

## ABSTRACTS

## ORAL ABSTRACTS

O001/#325 | IPSO

IPSO: FREE PAPER SESSION 01 - BASIC SCIENCE AND  
NEUROBLASTOMA

11-10-2023 08:15 - 09:45

## CIRCULATING TUMOUR CELLS IN OSTEOSARCOMA

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**Background and Aims:** Circulating tumour cells (CTCs) are part of the growing field of liquid biopsy research. Osteosarcoma is the most common bony malignancy of the paediatric population. Metastatic disease has a poor prognosis with a 20-30% survival, which would benefit from early diagnosis and improved disease monitoring. The aim of this project is to develop a technique to identify osteosarcoma CTCs.

**Methods:** Osteosarcoma cell lines were assessed for potential surface markers using flow cytometry. Cell lines used include 143B, HOS and MG63. Following this normal control blood samples were spiked with osteosarcoma cells. Cell recovery was tested using different preanalytical techniques and processing time points. Techniques compared include red blood cell (RBC) lysis and Ficoll density gradient processing. Timepoints included fresh processing, after 24 hours and frozen samples. Finally patient blood samples that were collected at different timepoints of the clinical course. All samples were processed using RBC lysis and stained with dioganglioside (GD2), Ephrin type-a receptor 2 (EphA2) and CD45. All samples were run through BD FACS Symphony and data was analysed using FlowJo software.

**Results:** The use of GD2, EphA2 as positive markers and CD45 as a negative marker was effective in identifying osteosarcoma CTCs. The use of RBC lysis processing with fresh sample processing yielded the best cell recovery rate. Within our patient samples we noted that presence of CTCs in 16/18 samples which were collected from seven patients. There was no correlation between the timepoint of collection and the number of CTCs identified in relation to comparing risk of recurrence and active disease and samples taken when in remission.

**Conclusions:** A reproducible technique to identify osteosarcoma CTC was developed. This was seen with both spiked normal control samples and patient samples. Further work on downstream analysis and large sample numbers would assist in further clinical translation of these findings.

O002/#1429 | IPSO

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NEUROBLASTOMA

11-10-2023 08:15 - 09:45

PRELIMINARY ANALYSIS OF MICRORNA EXPRESSION PROFILE  
OF OVARIAN IMMATURE TERATOMA IN CHILDREN BASED ON  
MICROARRAY AND ITS MOLECULAR MARKER SCREENINGJing Xiong

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**Background and Aims:** The clinical diagnosis of children's ovarian immature teratoma is often confusing, some reliable and effective biological indicators are needed to help promote the accuracy, so we analysed the miRNA expression profile and screen for specific molecular markers of ovarian immature teratoma in children.

**Methods:** A total of 20 children's ovarian tumor tissue samples were collected, of which 18 were formalin-fixed paraffin-embedded tumour tissue, including 2 cases of ovarian cyst, 3 cases of mature teratoma, 6 cases of immature teratoma, 3 cases of yolk sac tumor, 3 cases of juvenile granulosa cell tumor, and 1 case of dysgerminoma; 2 were fresh frozen tissue samples, including one mature teratoma and one yolk sac tumor. Differentially expressed miRNAs in samples were screened by Agilent gene chip, which were divided into three groups for statistical analysis. The most important one is the comparison between immature teratomas and the other ovarian tumors (ovarian cyst, mature teratoma, yolk sac tumor, juvenile granulosa cell tumor, dysgerminoma). Then target gene prediction, GO (Gene Ontology) analysis, KEGG (Kyoto Encyclopedia of Genes and Genomes) analysis, miRNA-gene-pathway analysis were performed in miRWalk, miRDB, and DAVID databases to obtain its biological information. Find the miRNAs related to the pathogenesis, diagnosis, treatment, and prognosis of immature teratoma in children.

**Results:** 13 different miRNA are specific for immature teratomas (compared with the other 5 types) and 18 miRNA differences among different pathological grades of immature teratoma.

**Conclusions:** The miRNA expression profile of immature teratoma in children for the first time through a microarray analysis of formalin-fixed paraffin-embedded samples and 13 specific miRNAs were obtained. Important miRNAs were found including miR-129-5p, miR-124-3p, miR-7-5p, miR-4698, may be biomarkers for distinguishing ovarian immature teratoma from other ovarian tumors, and laid the foundation for subsequent experiments in blood and fresh tissue samples.

O003/#1008 | IPSO

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#### EXPRESSION OF H19 LONG NON-CODING RNA IN PATIENTS OF WILMS TUMOR AND ITS CLINICAL IMPLICATION - A PILOT STUDY

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**Background and Aims:** To study the expression of H19 Long Non-Coding Ribonucleic Acid (lncRNA) in patients of Wilms Tumor and to assess its association with the clinical characteristics and outcomes.

**Methods:** A single-centre prospective study was conducted, including patients with primary Wilms Tumor, managed from January 2020 to March 2021. The tumor specimen obtained during Nephroureterectomy was taken as a test sample, while the controls were divided into two types; self-controls (normal renal parenchyma in the Nephroureterectomy specimen) and normal controls (Non-Wilms Tumor patients undergoing nephrectomy for non-malignant indications). The H19 levels were evaluated in the specimens using qRT-PCR to assess amplification. This was then correlated with the prospectively collected clinical features and outcomes data.

**Results:** A total of 31 patients were included in the study, with a mean age at the inclusion of 40.1 +/- 27.7 Months. Of these, 81% (n=25/31) patients had received neoadjuvant chemotherapy, while the remaining 19% (n=6/31) underwent upfront surgery. All the patients underwent complete excision of the tumor. On qRT-PCR analysis, tumor specimen had a 5.3-fold decrease (p=0.025) in the expression as compared

to normal controls (n=6). Also, self-control samples had a 4.7-fold decrease (p=0.039) as compared to normal controls. However, there was no change in the expression levels between the tumor samples and self-control. However, on correlating with histopathology, there was no difference in the expression levels of those with and without anaplasia. It was further noted that patients with progressive disease had a rather 3.7-fold increase (p=0.037) in the expression as compared to patients with complete response.

**Conclusions:** In patients with Wilms Tumor, there is a definitive decrease in the expression levels of H19 lncRNA as compared to normal kidneys, hence suggesting that H19 lncRNA plays an essential role in the tumorigenesis of Wilms Tumor.

O004/#1383 | IPSO

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11-10-2023 08:15 - 09:45

#### THE IMPACT OF A NATIONAL REFERENCE-SURGICAL REVIEW ON RESECTION STATUS AND SURGICAL RESULTS IN CHILDREN WITH COMPLEX NEUROBLASTOMA

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**Background and Aims:** Neuroblastoma (NB) are usually treated according to risk adapted multimodal therapy protocols. Central review is increasingly performed for recommending local treatment of children with complex tumor conditions (involvement/encasement of vital structures, presence of Image Defined Risk Factors). Aim of this study was to investigate the impact of a national reference-surgical tumor board on surgical treatment outcomes in children with complex neuroblastoma.

**Methods:** We retrospectively analyzed resection rates and surgical outcomes of children with complex NB, who underwent central reference-surgical review and received an according recommendation by the national multidisciplinary neuroblastoma tumor board of the Society of Pediatric Oncology and Hematology (GPOH) between 2019 and 2021.

**Results:** Data of 118 children were analyzed. Resection at a reference surgical center was recommended in 86 cases, this recommendation was followed in 70%. A tumor resection rate of 95% or greater was achieved in 80% of cases when surgery was performed at a surgical reference center as recommended (group 1), but in only 27% of cases

when surgery was performed at a local center contrary to the recommendation of the reference board (group 2). At last follow-up the rate of children without evidence of disease was 59% in group 1 and 18% in group 2. Higher resection rates in reference centers were not associated with higher rates of surgery-related complications.

**Conclusions:** Our data underline that a reference-surgical review board represents an important institution regarding quality of surgical care for children with complex NB. Inferior surgical success rates in children undergoing surgery against central review recommendation may result in more intensified treatment approaches (e.g. irradiation).

O005/#1153 | IPSO

#### IPSO: FREE PAPER SESSION 01 - BASIC SCIENCE AND NEUROBLASTOMA

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#### PROLIFERATIVE EFFECTS OF MESENCHYMAL STEM/STROMAL CELLS ON NEUROBLASTOMA CELL LINES

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**Background and Aims:** Neuroblastoma is a devastating pediatric cancer with survival rates of less than 50% for high-risk disease. Mesenchymal stem/stromal cells (MSCs) may be a novel cellular delivery vehicle given their innate tumor homing properties, but MSCs have shown variable effects on tumor growth. We compared the effects of placental MSCs (PMSCs) and bone marrow MSCs (BM-MSCs) on the proliferation of neuroblastoma (NB) cells in vitro.

**Methods:** Proliferative effect were assessed by indirect co-culture with inserts with no MSCs as controls. NB cell proliferation was assessed using MTS assay and fold change (fc) over control was calculated. 3 NB cell lines (NB1643, SH-SY5Y, and CHLA90) were co-cultured with early-gestation PMSC (n=9), term PMSC (n=5) or BM-MSC (n=4) cells. Early PMSCs were sub-grouped by neuroprotective effects: strong (n=2), intermediate (n=3), and weak (n=4). A linear mixed effects model was used to assess the relationship between MSC type, PMSC neuroprotective level, and PMSC gestational age on NB cell proliferation.

**Results:** Proliferative effects varied between MSC groups and NB cell lines. BM-MSCs had a lower proliferative effect (fc 1.18) on all NB cell lines compared to early (fc 1.4, p=0.002) and term PMSCs (fc 1.51, p<0.001). Levels of neuroprotective effect of PMSCs did not significantly affect proliferation. BM-MSCs had the lowest proliferative effects on CHLA90 (fc 1.01), compared to NB1643 (fc 1.33) and SH-SY5Y (fc 1.20). For NB1643, there was no difference in proliferation

between PMSCs and BM-MSCs, however, term PMSCs significantly increased NB proliferation vs. early PMSCs (p=0.0376).

**Conclusions:** Effects of MSCs on NB cell proliferation varies by MSC source and NB cell line. BM-MSCs showed lower proliferative effects than most PMSCs, except with NB1643, suggesting the effects of PMSCs on NB cell growth may vary by tumor histology. Further characterization of these MSCs may provide insight for which cells are best suited for drug delivery.

O006/#252 | IPSO

#### IPSO: FREE PAPER SESSION 01 - BASIC SCIENCE AND NEUROBLASTOMA

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#### INCIDENCE AND RISK FACTORS FOR CHYLOUS ASCITES AFTER SURGICAL RESECTION OF NEUROBLASTIC TUMOURS - A SYSTEMATIC REVIEW OF PUBLISHED STUDIES

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**Background and Aims:** Chyle leakage/ascites after surgical resection of neuroblastic tumours may delay the start of chemotherapy and worsen prognosis. Previous studies have reported a highly variable incidence (%) and risk factors remain largely unknown. This study aims to analyse the true incidence of chylous ascites and seeks to identify risk factors and optimal treatment strategies.

**Methods:** Medline/Embase databases were searched according to PRISMA guidelines. Literature reviews, case reports, and non-English papers were excluded. Data were extracted independently following paper selection by 2 authors.

**Results:** The final analysis yielded 15 studies with N = 1468 patients. Chylous ascites was recorded postoperatively in 171 patients (12%). Of those 7 (4%) cases required operative exploration to control the chyle leak. The majority of patients experiencing chyle leaks were successfully treated conservatively with drainage, bowel rest, parenteral nutrition and octreotide with variable combinations of these treatment options. In risk factor analysis, higher tumour stage (INSS III or IV) was significantly associated with the risk of chyle leak (P<0.0001) whereas no correlation was observed with adrenal vs non-adrenal tumour location, INRG risk groups and tumour laterality. Individual published studies reported that MYCN amplification and number of resected lymph nodes increased the risk of chylous ascites. A significant reduction in the incidence of lymphatic leakage (15.6% to 0%) was reported by one study group with mesenteric lymphatic ligation.

**Conclusions:** Chyle leakage after surgery for neuroblastic tumours is a common morbid complication occurring in some 12% of patients. Higher INSS tumour stage portends greater risk(s). Conservative therapy strategies appears successful in the majority of cases. To avert this complication meticulous mesenteric lymphatic ligation is recommended especially for those patients with higher tumour stage(s) requiring extensive surgery including retroperitoneal lymph node resection.

O007/#832 | IPSO

**IPSO: FREE PAPER SESSION 01 - BASIC SCIENCE AND NEUROBLASTOMA**

11-10-2023 08:15 - 09:45

**THE FIRST REPORT FROM 161 CASES OF ABDOMINAL AND PELVIC NEUROBLASTOMA SURGERY USING THE INTERNATIONAL NEUROBLASTOMA SURGICAL REPORT FORM (INSRF)**

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**Background and Aims:** The role of complete resection of the primary tumor is important in non-high risk neuroblastoma (NB) treatment, but it is still controversy in high-risk NB. To improve the quality of surgical reporting and facilitate the analysis of the role of extensive surgery in high-risk NB, the International Neuroblastoma Surgical Report Form (INSRF) was proposed. We aim to report the experience of using INSRF, and explore the relationship between INSRF items and the extent of surgical resection.

**Methods:** This was a prospective observational study, and our team used the INSRF to document patients with abdominal or pelvic NB who received surgery in our center from October 2021 to February 2023. The INSRF was reported within 24 hours after the completion of the operation, and the intraoperative and postoperative conditions of these patients were discussed in the weekly department case discussion meeting.

**Results:** There were 161 cases included in this study with the median age of 52 (36, 82) months, and the median length of stay after surgery was 11 (8, 17) days. This study collected a total of 298 INSRF reports. Among the 161 cases, 137 were documented by two surgeons, and the concordance rate was 16.78%. During the completion of the INSRF, the items with high inconsistency were mainly focused on the extent of tumor resection (29.20%), renal vein involvement (25.55%), and abdominal aorta involvement (16.79%). Through analyzing the relationship between the extent of surgical resection and INSRF items,

we found that more than 14 items involvement in the INSRF is an independent risk factor for poor surgical resection (>5cm<sup>3</sup>).

**Conclusions:** In general, INSRF is highly operable and valuable, but there are still some controversies on the judgement of surgical resection and some other items. Surgical residue is closely related to the number of items documented by the INSRF.

O008/#375 | IPSO

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**SURGICAL OUTCOME ACCORDING TO THE RELATIONSHIP BETWEEN THE RENAL VESSELS AND TUMOR IN THE LOW- AND THE INTERMEDIATE-RISK PATIENTS WITH ABDOMINAL NEUROBLASTOMA**

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**Background and Aims:** The Japan Children's Cancer Group (JCCG) Neuroblastoma Committee (JNBSG) conducted the JN-L-10 for low-risk patients and the JN-I-10 for intermediate-risk patients using Image-defined risk factors (IDRFs) as the main factor for determining treatment. We analyzed the treatment results of the patients who enrolled in both studies according to the relationship between the renal vessels and tumor in order to clarify whether or not "contact with renal vessels" should be considered an IDRF.

**Methods:** Thirty-seven low-risk and 39 intermediate-risk patients who had an abdominal primary tumor and precise information of relationship between renal vessels and tumor were selected. Patients were divided into the 3 groups according to the relationship between the renal vessels and tumor: Group S (14 low-, 10 intermediate-risk), separated; Group C (16 low-, 6 intermediate-risk), in contact; Group E (7 low-, 23 intermediate-risk), encased. We analyzed the surgical treatment results. In both studies, "contact with renal vessels" were not considered IDRF.

**Results:** In Groups S, C and E, 9 in low-, 5 in intermediate-risk, 13 in low-, 2 in intermediate-risk and 0 in low-, 11 in intermediate-risk patients underwent primary resection. Therefore, 22/37 (59.5%) in low-risk and 18/39 (46.2%) intermediate-risk patients underwent surgery rather than a biopsy. Surgical complications were observed in 4/22 (18.2%) low-risk, 6/18 (33.3%) intermediate-risk patients. There were 0 low-, one (20.0%) intermediate-risk in Group S, 4 (30.8%)

low-, one (50.0%) intermediate-risk in Group C and 0 low-, 4 (36.4%) intermediate risk patients in Group E.

**Conclusions:** Major surgical complications were observed more frequently in intermediate-risk patients. "Contact with renal vessels" might be a potential surgical risk for low- and intermediate-risk neuroblastoma.

O009/#446 | IPSO

#### IPSO: FREE PAPER SESSION 01 - BASIC SCIENCE AND NEUROBLASTOMA

11-10-2023 08:15 - 09:45

#### SYSTEMATIC LYMPHATIC REPAIR AND POSTOPERATIVE OUTCOMES OF NEUROBLASTOMA RESECTION

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**Background and Aims:** Gross total resection is critical to definitive management of neuroblastoma, but is associated with complications, particularly lymphatic leaks which may delay postoperative resumption of treatment. As an adjunct to prevent postoperative lymphatic leak, we introduced systematic lymphatic repair (SLR), which involved oversewing the entire edge of the disrupted lymphatic plane after neuroblastoma resection. We sought to study factors affecting timely postoperative return to treatment, particularly in relation to introduction of SLR.

**Methods:** We retrospectively reviewed 32 neuroblastoma patients with documented details of surgical resection at KK Women's and Children's Hospital. Patient, disease, and operative factors were correlated with surgical drainage, treatment delay and length of stay (LOS) using one-way ANOVA. Five patients who underwent resection after introduction of SLR were compared with 27 historical controls. Two-way ANOVA was used to study the interaction between categorical independent variables significantly associated with drainage, delay and LOS outcomes, in patients operated before and after introduction of SLR.

**Results:** Postoperative drain duration and volume were significantly higher in tumors with  $\geq 2$  image-derived risk factors (IDRFs,  $P < 0.05$ ) or vessel encasement ( $P < 0.05$ ). Prolonged LOS, whether in intensive care (ICU), non-ICU, or overall, was likewise associated with the presence of  $\geq 2$  IDRFs ( $P < 0.05$ ). MIBG-avid disease and favorable histology was associated with longer delay to resumption of chemotherapy ( $P < 0.05$ ).

All forms of suture repair of lymphatics and use of Tachosil™ were associated with significantly longer postoperative drain duration ( $P < 0.05$ ); the former was also associated with significantly higher total drain volume ( $P < 0.05$ ) – indicating appropriate use of these adjuncts in patients at risk of chyle leak. On two-way ANOVA analysis, suture repair of lymphatics together with the introduction of the SLR technique were significantly associated with reduced interval to chemotherapy resumption ( $P < 0.05$ ).

**Conclusions:** A systematic approach to repair of lymphatic channels following neuroblastoma resection can reduce time to postoperative resumption of treatment.

O010/#582 | IPSO

#### IPSO: FREE PAPER SESSION 01 - BASIC SCIENCE AND NEUROBLASTOMA

11-10-2023 08:15 - 09:45

#### PREOPERATIVE RISK FACTORS AND PERIOPERATIVE COMPLICATION RATES OF RETROPERITONEAL NEUROBLASTOMA IN CHILDREN

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**Background and Aims:** To evaluate the incidence of all the perioperative complications in patients undergoing retroperitoneal neuroblastoma tumor resection and identify risk factors associated with significant complications.

**Methods:** Patients undergoing neuroblastoma tumor resection between 2014 and 2021 were included for analysis. Data were collected and analyzed on the clinical characteristics and perioperative complications.

**Results:** A total of 571 patients were included in this study. Perioperative complications were observed in 255 patients (44.7%). Lymphatic leakage (28.4%), diarrhea (13.5%), and injury (7.5%) were the most frequent complications. There were 3 operation-related deaths (0.53%): massive hemorrhage ( $n = 1$ ), biliary tract perforation ( $n = 1$ ) and intestinal necrosis ( $n = 1$ ). Presence of IDRFs (odds ratio [OR],  $p < 0.01$ ), high stage of INRGSS (OR 0.454,  $p = 0.04$ ), retroperitoneal lymph node metastasis (OR 2.433,  $p = 0.026$ ), superior mesenteric artery encasement (OR 3.346,  $p = 0.003$ ) and inferior mesenteric artery encasement (OR 2.218,  $p = 0.019$ ) were identified as independent risk factors for perioperative complications.

**Conclusions:** Despite the high incidence of perioperative complications, the associated mortality rate was quite low. Perioperative complications of retroperitoneal neuroblastoma were associated with

IDRFs, INRGSS, retroperitoneal lymph node metastasis and vascular encasement. Patients with high-risk factors should be treated more seriously during surgery, but should not discourage the determination to pursue total resection of NB.

OO11/#1397 | IPSO

**IPSO: FREE PAPER SESSION 01 - BASIC SCIENCE AND NEUROBLASTOMA**

11-10-2023 08:15 - 09:45

**DANCING EYE DANCING FEET!! LESSONS LEARNED FROM 28 CONSECUTIVE PATIENTS OF NEUROBLASTOMA-OMAS**

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**Background and Aims:** Opsoclonus-myooclonus ataxia syndrome (OMAS) is a rare entity characterized by irregular and abnormal jerky eye and limb movements with gait imbalance and extreme irritability and behavioral changes. It is commonly seen in children diagnosed with neuroblastoma. These patients continue with several neuro-psychiatric manifestations even after adequate treatment.

**Methods:** This was a retrospective analysis of cases managed in the department over 6 years from January 2017-December 2022. The data were analyzed in terms of clinical features, radiology, neurological symptoms, surgical findings, histopathology, and outcomes.

**Results:** Total 28 patients with a diagnosis of opsoclonus-myooclonus were admitted over a period of 6 years. The median age at the presentation was 21 months. The duration of symptoms at the time of presentation was in the range of 1-6 months. Opsoclonus and myoclonus were present in all 28 patients, irritability in 21, and sleep disturbances in 5 of them. On evaluation with imaging (CECT abdomen, PET CT and MRI), they were found to have abdominal and thoracic neuroblastoma. After receiving medical management in the form of IVIG, and ACTH therapy, All patients underwent the excision of tumors via open or minimal access approach. 23 patients received injection ACTH alone, 11 received IVIG along with ACTH and three received only chemotherapy. Two patients received advanced neuromodulation with rituximab, without significant resolution of symptoms. Postoperatively the symptoms improved followed by a recurrence of sleep disturbances and irritability in 13 patients. On a 5-year follow up two patients died due to pneumonia and acute diarrheal disease.

**Conclusions:** OMAS syndrome has a complex treatment algorithm a complex and requires a multimodality treatment approach. High suspicion is required for diagnosis. Medical management followed

by surgical excision is adequate in most patients for the resolution of symptoms, in the initial post-operative. Sequelae like sleep disturbances, irritability, and occasional myoclonus may recur after the cessation of therapy.

OO12/#253 | IPSO

**IPSO: FREE PAPER SESSION 01 - BASIC SCIENCE AND NEUROBLASTOMA**

11-10-2023 08:15 - 09:45

**PRE AND POSTOPERATIVE DIARRHOEA ASSOCIATED WITH NEUROBLASTOMA RESECTION – A SYSTEMATIC REVIEW OF PUBLISHED STUDIES**

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**Background and Aims:** Neuroblastoma is a malignant tumour affecting 10.5/1 million children annually. It arises from sympathetic nervous system precursor cells and is most frequently found in the adrenal gland and abdominal paravertebral ganglia. Diarrhoea as a presenting symptom of neuroblastoma is rare and usually linked to vasoactive intestinal peptide (VIP) tumour secretion. Even more rarely, postoperative diarrhoea may follow neuroblastoma tumour resection. Published studies generally associate postoperative diarrhoea with subadventitial tumour resection. These findings are based on a handful of reports. This systematic review study therefore aims to analyze the true incidence of postoperative diarrhoea and its morbid correlation with the extent/type of surgical resection.

**Methods:** Medline/Embase databases were searched according to PRISMA guidelines. Literature reviews, case reports, and non-English papers were excluded. Data were extracted independently following paper selection by 2 authors.

**Results:** Final analysis consisted of 16 studies: N=779 patients. Post-operative diarrhoea was significantly more common in all patients who underwent subadventitial resection compared to non subadventitial resection,  $p < 0.001$  (OR 25.9, 95% CI 9.3–72.4). 5-year survival rates were similar in both groups. Preoperative diarrhoea was rarely reported in studies and always strongly linked to elevated VIP secretion. In the majority of neuroblastoma patients, preoperative diarrhoea ameliorated after gross tumour resection with elevated VIP normalized. The operative technique of subadventitial neuroblastoma resection portends significant risk(s) of post operative diarrhoea not seen in those patients undergoing other classical methods of tumour resection. 5-year survival rates are strikingly similar.

**Conclusions:** Postoperative diarrhoea is strongly linked with the subadventitial resection technique whereas preoperative diarrhoea encountered rarely in neuroblastoma is usually VIP-induced and cured by gross resection. These findings affirm that subadventitial tumour resection should be avoided when undertaking surgery for neuroblastoma to minimize the risk(s) of persistent postoperative diarrhoea.

O013/#1307 | IPSO

#### IPSO: FREE PAPER SESSION 01 - BASIC SCIENCE AND NEUROBLASTOMA

11-10-2023 08:15 - 09:45

#### IS RETROPERITONEOSCOPY A SAFE SURGICAL APPROACH FOR NEUROBLASTIC SUPRA RENAL TUMORS IN CHILDREN?

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**Background and Aims:** Despite well-known surgical and cosmetic advantages, retroperitoneoscopy in suprarenal tumors is not a standard of care and indications are not defined. The aims are to compare the results of transperitoneal laparoscopy or retroperitoneoscopy, and to define the indications of retroperitoneoscopy in the surgical management of suprarenal neuroblastic tumors in children.

**Methods:** This multicenter national retrospective study included children who underwent laparoscopic excision of a suprarenal neuroblastic tumor since 2010. Patients were divided into 2 groups: group TRANS (transperitoneal laparoscopy) and group RETRO (retroperitoneoscopy). Clinical, radiological, anatomopathological, operative data, and oncological results were compared.

**Results:** 118 patients were included (90 group TRANS; 28 group RETRO). Preoperative tumor diameter was higher in group TRANS (35mm) as compared to group RETRO (31.5mm) for tumor volumes of 24.7mL and 7.8mL respectively ( $p=0.09$ ). 39% of group RETRO were at high risk (INPC classification) versus 23.3% of group TRANS ( $p=0.6$ ). 23.3% of patients in group TRANS and 25% in group RETRO had one

IDRF only, and respectively 10% and 3.6% more than one ( $p=0.6$ ). Vascular and adjacent organ dissection difficulties were more frequent in group RETRO (35.7%) as compared to group TRANS (13.3%) ( $p=0.003$ ). Conversion rate was equivalent (10%). Blood loss was higher in group TRANS than group RETRO (36.7mL vs 0mL) ( $p=0.03$ ). Durations of hospitalization and oral intake were shorter in group RETRO (2.6 and 0.7 days) as compared to group TRANS (3 and 1 days) ( $p=0.05$ ;  $p=0.08$ ). More local recurrences occurred in group RETRO (2/28; intraspinal extensions) than group TRANS (1/100; high-risk) ( $p=0.08$ ). Risk factors associated with local recurrences were use of neoadjuvant chemotherapy and difficulties of intraoperative vascular dissection.

**Conclusions:** Retroperitoneoscopy for suprarenal neuroblastic tumors in children is feasible and safe in selected cases. We recommend it for tumors with a maximum diameter of 30-40mm for a volume of 10-15mL, localized (L1) (INRG classification), without IDRF.

O014/#1494 | IPSO

#### IPSO: FREE PAPER SESSION 02 - PERIOPERATIVE MANAGEMENT, TUMOUR LOCALIZATION, OPERATIVE TECHNIQUE AND LIVER, CARCINOID

11-10-2023 13:45 - 15:15

#### SALVAGE ORGAN TRANSPLANTATION AS BACKUP FOR EXTREME LIVER RESECTION IN CHILDREN WITH ADVANCED LIVER TUMORS

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**Background and Aims:** Extreme resection (as defined by the APSA criteria) and liver transplantation are surgical concepts for advanced pediatric liver tumors. In the interest of patient safety, the surgical concept of salvage liver transplant preparation as backup has been introduced in the context of extreme resections. In this study, we would like to present the content aspects of this concept at our institution.

**Methods:** The criteria for backup transplant preparation are i) a complicated tumor constellation with a borderline technical feasibility of resection, which can only be verified during surgical exploration, and ii) a borderline volume of the expected liver remnant after resection with uncertain predictability of postoperative liver function. As part of the backup preparation, the patient and a living donor (usually one parent)

are evaluated as if undergoing liver transplantation according to internal standardized protocols (SOP). Backup transplantation is prepared as an ad hoc living donation in the event that either non-resectability should become apparent during tumor resection or acute liver failure should occur postoperatively.

**Results:** Between 2012 and 2022, 54 children with liver tumors were operated on at our institution. Of these children, 43 underwent liver resection and 11 received liver transplantation. We performed backup transplant preparation in 6 cases staged for extreme resection. Ultimately, all of these children underwent successful tumor resection without need for transplantation. All 6 are without evidence of disease and have a sufficient liver function after a median follow-up of more than 24 months.

**Conclusions:** The concept of backup liver transplantation allows a successful individualized surgical approach in children with complicated liver tumors. Overall, this concept should be reserved for a selected group of patients treated at centers providing the complete capabilities of high-end pediatric liver surgery.

O015/#1699 | IPSO

IPSO: FREE PAPER SESSION 02 - PERIOPERATIVE MANAGEMENT, TUMOUR LOCALIZATION, OPERATIVE TECHNIQUE AND LIVER, CARCINOID

11-10-2023 13:45 - 15:15

FACTORS ASSOCIATED WITH LONG-TERM SURVIVAL IN CHILDREN WITH BRONCHIAL AND LUNG CARCINOID TUMORS

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**Background and Aims:** Bronchial and lung carcinoid is rare in children and treatment is based on tumor behavior in adults. The purpose of this study was to determine factors and management strategies associated with long-term survival in the pediatric population using a national cohort.

**Methods:** Patients  $\leq 20$  years with bronchial or lung carcinoid tumors were identified in the 2004-2020 National Cancer Database using ICD-O-3 codes. Tumor characteristics and management were compared among typical (TC) and atypical (AC) histological subtypes using Chi square and Fischer exact tests. Kaplan-Meier and univariate Cox proportional hazards analyses assessed survival.

**Results:** Of 273 patients, 251 (92%) had TCs and 22(8%) had ACs. Median (IQR) age was 18 (16,19). Most patients underwent lobectomy

or bilobectomy (67%), followed by sublobar resection (17%), no resection or bronchoscopic destruction (8%), and pneumonectomy (7%). Margins were negative in 96%. Lymph node (LN) assessment was performed in 216 patients (84%), median(IQR) LNs examined was 7(3,13), and 50 (23%) had  $\geq 1$  positive LN. There was no difference in age, resection, margin status, LN assessment or positivity between TC and AC (all  $p > 0.05$ ). Ten-year survival was worse for AC than TC (79% (41,100) vs 98% (95,100), HR = 6.9 (95% CI: 1.2 - 38.3,  $p = 0.03$ ). Ten-year survival among those with and without LN assessment was 97% (94,100) vs 91% (81,100), HR = 4.0, 95%CI: 0.8 - 19.9,  $p = 0.09$ ). There were no deaths in those with negative LN while 10-year survival was 89% (72,100) in those with  $\geq 1$  positive LN.

**Conclusions:** Among children with carcinoid tumors of the lung or bronchus, survival is excellent with TC or negative LN. Atypical histology and positive LN are associated with worse survival and should prompt close monitoring. These risk factors may be missed in the absence of surgical resection with lymph node dissection.

O016/#755 | IPSO

IPSO: FREE PAPER SESSION 02 - PERIOPERATIVE MANAGEMENT, TUMOUR LOCALIZATION, OPERATIVE TECHNIQUE AND LIVER, CARCINOID

11-10-2023 13:45 - 15:15

EQUITABLE ACCESS TO STATE-OF-THE-ART SURGICAL TECHNOLOGY: A MEXICAN MINI PUBLIC PRIVATE PARTNERSHIP CASE STUDY

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**Background and Aims:** Surgery remains the cornerstone of treatment for all solid tumors, but outcomes in limited-resource settings have not reached high-income benchmarks. As a cutting-edge pediatric cancer center, we aim to establish an evidence-based case study to improve surgical outcomes for children with cancer from low-and-middle-income families in Mexico.

**Methods:** After individual case discussion on a multidisciplinary tumor board, patients  $< 18$  years of age with an oncologic diagnosis, were provided with free, state-of-the-art, multimodal treatment, and underwent surgery at ABC Cancer Center in Mexico between January 2018 and March 2023. Time to treatment initiation, patient demographics, disease epidemiology, and surgical outcomes were prospectively collected.

**Results:** We enrolled 51 boys and 46 girls from 25/32 Mexican States, with a median age of 9 years (0 - 17). Tumors included 67%



malignant - sarcomas (29%), embryonal tumors (13%), gonadal (6%), Lymphoma/Leukemia (15%), and carcinomas (4%). Median time for treatment initiation was seven days. Patients presented with advanced stage in 64% of cases. Surgical volume increased over time (24 procedures in 2018 vs 82 in 2022). We performed 131 major and 117 ancillary procedures (Average two per patient) (1-21). R0 status was achieved in 90% of major oncologic resections (85 procedures). Local recurrence rate was 8%. Overall complication rate was 10% (73% during major cases). Overall survival was 86%, with no 30-day perioperative deaths. Furthermore, 70% of patients are currently alive without evidence of disease, with a median Follow-up of 27 months (1 - 64).

**Conclusions:** The program delivered high-quality surgical care for children that had otherwise no access for the required technology and expertise, improving equity and access to care. High-income benchmarks for local control and surgical outcomes in underserved children with solid tumors can be achieved through public-private-partnerships.

O017/#444 | IPSO

**IPSO: FREE PAPER SESSION 02 - PERIOPERATIVE MANAGEMENT, TUMOUR LOCALIZATION, OPERATIVE TECHNIQUE AND LIVER, CARCINOID**

11-10-2023 13:45 - 15:15

**ERAS (ENHANCED RECOVERY AFTER SURGERY) PATHWAY IN PEDIATRIC SURGICAL ONCOLOGY-FEASIBILITY AND OUTCOME**

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**Background and Aims:** The concept of ERAS is well established across all specialities in adults. But there is paucity of literature in the field of pediatric surgical-oncology due to heterogeneity in age, physiology and procedures. Hence an attempt is made to implement ERAS in pediatric patients undergoing oncological procedures. **Aims:** To study the feasibility and compliance of ERAS pathway and its effect on duration of hospital stay and 30-day morbidity.

**Methods:** On a pilot basis, all patients requiring surgery from December 2022 to February 2023 were enrolled in the study, excluding all day-care surgeries. Components of ERAS pathway considered were education and counselling, nutritional and medical optimization, standard fasting protocol, carbohydrate loading, physiotherapy, no bowel preparation, multimodal analgesia, goal directed fluid therapy, post-operative nausea and vomiting (PONV) prophylaxis, maintenance of normothermia, minimization of opioids, avoidance of drains/ early removal, no nasogastric tubes, early removal of urinary catheter, early mobilization and physiotherapy, early enteral feeding with rapid esca-

lation to normal feeds. Data was compared to the historical control (pre-ERAS).

**Results:** A total of 50 patients were enrolled. Median age was 42 months (5-180). A large proportion of surgeries was abdominal- 34 (68%), followed by thoracic-10 (20%). Compliance to components of ERAS varied, poorest being for avoidance of drains (38%) and pre-operative physiotherapy (42%); maximum for avoidance of bowel preparation (100%), adherence to fasting protocol (98%) and maintenance of normothermia (98%). There was a statistically significant ( $p=0.0156$ ) reduction in duration of hospital stay in ERAS group (mean- 7.06days) compared to pre-ERAS group (mean- 9.4 days,  $n=100$ ) with comparable morbidity ( $p=0.505$ ).

**Conclusions:** Implementation of ERAS in pediatric surgical-oncology is challenging, considering the diverse age group and variable acceptance levels, affecting the compliance and outcome and requires frequent improvisations. ERAS pathway in children is feasible, resulting in shorter hospital stay and early recovery.

O018/#190 | IPSO

**IPSO: FREE PAPER SESSION 02 - PERIOPERATIVE MANAGEMENT, TUMOUR LOCALIZATION, OPERATIVE TECHNIQUE AND LIVER, CARCINOID**

11-10-2023 13:45 - 15:15

**INTERCOSTAL NERVE CRYOABLATION REDUCES OPIOID UTILIZATION AFTER THORACOTOMY IN CHILDREN WITH CANCER**

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**Background and Aims:** Intercostal nerve cryoablation (INC) has shown promise as an adjunct method for analgesia in adults undergoing thoracotomy but has yet to be widely used in children for this indication. We hypothesize that INC decreases opioid utilization in children undergoing thoracotomy for cancer operations.

**Methods:** An IRB-approved, institutional retrospective review was performed of children who underwent thoracotomy for a cancer diagnosis at a freestanding children's hospital from 2018-2023. Patient characteristics, intraoperative data, and data on clinical course were collected. Patients were divided into those who underwent INC and those who underwent routine care. Nonparametric statistical tests were used for analysis.

**Results:** Twenty-six patients underwent 38 procedures at a median age of 16 years (range 5-21 years). INC was performed in 23 cases over a median of 5 intercostal levels (range 2-7). Length of stay

was similar between patients with INC and routine care (4 versus 5 days,  $p=0.15$ ). Total oral morphine equivalents (OME) during inpatient admission were significantly lower in INC patients (137.6mg versus 514.5mg,  $p=0.002$ ). Ten patients (66.7%) in the routine care group had a regional block postoperatively, but even this subset of patients had a higher OME compared to the INC group (533.35mg vs 137.6mg,  $p=0.01$ ). Routine care patients were more likely to be discharged with an opioid prescription (30.4% versus 80.0%,  $p=0.008$ ). One patient in the INC group developed a temporary Horner syndrome. There were no differences in rates of reoperation or 30-day readmission (ED or inpatient).

**Conclusions:** INC is a feasible and safe adjunct for children undergoing thoracotomy for cancer. INC is associated with reduced postoperative opioid utilization with respect to both inpatient use and outpatient prescriptions. Further studies on long-term pain control and patient satisfaction are warranted.

O019/#1555 | IPSO

**IPSO: FREE PAPER SESSION 02 - PERIOPERATIVE MANAGEMENT, TUMOUR LOCALIZATION, OPERATIVE TECHNIQUE AND LIVER, CARCINOID**

11-10-2023 13:45 - 15:15

**ROBOTIC-ASSISTED PEDIATRIC THORACIC AND ABDOMINAL TUMOR RESECTION: AN INITIAL MULTI-CENTER REVIEW**

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**Background and Aims:** Utilization of robotic-assisted minimally invasive surgery (RA-MIS) for thoracic and abdominal tumor resection in the pediatric population is not well-described. We aimed to determine the feasibility and safety of utilizing RA-MIS in this population.

**Methods:** A multi-center retrospective review of patients <18 years undergoing RA-MIS for thoracic or abdominal tumor resection from December 2015 – March 2023 was performed. Patient demographics, perioperative variables, and complication rates were analyzed.

**Results:** Thirty-nine procedures were performed on 38 patients (17 thoracic, 22 abdominal); 37% female and 68% non-Hispanic White. Median age at surgery was 9.3 years (IQR 5.6, 15.7); the youngest was 1.7 years-old. Thoracic operations included resections of neu-

roblastic tumors ( $n=16$ ) and a paraganglioma ( $n=1$ ). Abdominal operations included resections of neuroblastic tumors ( $n=5$ ), pheochromocytomas ( $n=3$ ), angiomyolipomas ( $n=3$ ), and solid pseudopapillary tumor, renal cell carcinoma, Wilm's tumor, spindle cell neoplasm, and metanephric adenoma (all  $n=1$ ). Six patients underwent retroperitoneal lymph node dissection (RPLND) for paratesticular tumors. Median maximum tumor dimension was 5.8cm (IQR 4.3, 7.9) for thoracic tumors and 3.6cm (IQR 2.0, 7.7) for abdominal tumors. Median operating time was 2:04 hours (IQR 1:48, 2:53) for thoracic cases, 3:18 hours (IQR 2:26, 3:20) for abdominal cases, and 5:57 hours (IQR 3:12, 8:06) for RPLND. Two cases required open conversion due to poor visualization and lack of working domain (thoracic). All patients underwent complete tumor resection. A partial nephrectomy performed for Wilm's tumor had a positive margin. Postoperatively, two patients developed a chyle leak (1 thoracic, 1 RPLND). Median LOS was 1.5 days (IQR 1.1, 3.0).

**Conclusions:** Robotic-assisted minimally invasive surgery is safe and feasible for tumor resection in carefully selected patients, achieving complete resection with minimal morbidity and short LOS. Patients should be selected by tumor size and location, with resection performed by those with robotic expertise for optimal outcomes.

O020/#1629 | IPSO

**IPSO: FREE PAPER SESSION 02 - PERIOPERATIVE MANAGEMENT, TUMOUR LOCALIZATION, OPERATIVE TECHNIQUE AND LIVER, CARCINOID**

11-10-2023 13:45 - 15:15

**WHEN LESS IS MORE. CONSECUTIVE PROCEDURES AT ONCE: COST BENEFIT STUDY IN A NATIONAL REFERENCE CENTER**

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**Background and Aims:** Cancer patients require many procedures before, during and after treatment. The aim of our study was to evaluate the impact of performing multiple procedures at the same operating room (OR) time vs. several independent OR time procedures in cancer patients, considering OR hours, surgical complications, cost reduction and delay to start oncological treatment.

**Methods:** A retrospective single-center study of newly diagnosed cancer patients under 25 years-old from January/2021 to February/2022 was performed.

**Results:** Eighty-one patients with a median age of 9.7 years (range 1-22) were included (59% male-41% female) The most frequent diagnosis was lymphoma (28.3%), Ewing sarcoma (19.8%), Wilms tumor

(12.3%), osteosarcoma (11.21%), others (28.3%). Multiple procedures were performed during the same surgical session in 55.6% of the patients (group1: one OR time), and 44.4% had separate procedures (group2: more than one OR time). The procedures performed were biopsy, central line placement, and, if necessary, bone marrow aspiration/biopsy, lumbar puncture and ovarian cryopreservation. The main reason (35.5%) for not performing all the procedures in the same session was not having intraoperative histological confirmation. The median OR time in group1 was 140 minutes (range 43-344) versus 175 minutes (range 85-370) in group2. The performance of simultaneous procedures in one surgical time resulted in an estimated cost reduction of 20%. Treatment initiation time was less in group1 (median number of days: 3, range 0-18) than group2 (median number of days: 8 days, range 0-54 days).

**Conclusions:** Performing simultaneous procedures in one OR time may reduce anaesthesia hours and costs. It also decreases the time between diagnosis and the start of treatment, anxiety from waiting and from going through several anaesthetic procedures in children and their parents.

O021/#411 | IPSO

**IPSO: FREE PAPER SESSION 02 - PERIOPERATIVE MANAGEMENT, TUMOUR LOCALIZATION, OPERATIVE TECHNIQUE AND LIVER, CARCINOID**

11-10-2023 13:45 - 15:15

**TRACKED ULTRASOUND REGISTRATION FOR INTRAOPERATIVE NAVIGATION DURING BONE TUMOR RESECTION: A FEASIBILITY STUDY ON PORCINE CADAVERS**

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**Background and Aims:** Resection of pediatric osteosarcoma with soft tissue involvement in the extremities presents surgical challenges including difficult visualization and palpation of the tumor. Image-guided surgery (IGS) may be valuable to overcome these challenges and allow for accurate and complete tumor resection. However, current IGS systems require radiation and can take up to 15 minutes to initialize, interrupting the surgical workflow significantly. We propose IGS with tracked intraoperative ultrasound (iUS) combined with

three-dimensional (3D) patient-specific models to improve surgical decision-making and overcome aforementioned surgical challenges. In this study, we evaluated this proposed system on the surgical feasibility by performing a porcine cadaver study.

**Methods:** The developed iUS-based IGS system was validated using eight porcine tibias. The registration accuracy was evaluated with artificial surgical targets located on the bone surface. Six pediatric surgeons and two pediatric orthopedists were asked to locate one target without navigation and subsequently ten targets with navigation using an optically tracked surgical pointer and the iUS. Intraoperative performance and ease of this surgical tool was evaluated with a post-procedural questionnaire.

**Results:** Eight registration procedures were performed with a mean target registration error of 6.78 mm (STD = 0.70 mm). The surgeons agreed about the willingness for clinical implementation in their current clinical practice. They mentioned the additional clinical value of iUS in combination with the 3D model for the localization of the soft tissue components of the tumor. Moreover, the participated surgeons experienced the localization of the surgical targets to be faster and easier with the help of navigation.

**Conclusions:** The participating pediatric surgeons and orthopedists were convinced of the clinical value of the interaction between the iUS and the 3D model. Further research is required to improve the surgical accuracy and should elaborate on the clinical potential of iUS-based IGS systems for the surgical management of pediatric osteosarcoma.

O022/#969 | IPSO

**IPSO: FREE PAPER SESSION 02 - PERIOPERATIVE MANAGEMENT, TUMOUR LOCALIZATION, OPERATIVE TECHNIQUE AND LIVER, CARCINOID**

11-10-2023 13:45 - 15:15

**IDENTIFICATION OF PEDIATRIC TUMORS INTRAOPERATIVELY USING INDOCYANINE GREEN (ICG): SYSTEMATIC REVIEW AND PROPOSAL FOR A STUDY GROUP OF INNOVATIVE TECHNOLOGIES IN PEDIATRIC SURGICAL ONCOLOGY (ITEPS)**

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**Background and Aims:** Fluorescent-guided surgery with indocyanine green (ICG) is an increasingly adopted approach in pediatric surgical oncology. However, this approach has been mostly reported for liver and renal tumors management, with different limited case series. The application of novel technologies in pediatric surgical oncology is challenging when compared to adult surgical oncology, due to different case-load and economic burdens. In particular, there is no consensus on ICG-guided surgery adoption for solid tumors management in childhood. Therefore, this study reviewed literature evidence, discussing limitations and future perspectives of fluorescent-guided surgery.

**Methods:** Using PRISMA guidelines, we analyzed studies reporting ICG-guided surgery for solid tumor management in children. Reports, opinion articles, and narrative reviews were excluded from the study.

**Results:** Of 108 analyzed articles, 17 studies (14 retrospective and 3 prospective) met the inclusion criteria. The majority of centers adopted ICG for liver tumors management (70.6%), with variability in terms of timing and dose of fluorescent dye administration. Intraoperative outcomes in terms of imaging detection, defined as sensitivity and specificity were reported in 23.5% of analyzed studies. Fluorescent-guided surgery provided liver resections with negative margins in 90-100% of cases, allowing the detection of additional lung metastasis in 33% of studies. ICG appeared effective and safe for lymph node sampling and nephron-sparing surgery, while in otolaryngologic malignancies positive margins without fluorescent signal were reported in 25% of cases.

**Conclusions:** ICG use appears heterogeneous in the international pediatric surgical oncology community, however, fluorescent-guided surgery provides promising results. Nevertheless, the underreported intraoperative imaging outcomes and the wide spectrum of tumors in children with a lack of caseload adequacy represent challenges to reaching scientific evidence for ICG adoption in pediatric surgical oncology. Further collaborative international efforts are needed to study the applications and limitations of ICG adoption and to evaluate the encouraging results of fluorescent-guided surgery and novel technologies in pediatric surgical oncology.

O023/#1648 | IPSO

IPSO: FREE PAPER SESSION 02 - PERIOPERATIVE MANAGEMENT, TUMOUR LOCALIZATION, OPERATIVE TECHNIQUE AND LIVER, CARCINOID

11-10-2023 13:45 - 15:15

## SACROCOCCYGEAL AND PRESACRAL TUMOR RESECTION GUIDED WITH INTRAOPERATIVE RESONANCE IMAGING: A NEW TECHNIQUE

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**Background and Aims:** Complete resection of the tumor with the coccyx is the cornerstone of sacrococcygeal tumor surgery. A remnant of the coccyx may lead to local recurrence. Intraoperative magnetic resonance imaging (iMRI) was developed initially for nervous system tumor resection. We developed a technique to use iMRI on the presacral and sacrococcygeal tumors to recognize the transition between the coccyx and sacrum, confirm the total resection of the presacral tumor, and guided more extensive sacral resection. The aim of this study was to discuss the operative technique of image guidance with MRI in the surgical management of sacral and presacral tumors.

**Methods:** Retrospective analyses of the sacral and presacral tumors using iMRI with an integrated operating room.

**Results:** There were 11 patients, three males, and eight females. The age of the procedure was: 3 days to 4 years. Patients were anesthetized and positioned for posterior sagittal access. First, a sagittal T2 intraoperative resonance sequence was done. The surgical procedure was performed, and then a new intraoperative image. This resonance sequence lasted ten minutes. Five procedures were primary resection (three Altman III and two II). Four patients came to our hospital after the yolk sac tumor relapsed, and the procedure was after chemotherapy. One patient had a metastatic mixed germ tumor; the procedure was done after chemotherapy. One patient came with immature teratoma with incomplete resection. MRI was used to verify the coccyx resection in 9 patients, S5 sacral vertebra in 3, sacrectomy until S1, and complete tumor resection in all. In two cases the MRI demonstrated residual tumor and needed more resection.

**Conclusions:** Intraoperative MRI could facilitate total resection of the sacrococcygeal, identify remnant tumors in the surgical site, and permit a precise level of bone resection.

O024/#688 | IPSO

IPSO: FREE PAPER SESSION 02 - PERIOPERATIVE MANAGEMENT, TUMOUR LOCALIZATION, OPERATIVE TECHNIQUE AND LIVER, CARCINOID

11-10-2023 13:45 - 15:15

## THORACOSCOPIC RESECTION OF LUNG NODULES FOLLOWING CT-GUIDED LABELING IN CHILDREN AND ADOLESCENTS WITH SOLID TUMORS

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**Background and Aims:** Resection of lung metastases in children with solid tumors is regularly hampered by a limited intraoperative detectability and a relevant operative trauma of the open surgical access. CT-guided coil wire labeling of lung metastases prior to minimally invasive atypical resection has so far not been described and systematically analyzed in children. It provides the advantages of labeling the nodules with a more robust method of anchoring the markers within the lung parenchyma compared to other methods. Aim of this study was to analyze thoracoscopic resection of lung metastases in children following CT-guided labeling with coil wires.

**Methods:** We retrospectively analyzed data of children undergoing this approach at our institution between 2010 and 2022 with regard to technical aspects as well as surgical and oncological data.

**Results:** Within the study period, we performed the described procedure in 12 patients, in which we resected 18 lesions (1-5 per patient). Median age was 178 months (51-265). Median duration of coil wire placement was 41 minutes (30-173), median surgery time was 53 minutes (11-157). No conversions were necessary, no intraoperative complications occurred. Complete microscopic resection ( $R_0$ ) was achieved in all labeled lesions, malignant tumor components were found in 7/15 resected specimens.

**Conclusions:** Our study shows that with a careful patient selection, thoracoscopic resection of lung metastases after coil wire labeling is a safe and reproducible procedure in children. Using this approach lesions become resectable that are expected to have a reduced intraoperative detectability during open surgery. Patients benefit from the minimally-invasive surgical access and reduced operative trauma.

0025/#991 | IPSO

IPSO: FREE PAPER SESSION 02 - PERIOPERATIVE MANAGEMENT, TUMOUR LOCALIZATION, OPERATIVE TECHNIQUE AND LIVER, CARCINOID

11-10-2023 13:45 - 15:15

## FUNCTIONAL FOLLOW-UP IN PEDIATRIC SURGICAL ONCOLOGY: AN OVERVIEW OF CURRENT PRACTICE AND A CALL FOR AN INTERNATIONAL COLLABORATIVE STUDY CONSORTIUM

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**Background and Aims:** The burden of treatment-related morbidity from multimodal cancer therapies in pediatric survivors is increasing. However, there are few studies on the long-term consequences of surgery for solid tumors. Therefore, the objective of this study is to examine (i) current follow-up practice and (ii) variability in reporting frequency (%) of functional sequelae that may occur after solid tumor operations in international voluntary participating centers.

**Methods:** The International Society Of Pediatric Surgical Oncology - IPSO - designed and distributed among its members an electronic survey analyzing a wide range of major pediatric solid tumors stratified according to anatomical site location.

**Results:** The survey was completed by 123 surgeons representing some 119 referral centers for pediatric surgical oncology and 47 international countries. It was noteworthy among respondents that fertility assessments were not undertaken in cancer survivors and pulmonary function testing in some bladder/prostatic tumors (68%) including thoracic surgical operations (62%). No standardized care or follow-up practice was evident. By contrast surgery for liver tumors had structured and standardized follow-up practice (63%). Most pediatric surgical oncologists (98%) believe that functional surgical follow-up and aftercare needs significant improvement.

**Conclusions:** This study highlights significant variability in surgical practice regarding functional follow-up assessments in childhood cancer survivors. The survey confirms there is a critical need to develop better workload practice with structured post-operative functional screening for all pediatric tumors. To quantify and score metrics linking functional outcomes with structured follow-up guidelines an international collaborative consortium will be established.

O026/#245 | Free Paper Session (FPS)

### FPS 01: PSYCHO-ONCOLOGY - WORKING CLOSELY WITH YOUR AYA'S AND SURVIVORS

12-10-2023 09:40 - 11:10

#### EXPLORING TEENAGERS' EXPERIENCES IN PEDIATRIC ONCOLOGY WITH GERMLINE GENE PANEL SEQUENCING FOR CANCER PREDISPOSITION

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**Background and Aims:** In pediatric oncology, large-scale germline sequencing is gradually becoming part of routine practice. Still, the experiences of pediatric cancer patients undergoing germline sequencing have not received much attention in the literature. This qualitative interview study explores these experiences.

**Methods:** Twenty-one interviews were conducted with teenagers who were awaiting test results of a study in which germline gene panel sequencing (142 genes) was offered to all pediatric cancer patients in the Netherlands. Interviewees' ages ranged from 12 to 18 years, median age was 15, 52% percent female and 48% male. Inductive thematic analysis was used to analyze the data.

**Results:** In general, teenagers were positive about sequencing to detect cancer predisposition syndromes. They seemed to approach sequencing with a certain casualness, for example by comparing sequencing decisions and experiences with other (more demanding) elements of cancer care and research. At the same time, patients were well-aware of the meaning of genetic sequencing, even though its potential implications in the (distant) future seemed to be less important to them. Patients stated that having information about a predisposition to cancer would be good-to-know, but often did not specify what good-to-know entails. Teenagers stressed the importance of making their own decisions regarding genetic testing and felt that patients

younger than themselves should also be involved in making these decisions. They articulated that future counseling materials should be concise and visually attractive, for example by using infographics, videos or websites.

**Conclusions:** Teenagers reflect positively on their participation in sequencing. They want to be actively involved in decision-making regarding genetics. This study provides insights for developing novel counseling tools tailored to teen cancer patients' unique perspectives and needs. We suggest using visual information materials that also address potential long-term implications of genetic testing.

O027/#760 | Free Paper Session (FPS)

### FPS 01: PSYCHO-ONCOLOGY - WORKING CLOSELY WITH YOUR AYA'S AND SURVIVORS

12-10-2023 09:40 - 11:10

#### FACE PROCESSING AND SOCIAL ATTENTION: MARKERS OF SOCIAL IMPAIRMENTS IN PEDIATRIC BRAIN TUMOR SURVIVORS

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**Background and Aims:** Pediatric brain tumor survivors (PBTS) experience significant social challenges, including fewer friends and greater isolation from peers. Research is needed to understand the factors contributing to these problems. Difficulties in face processing and visual social attention have been implicated in research with autism spectrum disorder and PBTS. This study evaluated facial affect recognition, social attention, and their associations with social impairments in PBTS.

**Methods:** PBTS (N = 54; ages 7-16) at least two years post-treatment completed a facial expression recognition measure, while parents completed measures of social functioning. A subset (N = 30) completed a social attention assessment that recorded eye gaze patterns while watching videos depicting pairs of interacting children. Social Prioritization scores were calculated, with higher scores indicating more face looking and less background looking. Correlations and regression analyses evaluated associations between variables, while PROCESS analyses evaluated the indirect effects of social attention on social impairments through face processing.

**Results:** Poorer accuracy in recognizing Angry and Sad expressions were significantly correlated with more social impairments ( $r_s = -.49$  and  $-.46$ ,  $p < .001$ ). This effect remained significant ( $p_s < .05$ ) in a stepwise linear regression model ( $F [2, 50] = 11.21$ ,  $p < .001$ ) accounting for accuracy across emotions. Social prioritization was correlated with recognition accuracy for Angry expressions ( $r = .40$ ,  $p < .05$ ) but

not with recognition accuracy for other emotions. In the PROCESS analyses, social prioritization had significant indirect effects on social impairments through Angry expression recognition accuracy.

**Conclusions:** Findings suggest interventions aimed at improving recognition of specific emotions may enhance social functioning in PBTS. Further, disrupted social attention could be a factor in reduced accuracy in face processing and relevant to social impairments. Longitudinal research is needed to elucidate temporal associations between social attention, face processing, and social impairments.

O028/#1659 | Free Paper Session (FPS)

#### FPS 01: PSYCHO-ONCOLOGY - WORKING CLOSELY WITH YOUR AYA'S AND SURVIVORS

12-10-2023 09:40 - 11:10

#### BARRIERS TO INITIATING ROMANTIC RELATIONSHIPS FOR YOUNG ADULT CANCER SURVIVORS: A QUALITATIVE STUDY

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<sup>1</sup>Dana-Farber/Harvard Cancer Center, Pediatric Oncology, Boston, United States of America, <sup>2</sup>Dana-Farber Cancer Institute, Psychosocial Oncology, Boston, United States of America

**Background and Aims:** Cancer treatment early in life causes significant disruptions to physical, social, and sexual development. However, the long-term effects of these disruptions on subsequent romantic relationships are not well understood. The current study aims to describe the experiences of young adult cancer survivors (YACS) in initiating romantic relationships after cancer treatment.

**Methods:** As part of an ongoing study, semi-structured qualitative interviews were conducted with 18 YACS (ages 24-39, 60% female) to better understand survivors' sexual health and relationship concerns. Interviews were recorded and transcribed verbatim. A coding framework was generated and applied to all transcripts; applied thematic analysis was used to identify emergent themes regarding romantic relationships in YACS.

**Results:** Preliminary findings reveal three major themes. 1) YACS experience difficulties initiating romantic relationships that cause them to feel behind peers in sexual and romantic experiences. 2) Low self-esteem, lack of sexual and romantic self-efficacy, and difficulty disclosing cancer history prevent YACS initiating relationships. 3) YACS want guidance on romantic relationships as part of routine survivorship care. Many were particularly interested in learning how to discuss their cancer history and lack of sexual and romantic experience with potential partners.

**Conclusions:** Findings highlight the profound impact that cancer has on initiating romantic relationships for YACS, even years or decades after treatment. Inability to initiate romantic relationships was widely

reported in this group and identified as a source of significant distress and impairment. Though currently unaddressed in mainstream survivorship care, YACS voiced a clear need for concrete advice and support regarding how to initiate and maintain healthy relationships after childhood cancer.

O029/#379 | Free Paper Session (FPS)

#### FPS 01: PSYCHO-ONCOLOGY - WORKING CLOSELY WITH YOUR AYA'S AND SURVIVORS

12-10-2023 09:40 - 11:10

#### MEASURING WHAT MATTERS TO ADOLESCENTS AND YOUNG ADULTS WITH CANCER: THE IMPORTANCE OF CAPTURING POSITIVE EXPERIENCES

Samantha Sodergren<sup>1</sup>, Olga Husson<sup>2</sup>, Gudrun Rohde<sup>3</sup>, Ali Alkan<sup>4</sup>, Amal Al Omari<sup>5</sup>, Irit Ben-Aharon<sup>6</sup>, Marianne Guren<sup>7</sup>, Georgios Ioannidis<sup>8</sup>, Hiroto Ishiki<sup>9</sup>, Michael Koehler<sup>10</sup>, Nookala Krishnamurthy<sup>11</sup>, Alessandra Majorana<sup>12</sup>, Nikolaos Memos<sup>13</sup>, Helle Pappot<sup>14</sup>, Duška Petranović<sup>15</sup>, Diana Richter<sup>16</sup>, Dan Stark<sup>17</sup>, Serdar Turhal<sup>18</sup>, Jeanette Winterling<sup>19</sup>, Anne-Sophie Darlington<sup>20</sup>

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**Background and Aims:** Background: While the negative sequelae of cancer on the quality of life (QoL) of adolescents and young adults (AYAs) are well recognised, positive psychosocial changes are also reported. To provide a comprehensive assessment of QoL as perceived by AYAs with cancer, we need to widen our focus beyond the negative constructs. We have developed a 50-item QoL questionnaire for

AYAs 14-39 years with cancer, of which, 12 questions are positive in focus. Aims: To identify whether there is a place for positive psychosocial constructs in a QoL measure designed to capture the voice of AYAs receiving treatment or palliative care for cancer.

**Methods:** AYAs from 16 countries rated the incidence and importance of each QoL construct on a 4-point response scale ("Not at all" to "Very much") as well as their relevance (yes/no). Mean incidence and importance and percentage relevance were calculated.

**Results:** The questionnaire was completed by 169 AYAs, mean (SD) age 27.77 (7.61) years, 51% females. Twelve cancer subtypes were represented, 82% on treatment and 74% on a curative pathway. "Distinguishing between important and non-important things in life" had the highest incidence of all the questions asked followed by "Feeling more motivated to live life to the full" (both rated on average as "Quite a bit") and were rated important by 85% and 81% of AYAs respectively. For AYAs (n=107) with spiritual/religious beliefs, 58% indicated that these had been strengthened. Positive questions were rated as relevant by the majority of AYAs; the lowest rating attributed to "Have you made new friends?" (60%).

**Conclusions:** This study underlines the importance of asking about positive experiences to gain a complete understanding of the impact of cancer on quality of life through the eyes of AYAs.

O030/#885 | Free Paper Session (FPS)

#### FPS 01: PSYCHO-ONCOLOGY - WORKING CLOSELY WITH YOUR AYA'S AND SURVIVORS

12-10-2023 09:40 - 11:10

#### POSITIVE AND NEGATIVE SURVIVOR-SPECIFIC PSYCHOSOCIAL CONSEQUENCES OF CHILDHOOD CANCER: THE DCCSS-LATER 2 PSYCHO-ONCOLOGY STUDY

Anne Maas<sup>1</sup>, Heleen Maurice-Stam<sup>1</sup>, Alied Van Der Aa-Van Delden<sup>1</sup>, Elvira Van Dalen<sup>1</sup>, Eline Van Dulmen-Den Broeder<sup>2</sup>, Wim Tissing<sup>1,3</sup>, Jacqueline Loonen<sup>4</sup>, Heleen Van Der Pal<sup>1</sup>, Andrica De Vries<sup>1,5</sup>, Marry Van Den Heuvel-Eibrink<sup>1,5</sup>, Geert Janssens<sup>1,6</sup>, Cecile Ronckers<sup>1,7</sup>, Sebastian Neggers<sup>1,8</sup>, Dorine Bresters<sup>1,9</sup>, Marloes Louwerens<sup>10</sup>, Birgitta Versluijs<sup>1,11</sup>, Margriet Van Der Heiden-Van Der Loo<sup>1</sup>, Leontien Kremer<sup>1,12</sup>, Marloes Van Gorp<sup>1</sup>, Martha Grootenhuis<sup>1</sup>  
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**Background and Aims:** Numerous studies investigated generic psychosocial outcomes in survivors of childhood cancer (CCS). The present study aimed to gain insight into survivor-specific psychosocial consequences, and to identify socio-demographic and medical associated factors.

**Methods:** CCS from the Dutch Childhood Cancer Survivor Study (DCCSS)-LATER cohort (diagnosed 1963-2001) part 2 (age  $\geq 18$ , diagnosed  $< 18$ ,  $\geq 5$  years since diagnosis) completed the Benefit & Burden Scale (BBSC) and the Impact of Cancer-Childhood Cancer (IOC-CS). Items were scored on a 5-point Likert scale (range 1-5). We examined outcomes with descriptive statistics, and socio-demographic and medical associated factors with regression analyses ( $p < 0.004$ ).

**Results:** CCS, N=1,713, mean age 36.0 years, 49.0% female, all  $\geq 15$  years since diagnosis, participated. CCS reported more Benefit (M=2.86) than Burden of childhood cancer (M=1.48) on the BBSC. Accordingly, most positive impact ( $> 50\%$  quite a bit/ very much) was reported on the IOC-CS-domains representing positive impact, namely Socializing, Talking with Parents, and most items of Health Literacy and Body & Health. Most negative impact was reported on Thinking/Memory (13.3%-26.7%). On the other negative impact scales (Sibling Concerns, Life Challenges, Relationship Concerns, Financial Problems) no to a little bit of impact was reported, although subgroups experienced survivor-specific challenges e.g. worries about not having a relationship, fertility, and how cancer had affected siblings (15.4%-19.4%). Female sex was associated with more Benefit, Personal Growth, and more negative impact. CCS more highly educated, partnered, and employed had higher positive and lower negative impact. CCS older at diagnosis reported more positive impact. CNS tumor survivors and those who had head/cranium radiotherapy had higher negative impact. CNS tumor survivors reported less positive impact.

**Conclusions:** Overall, CCS reported more positive than negative impact. CCS demonstrate resiliency, but health care providers should be aware that they can also experience survivor-specific challenges that warrant monitoring/ screening, information provision and psychosocial support.



O031/#389 | Free Paper Session (FPS)

**FPS 01: PSYCHO-ONCOLOGY - WORKING CLOSELY WITH YOUR AYA'S AND SURVIVORS**

12-10-2023 09:40 - 11:10

**"SOMETIMES WE THINK ABOUT IT BUT DON'T TALK ABOUT IT" ASKING ADOLESCENTS AND YOUNG ADULTS WITH CANCER TO EVALUATE SENSITIVE AREAS OF LIFE**

Samantha Sodergren<sup>1</sup>, Olga Husson<sup>2</sup>, Gudrun Rohde<sup>3</sup>, Ali Alkan<sup>4</sup>, Amal Al Omari<sup>5</sup>, Irit Ben-Aharon<sup>6</sup>, Marianne Guren<sup>7</sup>, Georgios Ioannidis<sup>8</sup>, Hiroto Ishiki<sup>9</sup>, Michael Koehler<sup>10</sup>, Nookala Krishnamurthy<sup>11</sup>, Alessandra Majorana<sup>12</sup>, Nikolaos Memos<sup>13</sup>, Helle Pappot<sup>14</sup>, Duška Petranović<sup>15</sup>, Diana Richter<sup>16</sup>, Dan Stark<sup>17</sup>, Serdar Turhal<sup>18</sup>, Jeanette Winterling<sup>19</sup>, Anne-Sophie Darlington<sup>1</sup>

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**Background and Aims:** Adolescents and Young Adults (AYAs) with cancer face a unique and complex array of concerns which impact their quality of life (QoL). Given their precarious position developmentally, they find themselves addressing sensitive, previously unexplored concerns. The study examines whether AYAs find it acceptable to include the following sensitive questions: "Have you worried about dying?", "Has your romantic life been negatively affected?", "Has your sex life been negatively affected?", and "Have you worried about your ability to have children?" in the European Organisation for Research and Treatment of Cancer (EORTC) Quality of Life Group (QLG) AYA questionnaire.

**Methods:** AYAs 14 and 39 years from 16 countries completed the 50-item AYA questionnaire and provided feedback on the acceptability of the questions. Age groups (14-18; 19-25; 26-39 years) and prognosis

(curative vs. palliative) were compared according to incidence ("Not at all", "A little", "Quite a bit", "Very much") using Chi-square tests.

**Results:** The study involved 169 AYAs, 24% palliative, 51% females. Each sensitive question was recognised by at least 50% of AYAs. More AYAs in the older group indicated an impact on sexual relationships,  $\chi^2(6, N=155) = 27.29, p < 0.001$ , and expressed fertility concerns,  $\chi^2(6, N=160) = 15.59, p < 0.05$ . Fear of dying was more common amongst AYAs in the palliative setting,  $\chi^2(3, N=159) = 15.70, p < 0.001$ . Only 10% AYAs expressed concern over the appropriateness of the sensitive questions. Impact on sexual activity was identified as too personal by 7% AYAs due to age, marital status, culture, or religion. The question about death was described as uncomfortable by 4% AYAs. **Conclusions:** Asking AYAs to rate the impact of cancer on sensitive areas was largely acceptable. The EORTC QLG AYA questionnaire provides the opportunity to gain a comprehensive understanding of the issues of importance to AYAs as well as opening up difficult conversations.

O032/#1846 | IPSO

**IPSO: FREE PAPER SESSION 03 - THE ROBERT ARCECI BEST OF IPSO**

12-10-2023 09:40 - 11:10

**EXTRACELLULAR VESICLES FROM METASTATIC OSTEOSARCOMA CONTRIBUTE TO CREATION OF A PRE-METASTATIC NICHE**

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**Background and Aims:** Osteosarcoma (OS) is a highly metastatic tumor affecting adolescents. Metastasis at diagnosis carries high mortality. However, even for patients without initial metastasis, recurrence is common and often occurs at distant sites—primarily the lungs. Extracellular Vesicles (EVs) have been linked to tumor growth and metastases in many different cancers. We aim to understand the effect EVs have on the pre-metastatic niche in OS.

**Methods:** EVs were collected from two murine OS cell lines, highly metastatic K7M2 and less metastatic K12.  $1 \times 10^{10}$  EVs or liposomes were injected into the tail veins of mice ten times over three weeks for pre-tumor "education" followed by intratibial implantation of either  $3 \times 10^5$  K7M2 or K12 cells. After five weeks, mice were euthanized, and lungs harvested for hematoxylin and eosin histologic staining. Metastatic burden was assessed via microscopy and Image J analysis.

**Results:** Mice that received "education" with K7M2 EVs had a higher metastatic burden compared to baseline in both K12 (0.8% vs 0%  $p=0.0004$ ) and K7M2 tumors (41.7% vs 3.8%,  $p=0.0139$ ). Mice

educated with K12 EVs also had slightly increased metastatic burden compared to baseline in K12 tumors (0.25% vs 0%), but not as significant as K7M2 EVs.

**Conclusions:** EVs from highly metastatic OS may prime the pre-metastatic site for tumor cell infiltration leading to increased metastasis. Determining molecular differences in EVs from highly metastatic and low metastatic cell lines may provide prognostic value and a novel therapeutic target for metastatic OS.

O033/#1498 | IPSO

IPSO: FREE PAPER SESSION 03 - THE ROBERT ARCECI BEST OF IPSO

12-10-2023 09:40 - 11:10

#### USE OF RADIO-GAMMA PROBE FOR SURGICAL EXCISION OF SMALL AND DIFFICULT TO LOCATE NEUROBLASTOMA METAIODOBENZYLGUANIDINE (MIBG) POSITIVE LESIONS

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**Background and Aims:** Immunotherapy anti-GD2 has improved outcomes in high-risk neuroblastoma (NB). Precision oncology studies for refractory disease or after relapse is of major importance for this protracted population. Surgeons are facing new challenges due to the increased need for procedures to obtain new samples that permit identifying potential targets. We aim to describe our experience using radio gamma for the detection and excision of small and difficult to locate MIBG-positive lesions.

**Methods:** 3-year (feb 20-jan 23) case series review of high-risk neuroblastoma patients with metastatic lesions who underwent surgery using radio-gamma probe (Euronad® Europrobe 3.2) for peri-operative detection after MIBG injection.

**Results:** 10 patients were included (40% male, 60% female), mean age 8,48 +/- 3,67 years. All locations of primary tumour were retroperitoneal, and 9 of them were metastatic at diagnosis. 70% of patients had prior surgery, and 40% have received radiotherapy. Locations were supraclavicular (30%), cervical (10%), hepatic hilum (10%), lung (10%), psoas muscle (20%), pelvic (10%) and inguinal (10%). 80% of procedures were open and 20% were laparoscopic. Mean surgical time was: 111,7 +/- 82,18 min. The size of the lesions were as follows: <1 cm (20%) and 1-3 cm (80%). There was one complication (enterocutaneous fistula in multioperated and multiradiated patient). Biopsy showed poorly undifferentiated neuroblastoma (60%) and differentiating neuroblastoma (40%). Molecular studies could be

performed in all samples. MIBG after surgery was negative in all patients.

**Conclusions:** Small NB lesions can be difficult to locate. Moreover, not all image suspected lesions are pathologic. Surgery in specific locations can be difficult. Incorporating nuclear medicine team to operating room can improve the goal of efficient sampling in this difficult group. Radio-gamma probe guided surgery has proven to be a necessary tool for successful small and difficult to locate lesion excision.

O034/#866 | IPSO

IPSO: FREE PAPER SESSION 03 - THE ROBERT ARCECI BEST OF IPSO

12-10-2023 09:40 - 11:10

#### AUGMENTED REALITY GUIDANCE FOR THE SURGICAL LOCALIZATION OF PEDIATRIC CHEST WALL TUMORS

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**Background and Aims:** Surgical treatment of pediatric chest wall tumors requires accurate surgical planning and tumor localization to achieve radical resections while sparing as much healthy tissue as possible. Augmented Reality (AR) could aid in surgical decision making through patient-specific 3D-visualization and intraoperative tumor localization. We present our early experience with a pre-incisional AR system and discuss the feasibility of AR guidance for the intraoperative localization of pediatric chest wall tumors.

**Methods:** Up to date, we have used the HoloLens 2 (Microsoft Corporation, Redmond, WA, USA) to intraoperatively localize chest wall tumors in six patients. For all patients, a patient-specific 3D-model was created by segmenting the tumor and relevant anatomy from preoperative computed tomography images with the patient lying in surgical position. Subsequently, the 3D-model was projected onto the patient in the operating room by a pre-incisional point-registration method based on anatomical landmarks.

**Results:** Pre-incisional registration and holographic overlay were achieved in all six patients. For most patients, the overlay visually matched the expected location based on palpation and thoracoscopy. The projection was most accurate when the registration landmarks were positioned in a non-symmetric configuration in proximity to the tumor. In some cases, minor disagreements between the overlay and expected tumor location were found, possibly caused by inaccuracies and user-dependent errors during the registration procedure.

Attempts at post-incisional registration and visualization were still unsatisfactory and require additional improvements in software development and workflow.

**Conclusions:** Our results demonstrate the applicability of AR guidance for the pre-incisional localization of pediatric chest wall tumors during surgery. The system has the potential to enable intraoperative 3D-visualization and facilitate the surgical management of chest wall resections. We are currently exploring the feasibility of different registration methods to overcome user-dependent errors and to enable post-incisional registration. Moreover, we are working on validation methods quantify our system's accuracy and performance.

O035/#1493 | IPSO

IPSO: FREE PAPER SESSION 03 - THE ROBERT ARCECI BEST OF IPSO

12-10-2023 09:40 - 11:10

#### MULTI-MODAL 3-DIMENSIONAL VISUALIZATION OF PEDIATRIC NEUROBLASTOMA: AIDING SURGICAL PLANNING BEYOND ANATOMICAL INFORMATION

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**Background and Aims:** Patient-specific 3-dimensional (3D) models of neuroblastoma and relevant anatomy are useful tools for surgical planning, particularly tumors encasing blood vessels or in close proximity to vital organs. However, these models do not represent the heterogenous biology of neuroblastoma. Clinically, this heterogeneity is visualized with the Apparent Diffusion Coefficient (ADC) and <sup>123</sup>I-MIBG-SPECT scans. By combining this multi-modal data to form a preoperative 3D model, we may allow differentiation of areas of viable and non-viable tumor tissue. In this study, we developed a workflow to create multi-modal preoperative 3D models for neuroblastoma surgery.

**Methods:** We included patients who underwent neuroblastoma surgery between 2022 and 2023. We developed a 3D model based on gadolinium enhanced T<sub>1</sub>-weighted MRI scan. Subsequently, we aligned this with corresponding ADC and <sup>123</sup>I-MIBG-SPECT images based on a rigid transformation using Elastix (<https://elastix.lumc.nl>). We estimated registration precision via Dice coefficient on the unaffected kidney and with the target registration error (TRE) of vascular bifurca-

tions of the renal vessels and the aorta. 3D heatmaps were computed based on ADC and <sup>123</sup>I-MIBG uptake.

**Results:** Multi-modal 3D models were developed for 5 patients with neuroblastoma. The registration algorithm had a median Dice coefficient for the kidney of 0.81 (STD=0.06) and 0.81 (STD=0.12) for the ADC and the <sup>123</sup>I-MIBG-SPECT respectively. For the ADC registration, the median TRE of renal vessels was 5.75 mm (STD=2.22) and for the aorta 5.24 mm (STD=3.29). For the <sup>123</sup>I-MIBG-SPECT imaging the TRE was 3.30 mm (STD=3.16) and 5.20 mm (STD=1.99) respectively.

**Conclusions:** We successfully developed a registration workflow to develop multi-modal 3D models which allows the surgeon to visualize the tumor and its biological behavior in relation to its surrounding tissue. Future research will include linking of pathological results to imaging data, in order to validate the reliability of this multi-modal 3D model.

O036/#978 | IPSO

IPSO: FREE PAPER SESSION 03 - THE ROBERT ARCECI BEST OF IPSO

12-10-2023 09:40 - 11:10

#### CLINICAL FACTORS DETERMINING ACCESS TO SURGERY AND HEALTHCARE PERCEPTIONS ON CHILDREN DIAGNOSED WITH NEUROBLASTOMA IN SOUTH AFRICA

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**Background and Aims:** Surgical control in neuroblastoma (NB) predicts survival. Nearly 80% of patients are diagnosed with high-risk (HR) NB who are often not operated on. The study evaluated healthcare workers' perceptions on and identified factors that determine access to surgery.

**Methods:** A retrospective, multicenter chart review of 204 children diagnosed with HR-NB between 2000 and 2016, who completed induction chemotherapy, was performed with surgery as endpoint. A national questionnaire on NB surgical practices was distributed to pediatric oncologists and surgeons.

**Results:** The male-to-female ratio was 1:0.96 and median age 32.4 months (IQR 15.1 – 53.5 months). Surgical resection of the primary was achieved in 76.9% of patients between 0-18 months of age and 51.7% older than 18 months ( $p < 0.001$ ). Only 43.2% of stage 4 disease had surgery done ( $p < 0.001$ ). LDH ( $> 750$  U/L) and ferritin ( $> 120$  g/dL) were increased in 46.8% and 53.1% respectively in operated patients ( $p = 0.005$ ). The majority (80.4%), who had achieved post-induction metastatic complete remission (mCR), were operated, while 28.7% with no mCR had surgery ( $p < 0.001$ ). Age ( $p < 0.001$ ), stage ( $p < 0.001$ ), mCR ( $p < 0.001$ ) and treatment setting ( $p < 0.001$ ) predicted resection rates. Tumour site, MYCN amplification and number of image-defined risk factors didn't predict prognosis. On multivariate analysis only post-induction mCR was significantly associated with surgical resection and five-year OS ( $p < 0.001$ ). The median experience of persons surveyed was 7.5 years (range 1 - 22 years). Main barriers to surgery were tumour operability ( $n = 17/34$ ; 50.0%) and operating time ( $n = 7$ ; 20.6%). Rates and indications for resection varied between hospitals. Vascular encasement was the greatest resection deterrent ( $n = 15/34$ ; 44.1%). Only 41.2% ( $n = 14/34$ ) were in favour of centralising NB surgical management.

**Conclusions:** Less than 50% of HR-NB patients are operated on; mostly determined by post-induction MCR and vascular encasement.

Non-standard surgical practices determine eventual surgery. Increased resection rates can be achieved by more resources and operating time.

O037/#1423 | IPSO

IPSO: FREE PAPER SESSION 03 - THE ROBERT ARCECI BEST OF IPSO

12-10-2023 09:40 - 11:10

### NATIONAL TRENDS IN MANAGEMENT OF THE NODAL BASIN FOR PEDIATRIC PATIENTS WITH OCCULT STAGE III MELANOMA IN THE UNITED STATES

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**Background and Aims:** Following publication of recent trials (MSLT-I, MSLT-II, DeCOG), routine completion lymph node dissection (CLND) after positive sentinel lymph node biopsy (SLNB) is no longer recommended for adults with melanoma, while adjuvant immunotherapy (IO) was approved for selected patients with positive SLNB. Given exclusion of pediatric patients from these studies, we aimed to characterize trends in nodal management for pediatric patients with melanoma.

**Methods:** The National Cancer Database (NCDB) was queried for pediatric patients (age  $\leq 20$  years) with melanoma (clinical stage I/II; pathologic stage III) that underwent resection between 2012-2019. The primary objective was to examine trends in extent of nodal surgery, number of lymph nodes examined, and adjuvant IO utilization. Secondary objectives included comparing overall survival (OS) by nodal management and receipt of adjuvant IO using Kaplan-Meier methods.

**Results:** Overall, 98 patients met inclusion criteria. Median age was 18 years (IQR 15-19). Median Breslow depth was 2.36 mm (IQR 1.48-4.00) and 28.6% were ulcerated. Altogether, 35.7% of patients had SLNB alone, 25.5% had CLND after SLNB, and 37.5% had total lymph node dissection (TLND) without SLNB. From 2012 to 2019, patients receiving SLNB alone increased from 13.3% of patients to 88.9%; conversely, TLND decreased from 60% to 0%, and CLND after SLNB decreased from 26.7% to 11.1%. Accordingly, median lymph nodes examined decreased from 22 in 2012 to 2 in 2019. Receipt of adjuvant IO increased from 33.3% of patients in 2012 to 44.4% in 2019 (range 16.7%-47.1%). There was no significant difference in OS by nodal management nor adjuvant IO.

**Conclusions:** The findings of this study support clinical observation after SLNB in pediatric patients with melanoma, as we noted de-escalation in extent of nodal surgery without compromising OS. We also noted increasing utilization of adjuvant IO among patients with

positive SLNB. Multidisciplinary discussion remains vital for managing melanoma in pediatric patients.

O038/#163 | IP SO

### IPSO: FREE PAPER SESSION 03 - THE ROBERT ARCECI BEST OF IP SO

12-10-2023 09:40 - 11:10

#### WHEN TO PERFORM NEPHRON-SPARING SURGERY FOR PATIENTS WITH WILMS' TUMORS, A DELPHI STUDY CONSENSUS STATEMENT

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**Background and Aims:** Within the current SIOP-RTSG treatment protocol, patients with nonsyndromic unilateral Wilms tumor (nsuWT) require a tumor volume <300ml at diagnosis to be considered for nephron-sparing surgery (NSS). This volumetric directive does not account for surgical feasibility, possibly reducing the utilization of NSS. To potentially change this directive, a definition of surgical feasibility is required. This study aimed to define surgical consensus statements for the assessment of patients with WT for NSS.

**Methods:** A Delphi study was performed for which 34 potential experts were approached. Surgeons were included in the expert panel if 3 or more NSS cases per year were performed in their hospital. The first questionnaire contained 5 open-ended questions regarding surgery, oncology, contraindications for NSS, technique, and organization. Follow-up questionnaires contained closed-ended statements based on previous answers.

**Results:** Nineteen potential experts responded to the first questionnaire. Eleven surgeons were included in the expert panel and continued

with three follow-up questionnaires containing 72 statements in total. A median of seven (3 min - 10 max) NSS procedures were performed per year in the hospitals of the experts. Among COG surgeons, NSS was not advocated for nsuWT. However, these consensus statements were derived from responses across the entire international panel. Meaningful consensus statements were: 1) bilateral patients should always be considered for NSS regardless of the expected margin. 2) NsuWT patients should receive four weeks of neoadjuvant chemotherapy and have a preoperative tumor of volume <200 mL. 3) Preoperative volume is more important than the volume at diagnosis. 4) Partial nephrectomy with wide resection margin (>5mm) is the preferred technique for nsuWT patients.

**Conclusions:** Using a Delphi method, surgical experts defined consensus statements regarding NSS for patients with WT. These statements can be used to implement surgical feasibility in future treatment protocols and expand the safe utilization of oncologically appropriate NSS.

O039/#278 | IP SO

### IPSO: FREE PAPER SESSION 03 - THE ROBERT ARCECI BEST OF IP SO

12-10-2023 09:40 - 11:10

#### GLOBAL CHILDHOOD CANCER SURGICAL LANDSCAPE: A PROFILE SECONDARY ANALYSIS OF NON-BIOLOGICAL FACTORS THAT INFLUENCE OUTCOMES

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**Background and Aims:** ProFILE is a tool to evaluate non-biological factors that influence childhood cancer outcomes, collecting data from diverse global settings. We describe global surgical capacity utilizing ProFILE.

**Methods:** From 2019 to 2021, 112 institutions from 23 countries collected data utilizing the Abbreviated Version of ProFILE. A secondary analysis focused on surgical variables of previously collected data was made.

**Results:** Hospitals included were in low-income (6), lower-middle-income (34), upper-middle-income (55), and high-income countries (17) and were classified as cancer (19%), children's (22%), general

(45%), and pediatric oncology (12%) hospitals. The median number of newly diagnosed cancer cases per year was 86 (range, 0-1400), and the median number of annual pediatric oncologic surgeries was 37 (range, 0-1800). Most hospitals covered surgical costs utilizing governmental funds (83%). Most were teaching facilities (90%), but fewer had accredited fellowship programs for general pediatric surgery (45%), orthopedics (20%), ophthalmology (13%), and neurosurgery (11%). Inhouse surgical rooms were available in 85%, timely access to a blood bank was available in 79%, and safe vascular access supplies in 71%. Anesthesiologists were available in 72%. Pediatric surgeons were available in 71%, but only 28% were exposed to pediatric oncology surgery training. Orthopedics, neurosurgery, and ophthalmology surgeons were available in 63%, 50% and 47% of hospitals, respectively. Pediatric radiologists specialized in oncology were only available in 16%. Tumor boards occur in 46% of the hospitals; 63% every week. Direct and effective communication between oncologists and surgeons occur consistently before surgery in 69% of hospitals and after surgery in 55%.

**Conclusions:** Most hospitals have some key elements for delivery of surgical care, but disparities have been observed and communication among members of multidisciplinary team and tumor boards, are still lagging desirable thresholds. A specific surgical tool (PrOFILe-ST) is being piloted to support a thorough assessment of service and training infrastructure.

O040/#256 | Free Paper Session (FPS)

## FPS 02: PROGNOSTIC FACTORS IN LEUKEMIA

12-10-2023 09:40 - 11:10

### PROGNOSTIC SIGNIFICANCE OF ETP STATUS AND MINIMAL RESIDUAL DISEASE AT END-INDUCTION AND END-CONSOLIDATION IN CHILDREN'S ONCOLOGY GROUP (COG) STUDY AALL1231

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**Background and Aims:** In the COG AALL0434 T-ALL trial (prednisone-based backbone), ETP status was not predictive of survival. We assessed the impact of ETP status in patients treated on the successor trial COG AALL1231 (dexamethasone-based backbone +/- bortezomib).

**Methods:** 615 T-ALL patients from AALL1231 were categorized as ETP (12%), Near-ETP (13.8%), Not-ETP (70.1%), or unknown (4.1%). Bone marrow MRD and ETP status were assessed centrally by flow cytometry at end of induction (EOI) and consolidation (EOC). Four-year event-free survival (EFS) and overall survival (OS) were estimated using Kaplan-Meier analysis.

**Results:** ETP patients had inferior EFS ( $p=0.0373$ )/OS ( $p=0.0090$ ) ( $73.8 \pm 5.3\%/78.0 \pm 5.0\%$ ) compared to Near-ETP ( $85.9 \pm 3.8\%/90.6 \pm 3.2\%$ ) and Not-ETP ( $82.9 \pm 1.9\%/89.3 \pm 1.5\%$ ). ETP patients had higher cumulative incidence of relapse (CIR) rates ( $11.1 \pm 3.7\%$ ) than Near-ETP ( $4.7 \pm 2.3\%$ ) or Not-ETP ( $8.8 \pm 1.4\%$ ;  $p=0.1490$ ) and were more likely than Near-ETP or Not-ETP to have MRD $\geq 0.1\%$  at EOI ( $p<0.001$ ), but not EOC ( $p=0.110$ ). EOI MRD $\geq 0.1\%$  was predictive of inferior EFS/OS for ETP and Not-ETP, but not Near-ETP. EOC MRD $\geq 0.01\%$  was associated with dismal outcomes for all patients. ETP status was not predictive of EFS, OS, or CIR on Arm A (no bortezomib). ETP patients on Arm B (+bortezomib) had inferior EFS ( $p=0.0054$ )/OS ( $p=0.0045$ ) but not CIR ( $p=0.2461$ ), driven by increased toxic deaths in ETP patients. Because of this discrepancy we conducted *ex vivo* drug profiling of T-ALL patient samples ( $n=18$ ) with bortezomib and corticosteroids. We

hypothesize intensified corticosteroids did not benefit ETP patients, compounded by the addition of bortezomib. ETP status did not predict sensitivity to bortezomib. Consistent with prior reports, ETP samples were more corticosteroid-resistant.

**Conclusions:** On AALL1231 ETP status was predictive of EFS and OS, primarily driven by the bortezomib arm, though this may reflect small sample sizes in subset analyses. EOIMRD $\geq$ 0.1% was prognostically significant in ETP and Not-ETP. EOC MRD-positivity was associated with poor prognosis for all patients.

O041/#1464 | Free Paper Session (FPS)

## FPS 02: PROGNOSTIC FACTORS IN LEUKEMIA

12-10-2023 09:40 - 11:10

### PROGNOSTIC FEATURES OF CD9 IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA - A RETROSPECTIVE ANALYSIS OF A NATION-WIDE MULTICENTER STUDY IN CHINA

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**Background and Aims:** The outcomes of children with acute lymphoblastic leukemia (ALL) have been incrementally improved with risk-stratified chemotherapy. However, the treatment responses even within defined risk groups are highly heterogeneous. We previously identified that, in a single-center cohort of B-ALL patients (n=153), CD9 positivity is associated with an inferior relapse-free survival rate (65.4% vs. 88.0%,  $P=0.019$ ) (Leung et al, *Leukemia*, 2020). This initial discovery points towards a multi-center study to consolidate its prognostic impact and address new questions.

**Methods:** The CCCG-ALL-2015 study enrolled 7,640 patients from 20 tertiary hospitals in China from 2015 to 2019 (Tang et al, *Blood*, 2021), with 3,781 subjects (49.5%) had flow cytometry data on lymphoblast CD9 at diagnosis. We conducted in-depth correlative analyses on the study cohort comprising 3,395 B-ALL and 386 T-ALL patients with a median follow-up of 53.9 months, linking CD9 status with clinical variables.

**Results:** CD9 is expressed in 88.5% of B-ALL and 27.9% of T-ALL cases. CD9 confers a dismal event-free survival (82.1% vs. 89.3%,  $P=0.001$ ) and a higher incidence of relapse (15.5% vs. 7.8%,  $P<0.001$ ) in B-ALL but not T-ALL patients. The prognostic impact of CD9

is much more prominent in subjects with adverse presenting features or poor early treatment responses, as best exemplified in those assigned to the intermediate/high-risk arms (CIR: 23.1% vs. 10.2%,  $P=0.003$ ) or those with minimal residual diseases (CIR: 30.3% vs. 9.7%,  $P=0.008$ ). The adverse impact of CD9 is confined to specific cytogenetics, as illustrated by its differential effect on BCR-ABL1 (CIR: 39.5% vs. 0%,  $P=0.019$ ) and KMT2A-rearranged (CIR: 30.3% vs. 36.4%,  $P=0.566$ ) leukemia. In multivariate analyses, CD9 remains an independent factor predicting a higher relapse rate (HR=2.188,  $P<0.001$ ).

**Conclusions:** CD9 should be incorporated into the diagnostic flow marker panel of childhood ALL to refine the current risk stratification system and inform appropriate treatment intensity.

O042/#791 | Free Paper Session (FPS)

## FPS 02: PROGNOSTIC FACTORS IN LEUKEMIA

12-10-2023 09:40 - 11:10

### PROGNOSTIC IMPACT OF T(1;19)/TCF3::PBX1 IN PEDIATRIC B-CELL LYMPHOBLASTIC LEUKEMIA (B-ALL) PATIENTS TREATED ON CONTEMPORARY CHILDREN'S ONCOLOGY GROUP (COG) STANDARD RISK PROTOCOLS

Ashley Pinchinat<sup>1</sup>, John Kairalla<sup>2</sup>, Meenakshi Devidas<sup>3</sup>, Andrew Carroll<sup>4</sup>, Zhiguo Chen<sup>2</sup>, Mary Shago<sup>5</sup>, Anne Angiolillo<sup>6</sup>, Michael Burke<sup>7</sup>, Wanda Salzer<sup>8</sup>, Naomi Winick<sup>9</sup>, Sumit Gupta<sup>10</sup>, Mignon Loh<sup>11</sup>, Elizabeth Raetz<sup>1</sup>, Karen Rabin<sup>12</sup>, Rachel Rau<sup>12</sup>

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**Background and Aims:** Translocation t(1;19)(q23;p13.3) resulting in the *TCF3::PBX1* fusion is a recurrent cytogenetic alteration in B-ALL. Data regarding the prognostic impact and need for therapy intensification are conflicting. We aimed to determine the t(1;19) outcomes with contemporary COG therapy.

**Methods:** We performed a retrospective outcome analysis of NCI standard risk (SR) B-ALL patients enrolled on COG AALL0932 from 2010 to 2018. Children with Philadelphia-positive, central nervous system (CNS3), and testicular leukemia were ineligible. Remaining patients were risk stratified based on day 8 blood and day 29 marrow MRD and cytogenetics. T(1;19), confirmed by central review, was considered a neutral cytogenetic lesion not impacting stratification.

**Results:** One-hundred thirty-one patients (2.7% of 4871 patients) had t(1;19), including 44 (34%) and 86 (66%) with a balanced and unbalanced translocation, respectively, and one with both. The 5-year disease-free (DFS) and overall survival (OS) for all patients with t(1;19) were not significantly different than those without t(1;19) (DFS  $96.9 \pm 1.6\%$  vs.  $93.6 \pm 0.4\%$ ,  $p=0.08$ ; OS  $97.6 \pm 1.4\%$  vs.  $98.0 \pm 0.2\%$ ,  $p=0.93$ ). However, t(1;19) DFS was significantly superior to that of other patients with neutral cytogenetics ( $n=1661$ ) (other neutral cytogenetics DFS  $90.2 \pm 0.8\%$ ,  $p=0.009$ ). There was a significant difference in DFS for balanced vs unbalanced translocations compared with other neutral cytogenetics. The 5-year DFS was  $100\%$  vs  $95.2 \pm 2.5\%$  vs  $90.2 \pm 0.8\%$  ( $p=0.02$ ), although no significant difference was noted in OS. In the unbalanced group, there were 3 isolated bone marrow and 1 isolated CNS relapse.

**Conclusions:** For NCI SR patients treated on recent COG regimens, t(1;19) did not confer a poorer prognosis and instead showed improved DFS vs. those with other neutral cytogenetics and comparable to patients with favorable cytogenetics. Our data confirm that NCI SR patients do not need intensification on the basis of t(1;19) alone when treated on contemporary COG regimens.

O043/#1204 | Free Paper Session (FPS)

FPS 02: PROGNOSTIC FACTORS IN LEUKEMIA

12-10-2023 09:40 - 11:10

#### RELEVANCE OF CD20 EXPRESSION AMONG PEDIATRIC PRECURSOR B-LINEAGE ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS

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**Background and Aims:** CD20 is expressed in nearly 50% of adult precursor B-lineage acute lymphoblastic leukemia (B-ALL) patients and is associated with adverse outcomes. Literature regarding the frequency

and prognostic relevance of CD20 expression among pediatric patients diagnosed with B-ALL is sparse and contradictory.

**Methods:** Baseline clinical and laboratory characteristics among consecutive pediatric patients diagnosed with B-ALL between January 2018 to February 2022 were analyzed. Patients with CD20 expression in >20% B-lymphoblasts as assessed by flow cytometric immunophenotyping (FCM) were considered CD20 expressers (CD20+).

**Results:** Among 224 children diagnosed with treatment-naïve B-ALL during the study time frame, 50% ( $n=111$ ) had CD20 expression. Among CD20+ B-ALL patients, a median (IQR) of 67% (39-91) blasts had CD20 expression. Among 211 patients who were treated, 6 (3%) patients died during induction. In the remaining 205 patients, there was no significant difference in the day 8 circulating blast clearance and FCM end-of-induction measurable residual disease (EOI-MRD) status with respect to CD20 expression. During follow-up, there was a significantly increased frequency of relapse among our CD20+ B-ALL patients as compared to CD20- B-ALL patients (22% vs 9%,  $p=0.007$ ). By Kaplan-Meier survival analysis, there was a significant difference in the 4-year relapse-free survival (62% vs 75%,  $p=0.011$ ), but not in the overall survival (64% vs 80%,  $p=0.109$ ) between our CD20+ and CD20- B-ALL patients. On univariate analysis, expression of CD20 conferred an increased risk for poor 4-year relapse-free survival (HR: 2.650 with 95% CI of 1.218 - 5.764,  $p=0.014$ ) but did not influence the overall survival (HR: 1.739 with 95% CI of 0.876 - 3.453,  $p=0.114$ ).

**Conclusions:** CD20 was expressed in 50% of our pediatric B-ALL patients. Baseline clinical and laboratory parameters and EOI-MRD were not significantly different with respect to CD20 expression. However, expression of CD20 was associated with significantly increased disease relapse and inferior 4-year relapse-free survival.

O044/#997 | PROS

PROS: FREE PAPER SESSION 01

12-10-2023 13:00 - 14:30

#### OUTCOME OF A SURVEY ON RADIOTHERAPY APPROACHES FOR PEDIATRIC CRANIOPHARYNGIOMA ACROSS SIOP EUROPE AFFILIATED COUNTRIES

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**Background and Aims:** Despite excellent survival rates, quality-of-life of pediatric craniopharyngioma survivors can be severely hampered by tumor and/or treatment induced hypothalamic, vascular and visual damage. The aim of this survey is to map the current radiotherapy practice for pediatric craniopharyngioma across the SIOPE-affiliated countries.

**Methods:** In May 2022, a survey was distributed among 246 SIOPE-affiliated radiotherapy departments across 35 countries. The survey consisted of 30 questions and sub-questions focusing on treatment modalities, applied protocols and dose, margins for contouring, organs at risk, imaging, and radiotherapy contra-indications. Questions related to radiotherapy-induced hypothalamic damage were added.

**Results:** Sixty-two of 246 (25%) centers from 24 countries responded. Ten centers irradiate  $\geq 6$  patients/year, while 14 centers irradiate zero patients. Protons only, photons only, or a combination (depending on volume, age, capacity) are used in 15, 6 and 27 of 48 centers, respectively. Twenty-five centers (52%) use the GPOH-Kraniopharyngeom-2007 protocol. Prescribed dose was 54Gy in 58% of centers. Summing all margins (CTV+ITV+PTV) demonstrates a GTV-PTV margin of 2-5mm, 6-10mm, 11-15mm in 22%, 60%, and 18% of the centers, respectively. Only 4/48 centers delineate optic nerves/chiasm AND hypothalamus AND surrounding major arteries. Most centers (40/48) perform daily position verification using KV-CBCT (23/48) or 2D-KV (15/48) imaging. Extra imaging to adapt for cyst volume changes is performed in 86% of centers, at weekly base (57%), and using MRI (65%). Most common contra-indications for radiotherapy include age <5 years, large cystic lesions with no option to decompress during radiotherapy, and no prior attempt done for debulking. Whether radiotherapy as a single modality can damage the hypothalamic functions (temperature, appetite, circadian rhythm) is controversial among respondents (yes: 22/48).

**Conclusions:** In lack of a modern SIOPE radiotherapy guideline, heterogeneity in daily practice is observed across SIOPE-affiliated centers. The outcome of this survey illustrates the need for consensus and further research on radiotherapy effects on hypothalamic function.

O045/#531 | PROS

PROS: FREE PAPER SESSION 01

12-10-2023 13:00 - 14:30

#### DEVELOPMENT OF STANDARD OPERATING GUIDELINES TO IMPROVE QUALITY OF VMAT CRANIOSPINAL IRRADIATION IN A GLOBAL SETTING

Aduugna Fekadu<sup>1</sup>, Naba Ali<sup>2</sup>, Keyru Nasir<sup>1</sup>, Molalgn Gebresenbet<sup>1</sup>, Oluwatosin Kayode<sup>2</sup>, Munir Awol<sup>1</sup>, Sean Dresser<sup>2</sup>, Eduard Schreibmann<sup>2</sup>, Elias Amara<sup>1</sup>, Edom Seife<sup>1</sup>, Natia Esiashvili<sup>2</sup>

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**Background and Aims:** Background: The use of volumetric modulated arc therapy (VMAT) has improved the accuracy and ease of craniospinal irradiation (CSI). When carefully executed, adaptation of this technique in low-income countries (LIC) with high case volume and low resources may improve efficiency and reduce set up errors. We discuss our experience developing standard operating procedure guidelines (SOP) to improve the quality of VMAT CSI in a hospital in a LIC.

**Methods:** Physicists and senior oncologists at Black Lion Hospital and peers from twinning program from high-income country (HIC) reviewed prior CSI cases to assess current capabilities and needs for quality improvement. SOP from a partnering (HIC) was used as a guide to modify and adapted to address concerns unique to a LIC institution with recent implementation of VMAT techniques.

**Results:** The scope and purpose of the SOP was defined at the onset of creation. Following this the CSI procedure was divided in succinct steps including contouring, doses, documentation, shifts, treatment planning, plan evaluation, quality assurance and on-board imaging. Challenges encountered included minimal resident CSI contouring experience, lack of routine use of electronic documentation, minimal experience with auto-feathering technique, two energy capability (6 MV, 16 Mv), difficulty attaining homogeneity goals, and lack of kV on-board imaging. VMAT CSI plans were planned to be assessed by both internal and external peers at quarterly intervals to adjust SOP if needed.

**Conclusions:** SOPs have been routinely used in HIC to ensure safe and effective radiation treatments. The presented experience may serve as a model for LIC to establish similar procedures in low-resource environments.

O046/#220 | PROS

PROS: FREE PAPER SESSION 01

12-10-2023 13:00 - 14:30

#### EUROPEAN CLINICAL PRACTICE IN PENCIL BEAM SCANNING PROTON THERAPY FOR PEDIATRIC POSTERIOR FOSSA TUMORS

Laura Toussaint<sup>1,2</sup>, Witold Matysiak<sup>3</sup>, Claire Alapetite<sup>4</sup>, Javier Aristu<sup>5</sup>, Agata Bannink-Gawryszuk<sup>3</sup>, Stephanie Bolle<sup>4,6</sup>, Felipe Calvo<sup>5</sup>, Fernando Cerron Campoo<sup>6</sup>, Frances Charwood<sup>7</sup>, Charlotte Demoor-Goldschmidt<sup>8</sup>, Jérôme Doyen<sup>9</sup>, Katarzyna Drosik-Rutowicz<sup>10</sup>, Pauline Dutheil<sup>8</sup>, Anna Embring<sup>11</sup>, Jacob Engellau<sup>12</sup>, Anneleen Goedgebeur<sup>13</sup>, Farid Goudjil<sup>4</sup>, Semi Harrabi<sup>14</sup>, Renata Kopec<sup>15</sup>, Ingrid Kristensen<sup>12</sup>, Peter Længsmand<sup>1,2</sup>, Carola Lütgendorf-Caucig<sup>16</sup>, Arturs Meijers<sup>17</sup>, Alfredo Miranda<sup>18</sup>, Ludvig

Muren<sup>1,2</sup>, Barbora Ondrova<sup>19</sup>, Ester Orlandi<sup>18</sup>, Erik Pettersson<sup>20,21</sup>, Sandija Plaude<sup>22</sup>, Roberto Righetto<sup>23</sup>, Barbara Rombi<sup>24</sup>, Beate Timmermann<sup>25</sup>, Karen Van Beek<sup>13</sup>, Sabina Vennarini<sup>26</sup>, Anne Vestergaard<sup>2</sup>, Marie Vidal<sup>9</sup>, Vladimir Vondracek<sup>19</sup>, Damien Weber<sup>17</sup>, Gillian Whitfield<sup>7,27</sup>, Jens Zimmerman<sup>28</sup>, John Maduro<sup>3</sup>, Yasmin Lassen-Ramshad<sup>2</sup>

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**Background and Aims:** The posterior fossa (PF) is the most common brain tumor location in pediatric patients, with the target adjacent to critical organs at risk such as the brainstem. Yet, there are currently

no 'best-practice' guidelines on treatment planning for pencil beam scanning (PBS) proton therapy of PF tumors. This study aimed at mapping the current PBS standard of care across European centers when treating PF tumors, with a special focus on the brainstem.

**Methods:** An initial survey and a treatment-planning comparison exercise were distributed to nineteen European PBS centers treating pediatric patients. The survey assessed brainstem management, including delineations, dose constraints and treatment planning. For treatment-planning comparison, each center planned two PF cases for focal irradiation, according to their own clinical practice but based on a common structure-set. The prescription dose was 54 Gy(RBE) (Case 1) and 59.4 Gy(RBE) (Case 2). For both cases, planning strategies were compared.

**Results:** Seventeen centers answered the survey, and sixteen planned both cases. Thirteen centers reported using a common definition for brainstem delineation. Twelve centers reported using typically three beams, which was confirmed in the treatment-planning study with nine (Case 1) and thirteen (Case 2) centers using three beams. However, the beam angles and configuration varied widely across centers. The survey showed large variations in the applied brainstem dose constraints, which was also highlighted by the treatment-planning study: e.g. the brainstem volume receiving 54Gy(RBE) ranged from 0% to 25% (median 4% - Case 1), and from 26% to 60% (median 49% - Case 2). No center used biologically-weighted dose optimization for planning of the two cases.

**Conclusions:** This study explored the European landscape in PBS treatment of pediatric PF tumors. Consensus was seen in e.g. delineation-practice, while wider variations were reported for e.g. brainstem dose constraints. Collaboration between centers is still ongoing, striving towards common guidelines.

O047/#1337 | PROS

PROS: FREE PAPER SESSION 01

12-10-2023 13:00 - 14:30

#### DIFFUSE PONTINE GLIOMA (DPG): SHORTER OR LONGER TREATMENT TIME?

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**Background and Aims:** DPG is a lethal disease with a median overall survival (OS) of < 1 year. No curative treatment is available, and the aim of radiotherapy is symptom palliation. Hypofractionated radiotherapy (HR) was proposed to improve quality of life with shorter

treatment duration, fewer hospital visits and costs, particularly in low- and middle-income countries (LMICs). Still, many LMIC institutions use 54 Gy/30 fractions. The study aims to identify patients who may benefit from HR.

**Methods:** We reviewed data of MAHAK patients from 11/2010 until 02/2020. The diagnosis was based on clinical symptoms and MRI imaging. Biopsy was not mandatory.

**Results:** Of 107 patients identified, 33(31%) had a biopsy. The diagnosis was high-grade glioma/glioblastoma in 18(55%). H3K27M was identified in two patients and not evaluated in others. No seeding was detected at diagnosis. Hydrocephalus was present at diagnosis in 28(26%), 17(61%) underwent CSF diversion. Three-year OS (107 patients) and progression-free survival (PFS, 81 patients) were 4.7% (95% CI: 0.7-8.6) and 2.5% (0-5.8) respectively. The dose was 39, 45 and 50-54 Gy in 22(21%), 55(51%) and 30(28%) patients respectively. Symptoms improved in 96 patients (90%) after radiotherapy. No significant EFS/OS effect of fractionation was detected. Seventy-eight (73%) patients received chemotherapy and no EFS/OS benefit was observed. Poor-risk patients with shorter OS were patients >3 years, patients with presenting symptoms <3 months and those with the full triad of symptoms (cranial nerve deficit, ataxia, long tract signs) ( $p < 0.05$ ). Only 10 patients (9%, 8 with 39 or 45 HR) received re-irradiation at the time of progression.

**Conclusions:** Due to their shorter life expectancy, poor-risk patients may benefit from HR. Our data confirm the lack of benefit of chemotherapy. Re-irradiation should be considered at the time of progression. We proposed a scoring system based on prognostic factors to decide on HR vs. normal fractionation.

O048/#635 | PROS

PROS: FREE PAPER SESSION 01

12-10-2023 13:00 - 14:30

#### HIGHER RISK OF HEARING LOSS AFTER PROTON IRRADIATION AND CHEMOTHERAPY AMONG A SUBSET OF CHILDREN WITH MEDULLOBLASTOMA

Mohammad Abu-Arja<sup>1</sup>, Austin Brown<sup>1</sup>, Jack Su<sup>1</sup>, Mehmet Okcu<sup>1</sup>, Holly Lindsay<sup>1</sup>, Susan Mcgovern<sup>2</sup>, Mary Frances Mcaleer<sup>2</sup>, David Grosshans<sup>2</sup>, Murali Chintagumpala<sup>1</sup>, Arnold Paulino<sup>3</sup>

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**Background and Aims:** To evaluate the incidence and risk factors for hearing loss (HL) among children with medulloblastoma treated with proton irradiation and cisplatin.

**Methods:** We identified children with medulloblastoma, three years of age or older, treated at Texas Children's Hospital between 2007-2022. Audiograms were graded using the International Society of Pediatric Oncology-Boston scale (SIOP-Boston). Time to grades 3-4 HL was evaluated using Kaplan-Meier and multivariable Cox models to estimate hazard ratios (HR) and 95% confidence intervals (CI). Patients with less than 6 months of follow were excluded.

**Results:** Seventy-eight patients were treated with craniospinal irradiation (CSI) at a median age of 7.6 years (range: 3-21 years). The mean cochlear irradiation dose was 31.5+/-9 Gy, and the mean cumulative cisplatin dose was 295+/-50 mg/m<sup>2</sup>. Fifty-six patients (72%) received amifostine. Patients completed a median of 9 audiograms (range: 4-22) with a median audiogram follow-up of 49 months (range: 6-177 months). Grades 3-4 HL were documented in 25 patients (35%). In adjusted Cox models, mean cochlear irradiation dose (HR=1.12, 95% CI: 1.06-1.18) and the age at CSI (HR=0.81, 95% CI: 0.68-0.98) were associated with grades 3-4 HL. In children treated with CSI after 7 years of age, the probability of grades 3-4 HL three years post-CSI was 12.6% (95% CI: 4.1-34.6) in those with cochlear exposure < 36 Gy compared to 35.6% (95% CI: 17.4-63.6) in children with cochlear exposure > 36 Gy. In children treated with CSI at or prior to 7 years of age, the probability of grades 3-4 HL at three years post-CSI was 16.5% (95% CI: 35.4-93.7) in those with cochlear exposure < 36 Gy and 66.7% (95% CI: 35.4-93.7) in those with cochlear exposure > 36 Gy.

**Conclusions:** Long-term follow-up shows that children who received cochlear dose equal to or higher than 36 Gy before 7 years of age are at higher risk for HL.

O049/#1491 | PROS

PROS: FREE PAPER SESSION 01

12-10-2023 13:00 - 14:30

#### CORTICAL AND SUBCORTICAL GREY MATTER VOLUMES IN SURVIVORS OF A PEDIATRIC POSTERIOR FOSSA TUMOR

Kristien Bullens<sup>1</sup>, Charlotte Sleurs<sup>2</sup>, Jeroen Blommaert<sup>1</sup>, Jurgen Lemiere<sup>3</sup>, Karen Van Beek<sup>4</sup>, Anne Uytendroek<sup>1</sup>, Sandra Jacobs<sup>5</sup>

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**Background and Aims:** Craniospinal irradiation (CSI) for pediatric brain tumors can damage the brain tissue, contributing to later-life neurocognitive impairment. We investigated grey matter (GM) volumes and intelligence scores (IQ) in survivors of a PFS tumor, to further elucidate radiation-induced brain damage.

**Methods:** T1-weighted MRI (MPRAGE, resolution=.98x.98x1.2mm) and IQ (WAIS-IV) were analyzed for 21 survivors of PFS tumors (15

males, mean age  $25.2 \pm 4.7$ y, mean diagnosis age  $8.5 \pm 4.5$ y) and 21 matched controls (mean age  $25.4 \pm 4.8$ y). MRIs of 3 survivors were excluded. Supratentorial voxel-based morphometry (VBM, SPM12) and subcortical region-of-interest (ROI-) volumetry (Fastsurfer) were applied. GM volume and IQ were compared between PFS survivors and controls, and between non-irradiated survivors (NI-S) and craniospinal irradiated [JL1] -survivors (CSI-S), and Bonferroni corrected for multiple comparisons. Finally, associations between supratentorial irradiation-doses, total subcortical GM, and total subcortical GM volumes and IQ were also assessed.

**Results:** The VBM analyses indicated lower subcortical GM volume within the pallidum of patients. All subcortical ROIs were smaller in PFS survivors, significant in 11/14 regions after Bonferroni correction. While all subcortical ROIs were smaller in CSI-S compared to NI-S, this difference was not significant. No relationship between GM volumes and supratentorial RT-dose was observed. Total IQ and all subscales were significantly lower among survivors ( $p_{\text{unc}} < 0.0001$ ), and lower in CSI-S compared to NI-S albeit only significant for processing speed ( $p_{\text{unc}} < 0.003$ ). Finally, positive correlations were found between total subcortical GM volume and IQ, including subscales ( $p_{\text{unc}} < 0.04$ ). Negative correlations were found between supratentorial RT-doses and IQ ( $p_{\text{unc}} = 0.010$ ), verbal comprehension ( $p_{\text{unc}} = 0.024$ ), and working memory ( $p_{\text{unc}} = 0.024$ ).

**Conclusions:** In conclusion, we found smaller subcortical GM volume in PFS survivors, associated with lower IQ. Larger cohort studies are needed to further elucidate RT-related mechanisms of toxicity, and possible interactions with age.

O050/#518 | PROS

PROS: FREE PAPER SESSION 01

12-10-2023 13:00 - 14:30

#### BONE MINERAL DENSITY IN PAEDITRIC BRAIN TUMOR PATIENTS: A PROSPECTIVE STUDY AT A TERTIARY CARE CENTRE IN INDIA

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**Background and Aims:** Low bone mineral density (BMD) is considered as a late effect of cranial radiotherapy (RT). None of the study has assessed BMD at diagnosis or within few months of RT in brain tumor

patients. Therefore, we conducted this study to analyse the incidence of low BMD at diagnosis in children with brain tumors.

**Methods:** The study was conducted as a part of intramural funding programme at a tertiary care centre in India. Paediatric brain tumor patients were advised for dual energy X-ray absorptiometry scan (DXA) at diagnosis (prior to RT), however; in some patients, scan was delayed and done within few months of RT initiation. Repeat DXA after 12 months of RT, has also been planned as a part of the study.

**Results:** Twenty-eight patients were analysed. Median age at diagnosis was 11-years. Medulloblastoma was the commonest malignancy ( $n=14$ ), followed by glioma ( $n=8$ ), pineal tumors ( $n=3$ ) and ependymoma ( $n=3$ ). DXA was done at diagnosis or within 6-months of RT initiation in 22 and 6 patients respectively. BMD was assessed using Z score at hip and lumbar spine. Seven, four and nine patients had normal, low (Z score =  $-1$  to  $-1.99$ ) and very low (Z score =  $-2$  to  $-2.5$ ) BMD respectively. Eight patients had secondary osteoporosis (Z score  $\leq -2.5$ ). Two patients with secondary osteoporosis had low vitamin D levels though none of them had compression fracture. Statistical analysis did not show any correlation between BMD and age, sex and site of the tumor.

**Conclusions:** To the best of our knowledge, index study is the first to report occurrence of low BMD at the time of brain tumor diagnosis or within few months of RT initiation. Low BMD in significant proportion of children highlights the importance of early assessment and referral to the specialist for better quality of life.

O051/#499 | PROS

PROS: FREE PAPER SESSION 01

12-10-2023 13:00 - 14:30

#### RE-IRRADIATION WITH CSI AND BOOST OF BRAIN TUMOURS PREVIOUSLY TREATED WITH LOCAL PROTON AND/OR PHOTON THERAPY

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**Background and Aims:** Preparing a re-irradiation can in many occasions be difficult considering the previously given radiation treatment. Several recent papers indicate the feasibility for re-irradiation of pediatric brain tumors such as ependymoma and medulloblastoma. We present a treatment planning method for re-irradiation with protons, taking the previously irradiated volume into account.

**Methods:** Three patients with the diagnoses; ependymoma, medulloblastoma, AT/RT were previously treated to 54 GyRBE to the primary tumor. One patient with NGGCT were previously treated with a simultaneously integrated boost (SIB) technique to 54/60 GyRBE.

Re-irradiation was performed 4 months to nine years after the primary irradiation. Three patients were primarily treated with protons. One patient was primarily treated with photons and re-treated twice with photons. All four patients were re-irradiated with protons and received craniospinal irradiation (CSI). Two of them also received boost. CT-studies were registered, and target volumes copied to the latest CT-study made for treatment-planning. A safety margin of 1.5-2cm were applied for the CSI-target volume. National re-irradiation guidelines compiled from latest evidence were used for constraints and objectives. All patients were discussed at a national video conference. In addition, re-irradiations are evaluated annually in the national pediatric radiotherapy group.

**Results:** For these patients,  $D_{2\%}$  of the previously treated volumes received between 29.0 and 68.5 GyRBE in the summed treatment plans. The absorbed dose to the brainstem were kept below the stated maximum of 91.5 GyEQD<sub>2</sub>, (62-70 GyRBE) and there were no cumulative doses above 100 GyRBE (59-74 GyRBE). The absorbed doses to organs at risk were all below internationally accepted tolerance doses.

**Conclusions:** Re-irradiation with protons is feasible in complicated situations. However, due to the severity of their diseases only two patients are still alive, 1 and 2 years respectively after the re-irradiation. Both are free from disease, but are tired (grade 1) and have cognitive problems (grade 1).

O052/#454 | Free Paper Session (FPS)

FPS 03: LYMPHOMA

12-10-2023 13:30 - 15:00

#### PD-L1 AND PD-L2 GENOMIC ALTERATIONS CORRELATE WITH GENE EXPRESSION PROFILING AND IS ASSOCIATED WITH CLINICAL OUTCOMES IN PEDIATRIC HODGKIN LYMPHOMA

Nmazuo Ozuah<sup>1</sup>, Howard Lin<sup>1</sup>, Jennifer Agrusa<sup>2</sup>, Faith Hollingsworth<sup>3</sup>, Elmoataz Abdelfattah<sup>1</sup>, Jessica Velazquez<sup>1</sup>, Brooks Scull<sup>1</sup>, Ryan Fleischmann<sup>1</sup>, Tamiwe Tomoka<sup>4</sup>, Kala Kamdar<sup>1</sup>, Nader El-Mallawany<sup>1</sup>, Olive Eckstein<sup>1</sup>, Terzah Horton<sup>1</sup>, Kenneth McClain<sup>1</sup>, Jyotinder Punia<sup>3</sup>, Dolores Lopez-Terrada<sup>3</sup>, Carl Allen<sup>1</sup>  
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**Background and Aims:** Programmed death (*PD-L1/PD-L2*) genomic alterations at the 9p24.1 locus are not well-characterized in pediatric classical Hodgkin lymphoma (HL). While response-based chemotherapy in HL has resulted in omission of radiation therapy (RT) in some patients, a significant number of rapid early responders (RERs),

still experience relapses without RT. We hypothesize that *PD-L1/PD-L2* genomic alterations are associated with treatment outcomes in pediatric HL.

**Methods:** Using fluorescent in situ hybridization, *PD-L1/PD-L2* alterations in 46 biopsy specimens from children who received risk-adapted response-based therapy with ABVE-PC (Doxorubicin, Bleomycin, Vincristine, Etoposide-Prednisone, Cyclophosphamide) was evaluated for frequency of amplification and copy gain. These were assessed for associations with progression-free survival (PFS), and in RERs who did not receive RT, a relapse-free survival (RFS) was estimated. Gene expression profiling (GEP) of flow-sorted Reed-Sternberg cells, was available in 10 patients, and differential expression analysis of five previously validated prognostic genes in pediatric and adult HL (*ALDH1A1*, *CCL17*, *CXCL11*, *IFNG*, and *PRF1*), was performed, with *FDR-adjusted p-value* <0.05.

**Results:** *PD-L1/PD-L2* amplification was present in 5/46 (11%), relative copy gain in 27/46 (59%) and 14/46 (30%) lacked copy gain. All patients had varying degrees of aneuploidy, and patients with amplification had copy gain. Forty-four patients (96%) were included in the survival analysis. The 3-year PFS for "no copy gain" vs. "copy gain" was 100% vs. 76% ( $p=0.05$ ). In RERs ( $n=27$ , 61%) who did not receive RT, the 3-year RFS was 100% vs. 60% (no copy gain vs. copy gain),  $p=0.03$ . Four of five prognostic genes were differentially expressed relative to copy gain - *ALDH1A1*, *IFNG*, *PRF1* ( $p<0.01$ ), *CXCL11* ( $p=0.02$ ), *CCL17* ( $p=0.08$ ).

**Conclusions:** Genomic alterations in pediatric HL is distinct, with low frequency of 9p24.1 amplification. No copy gain of *PD-L1/PD-L2* was associated with better radiation-free survival and correlated with validated prognostic genes on GEP. This supports validation in a larger cohort.

O053/#1080 | Free Paper Session (FPS)

FPS 03: LYMPHOMA

12-10-2023 13:30 - 15:00

#### PEMBROLIZUMAB IN CHILDREN AND YOUNG ADULTS WITH CLASSICAL HODGKIN LYMPHOMA (CHL) WITH SLOW EARLY RESPONSE (SER) TO FRONT-LINE CHEMOTHERAPY (KEYNOTE-667)

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**Background and Aims:** High-risk cHL patients with SER to front-line therapy require extensive radiotherapy after chemotherapy cessation. KEYNOTE-667 (NCT03407144) is a phase 2 study evaluating pembrolizumab plus chemotherapy in patients with cHL and SER to front-line chemotherapy. Interim results for patients with high-risk cHL and SER (group 2) are reported.

**Methods:** Eligible patients were aged 3-17 (children) or 18-25 years (young adults) with newly diagnosed high-risk cHL. Patients received induction therapy with 2 cycles of vincristine, etoposide, prednisone/prednisolone, and doxorubicin (OEPA). Response was assessed by PET/MRI/CT. Patients with rapid early response to OEPA received nonstudy therapy and patients with SER to OEPA received consolidation with 4 cycles of cyclophosphamide, vincristine, prednisone/prednisolone, and dacarbazine (COPDAC-28) plus pembrolizumab 2 mg/kg up to 200 mg IV Q3W (children) or 200 mg IV Q3W (young adults). After consolidation, patients with PET positivity at late response assessment (LRA) received involved-site radiotherapy (28.8 Gy) to late PET-positive residua and continued pembrolizumab Q3W for 17 doses. Patients with PET negativity and SER didn't receive radiotherapy and continued pembrolizumab Q3W for 17 doses. The primary end point was ORR per Cheson 2007 IWG criteria by BICR in patients with SER. Secondary end points included PET negativity at LRA and safety.

**Results:** Group 2 included 49 patients with high-risk cHL with SER to OEPA. At data cutoff (September 2, 2022), the median follow-up was 15.3 months (range, 3.2-30.5). There were 42 patients (86%) with a LRA, of whom 27 (64%) were PET negative by BICR. Treatment-related AEs occurred in 30 patients (61%; grade 3/4: n=6 [12%]). Four patients (8%) had immune-mediated AEs (2 grade 1 hypothyroidism and 2 grade 2 hypothyroidism).

**Conclusions:** Pembrolizumab plus COPDAC-28 consolidation had manageable safety and promising efficacy in children and young adults with high-risk cHL and SER to front-line chemotherapy, suggesting it may augment responses in patients with high-risk cHL.

O054/#917 | Free Paper Session (FPS)

FPS 03: LYMPHOMA

12-10-2023 13:30 - 15:00

### A NATIONAL HARMONISED PROTOCOL FOR CLASSICAL HODGKIN LYMPHOMA RESULTS IN IMPROVED SURVIVAL RATES OF CHILDREN AND ADOLESCENTS IN SOUTH AFRICA

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Clinical Medicine, Faculty Of Health Sciences, Johannesburg, South Africa

**Background and Aims:** Historic South African five-year overall survival (OS) rates for Hodgkin lymphoma (HL) from 2000 to 2010 were 46% and 84% for HIV-positive and HIV-negative children, respectively, with an overall rate of 79%. We investigated whether a harmonised treatment protocol using risk stratification and response-adapted therapy could increase OS of childhood and adolescent HL.

**Methods:** Seventeen units prospectively enrolled patients <18 years, newly diagnosed with classical HL onto a risk-stratified, response-adapted treatment protocol from July 2016 to December 2022. Low- and medium-risk patients received four and six courses of adriamycin, bleomycin, vinblastine, and dacarbazine (ABVD), respectively. High-risk patients received two courses of ABVD, followed by four courses of cyclophosphamide, vincristine, prednisone, and dacarbazine (COPDac). Those with a slow early response and bulky disease received consolidation radiotherapy. HIV-positive patients could receive granulocyte-colony stimulating factor, and less intensive therapy for high-risk stratification, at the treating clinician's discretion. Kaplan-Meier survival analysis was performed to determine two-year OS with Cox regression to elucidate prognostic factors.

**Results:** The cohort comprised 132 patients (19 HIV-positive, 113 HIV-negative), median age 9.7 years with median follow-up of 2.2 years. Risk grouping comprised nine standard-risk (7%), 36 medium-risk (27%) and 87 high-risk (66%) with 71 (54%) rapid early responders and 45 (34%) slow early responders, with 16 undocumented (12%). Two-year OS was 100% for low-risk, 93% for medium-risk, and 91% for high-risk patients. OS for HIV-negative (93%) and HIV-positive (89%) patients were similar ( $p=0.53$ ). Total lymphocyte count  $>0.6 \times 10^9$  predicted survival (94 vs 83%,  $p=0.02$ ).

**Conclusions:** In the first South African harmonised HL treatment protocol, risk stratification correlated with prognosis. Two-year OS of both HIV-positive and HIV-negative patients has improved dramatically since 2010, which may partially be ascribed to standardised treatment and increased supportive care. The improved survival lends strength to the harmonisation movement and gives hope that South Africa may achieve the GICC goals.

O055/#781 | Free Paper Session (FPS)

FPS 03: LYMPHOMA

12-10-2023 13:30 - 15:00

#### CURRENT STATE OF INTERNATIONAL HARMONIZATION EFFORTS FOR PEDIATRIC AND YOUNG ADULT HODGKIN LYMPHOMA: A REPORT FROM THE SEARCH FOR CAYAHL GROUP

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**Background and Aims:** Initial evaluation and staging of patients with Hodgkin lymphoma (HL) provides the foundation for risk-adapted treatment. The Ann Arbor staging system, and later the Cotswolds modification criteria, have been used to classify patients into risk groups. As imaging techniques advance, refinements to HL staging are necessary to improve prognostication and risk group assignment. Published staging systems are not reflective of current pediatric practices, nor is there consistent application of staging and response criteria across pediatric consortia. Harmonization of staging and response assessment criteria in pediatric HL are imperative to facilitate cross-trial comparison of clinical studies globally.

**Methods:** Established in 2011, the SEARCH (Staging, Evaluation & Response Criteria Harmonization) for CAYAHL (Childhood, Adolescent & Young Adult HL) group is comprised of representatives from the Children's Oncology Group, European Network for Pediatric HL, Pediatric Hodgkin Consortium, and the Latin American Hemato-Oncologic Pediatric Diseases Consortium. Utilizing clinical data across consortium groups where available, and delphi consensus methods where data is lacking, SEARCH has proceeded with harmonization efforts across multiple areas of HL staging and response assessment.

**Results:** Through SEARCH working groups, we have now published harmonization projects for the involvement of liver, cortical bone

and Waldeyer's Ring. In 2023, harmonization efforts were completed for CNS involvement, E-lesions and lung lesions, with manuscripts in preparation.

**Conclusions:** SEARCH for CAYAHL has completed the majority of our initial harmonization projects and our next steps are to publish a comprehensive review of current practices. While staging and response criteria were updated in the Lugano 2014 publication, these guidelines do not include pediatric patients. Given that the peak age of patients with HL are within the AYA spectrum, and that care is often shared between the adult and pediatric groups, there is also a pressing need for pediatric oncology input and collaboration into future updates to HL staging and response assessment criteria.

O056/#467 | Free Paper Session (FPS)

FPS 03: LYMPHOMA

12-10-2023 13:30 - 15:00

#### PROGNOSTIC FACTORS IN CHILDREN AND ADOLESCENTS WITH LYMPHOMAS AND VERTICAL TRANSMISSION OF HIV IN BRAZIL: A MULTICENTRIC HOSPITAL-BASED SURVIVAL ANALYSIS STUDY

Nathalia Duarte<sup>1</sup>, Ana Paula Bueno<sup>1</sup>, Bárbara Sanches<sup>1</sup>, Gabriella Ramos<sup>1</sup>, Júlia Maria Dos Santos<sup>1</sup>, Henrique E Silva<sup>1</sup>, Janaína Pondé<sup>1</sup>, Elaine Da Costa<sup>1</sup>, Cristiane Milito<sup>2</sup>, Thalita De Abreu<sup>1</sup>, Marcelo Land<sup>1,2,3</sup>

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**Background and Aims:** Lymphomas related to HIV are usually more aggressive and have a poor prognosis despite the use of combined antiretroviral therapy (cART) and chemotherapy. Children, whose immune system is still developing, suffer severe consequences from this. We aimed to determine survival and prognostic factors in children and adolescents in Rio de Janeiro, Brazil, who live with HIV (CLWH) and developed lymphomas.

**Methods:** Retrospective and observational study of vertically infected patients, aging from 0 to 20 incomplete years, who attended five reference centers for the treatment of HIV/AIDS and pediatric cancer during 1995-2018.

**Results:** A cohort of 1,306 patients was observed. Twenty-five lymphomas were developed and 19 of them were AIDS-defining malignancies. The 5-year Overall Survival (OS) and the 5-year Event-Free Survival (EFS) probabilities were 32.00% (95% CI = 13.72%–50.23%). The 5-year Disease-Free Survival (DFS) probability was 53.30% (95%

CI = 28.02%–78.58%). In multivariate Cox regression analysis, Performance Status (PS) 4 was considered a poor prognostic factor in OS (HR 4.85, 95% CI 1.81–12.97,  $p = 0.002$ ) and in EFS (HR 4.95, 95% CI 1.84–13.34,  $p = 0.002$ ) and the higher CD4+ T-cell counts were considered a better prognostic factor in DFS (HR 0.86, 95% CI 0.76–0.97,  $p = 0.017$ ). Competitive risks for different outcomes were calculated. For death by disease progression or non-complete response, the risk was 40.00% (95% IC = 20.20%–59.80%), for death related to the treatment, it was 20.00% (95% IC = 3.65%–36.35%), and for relapse, 12.57% (95% IC = 0.00%–26.70%).

**Conclusions:** PS 4 as a poor prognostic factor for OS indicates that patients with high degrees of PS could benefit from low-intensity chemotherapy until improvement of the clinical condition. Low counts of CD4+ T-cells as a poor prognostic factor for DFS confirm the importance of cART adherence. This study demonstrates survival and prognostic factors of CLWH that developed lymphomas in Brazil.

O057/#1752 | Free Paper Session (FPS)

FPS 03: LYMPHOMA

12-10-2023 13:30 - 15:00

#### MNAVIGATOR: A DIGITAL HEALTH APPLICATION TO FACILITATE COMPLIANCE WITH STANDARDIZED PEDIATRIC CANCER TREATMENT PROTOCOLS IN TANZANIA

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**Background and Aims:** Low compliance with guideline-based treatment protocol is a well-established barrier contributing to the pediatric cancer survival gap between low- and high-income countries. We designed and implemented mNavigator, a digital case management system at Bugando Medical Centre, a regional cancer referral hospital in Tanzania, to facilitate health provider compliance with standardized pediatric cancer treatment protocols to treat Burkitt lymphoma (BL), the most common Tanzanian childhood cancer diagnosis. We report the impact of mNavigator on provider compliance and patient outcomes.

**Methods:** Patients <18 years of age diagnosed with BL were assigned to the historic cohort (March 2016 to July 2019) or prospectively consented to the study cohort (July 2019-June 2021). Patient demographics, laboratory studies, clinical staging, treatment received and outcomes were extracted for comparative analysis. A 21-section



checklist was created based on the Tanzanian BL National Treatment Guidelines to systematically evaluate protocol compliance. Pre and post mNavigator implementation compliance scores were calculated and analyzed using StataSE 17.

**Results:** A total of 99 patients diagnosed with BL were included in the analysis - 63 in the historic cohort and 36 in the study cohort, with no significant difference in age or sex. After mNavigator implementation, overall protocol compliance increased from 50% to 74% ( $p < 0.001$ ), with an increase in treatment completion from 38% ( $n = 24/63$ ) to 64% ( $n = 23/36$ ). Use of mNavigator led to a  $>40\%$  reduction in treatment abandonment (43% to 25%) and increase in overall end of therapy survival rate from 44% to 81%.

**Conclusions:** The use of mNavigator significantly improved the quality of pediatric BL treatment and patient outcomes at BMC, one of three childhood cancer referral centers in Tanzania. The mNavigator application can be easily adapted for use with other protocols, allowing for future adaptation and scale up to improve outcomes in similar settings with limited staffing capacity for trained pediatric cancer providers.

O058/#1306 | IPSO

#### IPSO: FREE PAPER SESSION 04 - RENAL, SARCOMA, GERM CELL TUMOURS AND FERTILITY

12-10-2023 13:30 - 15:30

#### CHALLENGES OF MANAGEMENT AND OUTCOMES OF RECURRENT WILMS TUMOR IN LOW MIDDLE INCOME COUNTRIES : EXPERIENCE FROM A TERTIARY CARE CENTRE

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**Background and Aims:** The incidence of recurrence in unilateral wilms tumor(WT) is about 15%. Most recurrences occur within 2 years from diagnosis. However the overall survival for patients with recurrent WT (RWT) is reported to be approximately 50 %. This study evaluates the problems in management of children with RWT in low middle income countries (LMIC).

**Methods:** Prospective study from tertiary care center in a LMIC including freshly diagnosed unilateral WT (UWT) patients treated with AIIMS WT-99 protocol from August 1999 through July 2017. Final evaluation was done in December 2022 with at least 5 years follow-up for the last

included patient. All patients who developed recurrence were included and evaluated for the time of recurrence, site, alternate chemotherapy and surgical treatment offered and outcome.

**Results:** During this period 273 UWT were treated, of whom 268 patients were operated. Amongst these 268, 46(17.2%) developed recurrences. Fifteen (32.6%) patients with recurrences refused for further treatment. Thirty-one(67.4%) with RWT were treated. Six of these 31 (19.5%) abandoned treatment after one or two courses of alternate chemotherapy. Of these 31, 17 (17/46=37%) were reoperated and overall 12(12/46= 26.1%) achieved disease free status (DFS). Of these 12, five further died (2 from sepsis, 3 from re-recurrences) ultimately leaving only 7 (7/46=15.2%) alive with DFS. Overall 27/46 (58.7%) have died (5 after DFS; 22 with progressive disease) and 19/46 (41.3%) were alive(7 DFS; 12 with progressive disease).

**Conclusions:** Survival of patients with RWT LMIC is much lower than reported. Around one third patients refuse treatment once recurrence is diagnosed and one-fifth who start treatment abandon it early. Though one-fourth achieve disease free status ultimately only 15% were alive and disease free. As outcome of RWT in LMIC is poor, partly because of refusal or abandonment of therapy all efforts should be made to decrease the incidence of recurrences in WT.

O059/#452 | IPSO

#### IPSO: FREE PAPER SESSION 04 - RENAL, SARCOMA, GERM CELL TUMOURS AND FERTILITY

12-10-2023 13:30 - 15:30

#### SARCOPENIA AS A PROGNOSTIC FACTOR IN PATIENTS WITH WILMS TUMOR: DOES IT INFLUENCE SURGICAL OUTCOMES AND SURVIVAL?

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**Background and Aims:** Sarcopenia (SP) has been described as a risk factor for bad outcomes in adult patients with cancer. Although recent studies have shown its role as a prognostic factor for some hematological malignancies and solid tumors in pediatric population, there is no data regarding Wilms Tumor (WT). Our aim was to study the association between sarcopenia and oncological outcomes in WT.

**Methods:** A retrospective study in patients diagnosed with WT in our institution between 2010-2022 was performed. Sarcopenia at

diagnosis was assessed by measuring psoas muscle area (PMA) at L4-L5 level on CT/MRI, and was defined as z-score values  $< -2$ . Demographic data, complications and outcomes were analyzed.

**Results:** Forty-eight patients (50% male) were included, with a mean age of  $44.91 \pm 31.12$  months and with associated genetic syndromes in 3 cases (6.25%). Twelve patients (25%) had SP at diagnosis vs. 36 (75%) who did not. Right kidney was involved in 22 patients (45.8%), left kidney in 20 (41.7%), and bilateral involvement was found in 6 (12.5%). Forty-one patients (85.4%) underwent total nephrectomy vs. 7 (14.6%) who underwent nephron-sparing surgery (NSS). No statistical differences were found in demographic data, staging, risk group or surgical treatment between SP-group and non-sarcopenic (NS) group. SP was associated with a higher rate of postsurgical complications (36.4% for SP-group vs. 5.71% for NS-group;  $p=0.023$ ) and with a higher rate of relapse (36.4% vs. 13.9% respectively;  $p=0.09$ ). With a median follow-up of 57.75 (1.87-150.8) months, event-free survival (EFS) was lower for SP group ( $84.20 \pm 17.45$  vs.  $135.40 \pm 8.65$  months respectively;  $p=0.08$ ). Only one patient died (2.1%), from SP-group. The 5-years overall survival (OS) was 89% for SP-group vs. 100% for NS-group.

**Conclusions:** SP has been shown to be a risk factor for postsurgical complications in patients with WT. Moreover, SP seems to be associated with poor outcomes, increasing the risk of relapse and decreasing EFS.

O060/#30 | IPSO

IPSO: FREE PAPER SESSION 04 - RENAL, SARCOMA, GERM CELL TUMOURS AND FERTILITY

12-10-2023 13:30 - 15:30

INTRAPARENCHYMAL ICG DURING MIS TUMOUR NEPHRECTOMY IMPROVES NODAL YIELDS: OUTCOMES FROM A FEASIBILITY STUDY

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**Background and Aims:** Lymph node sampling during tumour nephrectomy is mandatory with SIOP and COG recommending sampling a minimum of seven and five nodes, respectively. In children with stage 1/2 disease, absent or inadequate sampling results in a six-fold increase in disease relapse. We have performed laparoscopic (minimally invasive) partial (MISPN) and total tumour nephrectomy (MISN) since 2017 according to institutional guidelines. Intraparenchymal (IP) injection of Indocyanine Green (ICG) was described by the author in 2020 and has been used in all subsequent MISN/MISPN. Here we describe our results before (PreICG) and after (PostICG) introducing fluorescent

guided nodal mapping in patients who had MIS nodal sampling. Patients whose procedure was converted to open prior to nodal sampling were excluded.

**Methods:** All patients having MISN/MISPN between 01/2017 and 11/2022 at a single, tertiary referral centre were included. Data was collected prospectively and retrospectively analysed. Patients having IP ICG were enrolled on clinical trial NCT04854018. Demographics, diagnosis, disease status, treatment, operative data, length of procedure and histopathology results were analysed. Data is median(IQR).

**Results:** MISN in 16 patients and MISPN in 1(7M:14F). Diagnosis: Wilms in 14, Nephroblastomatosis in 2, mesoblastic nephroma. Tumours were left-sided in 8 and right-sided in 9. Patient weight 15.4kg(6) vs 10.5(0.3); tumour volume 85mls(125) vs 93(65); knife to skin time 180mins(71) vs 170(82); or length of stay 72hours(36) vs 90(87) were not significantly different between PreICG and PostICG. Number of nodes sampled was statistically significantly different 3(2.5) vs 9(6)  $p=0.02$  (Mann-Whitney U) Fluorescent nodes were located in stations 4,5,7 for left, and 1,2,3,6,8 for right-sided tumours and in three patients contained disease. No non-fluorescent sampled node contained disease. Follow up is too short to assess whether there is a difference in rates of disease relapse.

**Conclusions:** In this small preliminary comparison, IP ICG results in a significantly higher number of lymph nodes sampled.

O061/#1241 | IPSO

IPSO: FREE PAPER SESSION 04 - RENAL, SARCOMA, GERM CELL TUMOURS AND FERTILITY

12-10-2023 13:30 - 15:30

THE NOVEL TEMPLATE OF LYMPH NODE SAMPLING IN WILMS TUMOR:REVIEWING ITS USE AS A CONSISTENT AND REPRODUCIBLE PURSUIT

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**Background and Aims:** Lymph Node(LN) sampling is a crucial and most frequently omitted step in surgery for Wilms tumor, leading to inaccurate staging and increased relapse rates. The main reason for this

was absence of a proper template for systematic sampling. To circumvent this, in 2020, we prospectively devised a method for LN sampling to encourage routine sampling. In this study, we retrospectively re-evaluated the usage of our template from the beginning of previous study until now, and identified whether any changes in outcomes occurred, in a larger cohort.

**Methods:** In our previous prospective study, we evaluated 113 patients from 2015-2019; with addition of 79 patients: we now retrospectively evaluated 192 patients, all operated at a single tertiary-care cancer centre from 2015-2023. All patients underwent a systematic 5-station nodal sampling, as described earlier. All follow-up records were completed by March, 2023.

**Results:** Similar to our previous study, median LN yield was 8. Lymph node positivity rate was also comparable at both time points: overall it changed from 13.2% to 14.6% (28/192), [p=0.839] and in interaortocaval nodes from 46.7% (n=7) to 41%(n= 11) [p=1]. Skip metastases in this region remained high and comparable, with 28.6% (n = 4) then and now 25% (n=7) of patients [p=0.70], which were more often seen with right-sided tumours. In both studies: Larger tumor size, high-risk pathology and presence of tumor thrombus were factors associated with LN metastasis [p=0.001, p < 0.001 and p=0.02 respectively].

**Conclusions:** The previously proposed method of systematic station-wise sampling provides a template to guide surgeons in performing LN harvesting, promoting routine nodal sampling for all Wilms tumors. Reproducible and consistent results are produced by following the template, as seen in updated data, in a larger cohort. Similar to our previous findings, interaortocaval nodes should be sampled routinely as the incidence of disease at this station is high.

O062/#1014 | IPSO

IPSO: FREE PAPER SESSION 04 - RENAL, SARCOMA, GERM CELL TUMOURS AND FERTILITY

12-10-2023 13:30 - 15:30

LONG-TERM OUTCOMES FOR BILATERAL FAVORABLE HISTOLOGY WILMS TUMOR, REPORT FROM COG STUDY AREN0534

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**Background and Aims:** The type and timing of events in Children with bilateral Wilms tumors (BWT) have not been well described. Small studies suggest a significant number of occur after 3 years. We report the long-term timing and patterns of relapse for children with BWT or unilateral WT with genetic predisposition to BWT enrolled on the AREN0534 prospective trial.

**Methods:** Smoothed hazard (risk) functions for event-free survival (EFS) were plotted for patients enrolled on AREN0534 with BWT or predisposed to BWT with a unilateral tumor, both overall and by patient and tumor characteristics so that timing of events by groups of interest could be visualized. Factors considered included unilateral vs bilateral disease, age at diagnosis, sex, histology, stage, post-chemotherapy risk classification, and lymph node status and margin status among patients with stage.

**Results:** 222 children (190 BWT and 32 unilateral WT with BWT predisposition) were followed for a median of 8.6 years. Fifty EFS events were reported of which 48 were relapse/progression, one was subsequent malignant neoplasm, and one was death. The highest hazard was from end of therapy to two years, when 68% of events occurred with 59% of these being recurrences in the kidney or tumor bed. A second risk peak was observed from approximately 5-8 years post-diagnosis, with 80% of these events involving the kidney or tumor bed. Risk of late events was higher for females and in children with negative margins or negative lymph nodes.

**Conclusions:** Although Most EFS events in children with BWT occur by two years, more than a quarter may occur later. These patterns suggests that late events may be second primary tumors rather than a recurrence of the primary tumor, although more investigation is required.

O063/#1025 | IP SO

## IPSO: FREE PAPER SESSION 04 - RENAL, SARCOMA, GERM CELL TUMOURS AND FERTILITY

12-10-2023 13:30 - 15:30

## CYTOREDUCTIVE SURGERY AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY IN PEDIATRIC ABDOMINAL RHABDOMYOSARCOMA. EXPERIENCE OF A REFERENCE PEDIATRIC ONCOSURGICAL CENTER

Cristian Urla<sup>1</sup>, Benedikt Wagner<sup>1</sup>, Gesche Jens<sup>2</sup>, Andreas Schmidt<sup>1</sup>, Felix Neunhoeffer<sup>3</sup>, Jürgen Schäfer<sup>4</sup>, Jörg Fuchs<sup>1</sup>

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**Background and Aims:** Advanced and relapsed intraabdominal rhabdomyosarcoma (RMS) in children represent an oncological challenge and options for local tumor control are limited. Cytoreductive surgery (CRS) combined with hyperthermic intraperitoneal chemotherapy (HIPEC) has been proven to be effective in adults with peritoneal carcinomatosis as well as in children/adolescents with desmoplastic small round cell tumors. Thereby we present the largest series on CRS and HIPEC in patients with abdominal RMS.

**Methods:** Between January 2013 and Mars 2023, 17 patients (9 female, 8 male) with abdominal RMS underwent CRS and HIPEC at our institution. All patients were treated according to the guidelines of the Society of Pediatric Hematology and Oncology (GPOH). The indication for surgery was established by a multidisciplinary tumor board. Surgery was performed by midline incision in all patients. HIPEC was performed using cisplatin (37.5-100mg/m<sup>2</sup>) and doxorubicin (15-30mg/m<sup>2</sup>) for 60 min. at 42°C. A retrospective review of patient's records was performed.

**Results:** The median age at operation was 6.3 years (1.3-20). A complete cytoreduction was achieved in all cases. Median length of hospital stay was 11 days (8-21). Median length of ICU stay was 2 days (2-4). No procedure-associated complications and no major short-/long-term toxicities were recorded. The median follow-up was 31 months (3-107). The 5-year overall (OS) and event-free survival (EFS) were 70% (58-82) and 50% (35-65), respectively. Patients >10 years and those with alveolar histology had the worst prognosis (OS 0%). Patients with relapse after HIPEC (6/17) had a significantly poorer prognosis compared with those without relapse [OS 33% (14-52) vs 100%, p=0.009]. IRS stage had no impact on survival (IRS III vs IRS IV, p=0.32).

**Conclusions:** CRS and HIPEC is effective in patients with abdominal RMS. Patients >10 years, those with alveolar RMS and those with relapse after HIPEC had the worst outcome.

O064/#964 | IP SO

## IPSO: FREE PAPER SESSION 04 - RENAL, SARCOMA, GERM CELL TUMOURS AND FERTILITY

12-10-2023 13:30 - 15:30

## PROGNOSTIC FACTORS IN HEAD AND NECK EWING SARCOMA: A RETROSPECTIVE ANALYSIS OF 85 PATIENTS

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**Background and Aims:** Head and neck (HN) Ewing sarcoma (ES) accounts for <10% of ES. It represents a challenging site in terms of achieving optimal local control while preserving functional outcomes. Due to rarity, prognostic factors and treatment outcomes are unknown.

**Methods:** This is a retrospective study including HN-ES patients registered at our centre between 2003-18. We extracted clinicodemographic details from the hospital database. Descriptive statistics were used for baseline characteristics. The baseline factors associated with event free (EFS) and overall survival (OS) were identified by stepwise univariable and multivariable Cox proportional hazards regression.

**Results:** Eight-five patients were included [58 males (68.24%); 27 females (31.76%)]. The primary tumour was extra-osseous in 35 patients (41.18%). The primary was in the maxilla in 21 patients (24.7%), mandible in 13(15.3%), orbit in 9(3%), sinonasal in 16(18.8%) and craniofacial bone/soft tissue in 21 (24.6%) patients. Baseline metastatic disease was seen in 9 patients (10.59%). Aside from 11 patients (34.4%) wherein upfront surgery was done, neoadjuvant chemotherapy was given to all. For local control, radiotherapy alone was used in 40 cases (48.82%), surgery plus radiotherapy in 13 (15.8%) and surgery alone in 7 (8.5%). The median EFS was 29.1 months (15.8-67.7) and OS was 37.4 months (25.8-98.7). On multivariable analysis, male gender (HR:0.50; p-value=0.049), osseous primary (HR:0.41; p-value=0.005) and TLC<10000/mm<sup>3</sup> (HR:0.34; p-value=0.002) were associated with better EFS. These three factors also predicted for better OS [male gender: HR 0.47; p-value=0.043, osseous primary: HR 0.42; p-value=0.011, TLC<10000: HR 0.32; p-value=0.002].

**Conclusions:** Our cohort is the largest HN-ES cohort described worldwide. The site has favourable disease biology with low

proportion of baseline metastatic disease. However, patients with elevated TLC, extra-osseous disease and/or female gender have poorer outcomes.

O065/#356 | IP SO

**IPSO: FREE PAPER SESSION 04 - RENAL, SARCOMA, GERM CELL TUMOURS AND FERTILITY**

12-10-2023 13:30 - 15:30

**DOES PULMONARY METASTASECTOMY IMPACT OUTCOMES FOR PATIENTS WITH RELAPSED EWING SARCOMA?**

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**Background and Aims:** Our objective was to describe the utilization of pulmonary metastasectomy for the 30-40% of patients with initially localized Ewing Sarcoma (EWS) who developed relapse isolated to the lungs.

**Methods:** This multi-center retrospective cohort study included patients <20 years with initially localized EWS treated from 2007-2020 at 19 institutions in the Pediatric Surgical Oncology Research Collaborative, who developed pulmonary relapse. Analyses included Chi-square or Wilcoxon rank-sum tests, and Kaplan-Meier curves for overall survival (OS).

**Results:** Forty-four patients were included with a median age of 17 years (interquartile range (IQR): 13-19.5). Most presented with tumors of the extremity (n=20, 45.5%), pelvis (n=10, 22.7%), or chest wall (n=6, 13.6%). Primary site local control was achieved with surgery in 17 (38.6%) patients, radiation in 17 (38.6%) patients, and both surgery and radiation in 10 (22.7%) patients. Pulmonary surgery included complete clearance in 15 patients, other diagnostic/therapeutic surgery in 8 patients, and unknown surgery in 2 patients, while 18 patients had no surgery. Patients with unilateral pulmonary metastases (80% vs. 42%, p=0.02) and fewer nodules (median 1, IQR: 1-2 vs. median 3.5, IQR: 2-6; p<0.01) were more likely to have complete clearance. Further pulmonary relapse occurred in 5 (29.2%) patients with complete clearance and 7 (38.5%) without complete clearance (p=0.52). Of patients with further relapse, 1 relapsed at the prior site, 7 at a new site, and 4 at both the prior and a new site. Three-year OS for patients with complete clearance was 57.4% compared to 23.1% with no or incomplete surgical clearance (p=0.046).

**Conclusions:** Complete surgical clearance of isolated pulmonary relapse in patients with initially localized EWS is associated with improved overall survival despite no documented reduction in rates of additional pulmonary relapse. Although this finding may reflect a selection bias, further research is needed to understand the optimal utilization of pulmonary surgery in relapsed EWS.

O066/#1434 | IP SO

**IPSO: FREE PAPER SESSION 04 - RENAL, SARCOMA, GERM CELL TUMOURS AND FERTILITY**

12-10-2023 13:30 - 15:30

**ENHANCING OUTCOMES WITH PULMONARY METASTASECTOMY FOR SOFT TISSUE SARCOMA: A CANCER CENTER EXPERIENCE IN ADOLESCENTES AND YOUNG ADULTS**

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**Background and Aims:** Soft tissue sarcomas (STS) account for less than 1% of adult cancers. However, about 15-20% occur in the AYA population. Incidence of pulmonary metastases in these patients can be as high as 80%. Pulmonary metastasectomy (PM) can be indicated for select patients. The purpose of this study was to evaluate the outcomes of this approach in a cancer center.

**Methods:** A retrospective, single-center observational cohort study of AYA patients with STS who underwent PM between March 2009 and December 2019. Primary endpoint was overall survival (OS) that was calculated from the date of PM to the date of death from disease or the last follow-up. Secondary endpoints included disease-free survival (DFS), as well as morbidity and mortality associated with PM.

**Results:** We included 49 patients. Most were male 59.2%. Mean age was 27.6 years (16-39). Synovial sarcoma was most common histology (59.2%), and most were in the lower limb (55.1%) Pulmonary metastases were metachronous (occurring after 6 months) in 51%, and bilateral in 59.25% of patients. Mean number of resected metastases was 6.5 (1-26) Most patients underwent wedge resections (77.6%), but 10.2% required a lobectomy and 4.1% a pneumonectomy for negative margins. A R0 resection was achieved in 73.5%. Mean follow-up was 53.0 months (35-70), 30 patients (61.2%) experienced a relapse, only 17 having isolated lung metastases and 14 underwent a re-do metastasectomy. Median OS was 53.0 and median DFS was 30.0 months. On univariate analysis, factors associated with improved OS were R0 resection (43.0 vs 11.0 months,  $p = 0.012$ ) and metachronous metastases (51.0 vs 20.0 months,  $p = 0.027$ ). The 90-day morbidity was 8.2% and there were no deaths.

**Conclusions:** These findings suggest that PM should be considered as part of the multimodal approach for these patients. Achieving R0 resec-

tion and having metachronous metastases were associated with an encouraging OS.

O067/#839 | IP SO

**IPSO: FREE PAPER SESSION 04 - RENAL, SARCOMA, GERM CELL TUMOURS AND FERTILITY**

12-10-2023 13:30 - 15:30

**FROZEN BONE-BIOLOGICAL RECONSTRUCTION IN PAEDIATRIC BONE SARCOMAS USING LIQUID NITROGEN. A REVIEW OF EARLY OUTCOMES IN LOW-MIDDLE INCOME COUNTRY**

Syed Ali Anwar Jillani<sup>1</sup>, Salman Javed<sup>1</sup>, Nida Zia<sup>2</sup>  
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**Background and Aims:** Autologus reimplantation of disease treated bone is the mainstay of limb salvage for bone sarcomas in LMIC. Autoclaving, Pasteurization and extracorporeal irradiation have been tried for reconstruction with mixed results. These methods however, decrease the structural quality of native bone prompting reconstructed limb to fail, due to multiple fragility fractures, implant failure and often non-union. We have tried a novel technique in our region, using liquid nitrogen dip, to rid native tumor bone of all living neoplastic cells, yet preserving strength of bone for good fixation and also bone morphogenetic protien that helps in timely bone healing preventing non union.

**Methods:** A retrospective review between january 2018 and December 2020. data retrieved from indus hospital HMIS records inclusion criterion: 1) age < 16 years 2) malignant bone tumors surgically treated with Liquid Nitrogen. 3) atleast 2 years followup all patients were called in out patient and assessed at latest followup.

**Results:** Total 28 patients , 18 males, 10 females mean age 14.5 18 femure,4 humerus,4 tibia, 3 pelvis 12 osteosarcoma,15 Ewing's and 1 condrosarcoma. 4 patients left treatment after surgery, 2 expired due to chemotherapy toxicity, 4 patients relapsed with chest metastasis. 18 patients were assessed off treatment and complete > 2 year follow-up 1 had local recurrence 5% 4 underwent amputation due to persistent resistant infection. 22% 13 patients off treated patients are full weight bearing mobilized. 72% 8 having good functional class and 4 having fair function. approx bone union time 4-5 months, where assessed.

**Conclusions:** Frozen bone reimplantation is a reliable technique in comparison to other recycling methods, for reconstruction of surgically created bone defects in bone sarcomas. Owing mainly to its anatomical fit, cost effectiveness, simple technique and mechanical strength, frozen bones despite having some problem with

infections, has a promising potentials in the future of pediatric orthopedic oncology.

O068/#1425 | IPSO

IPSO: FREE PAPER SESSION 04 - RENAL, SARCOMA, GERM CELL TUMOURS AND FERTILITY

12-10-2023 13:30 - 15:30

### PARTIAL VAGINECTOMY GUIDED BY FINE CHOLEDOCHOSCOPY: A NEW SURGICAL MANAGEMENT OF PRIMARY VAGINAL YOLK SAC TUMOR IN CHILDREN?

Jiangbin Liu

Shanghai Children's Hospital, school of medicine, Shanghai Jiao Tong University, Department Of General Surgery, shanghai, China

**Background and Aims:** Primary vaginal yolk sac tumor (YST) are extremely rare in the pediatric population, because of their low incidence, there is no consensus regarding the appropriate methods of therapy in spite of nonsurgical treatment with PEB chemotherapy was reported in most literature. Here, we review our experience on partial vaginectomy guided by fine choledochoscopy for the treatment of YST in children.

**Methods:** Medical records from 31 patients with YST were identified in our hospital from 2013 to 2022. 7 girls with YST who only received systemic chemotherapy(4-8 cycles) in their local hospitals and then admitted in my hospital for recurrence of tumor. The others are admitted in our hospital without any therapy. The median age of patients was 2.2years (range, 0.4–5.8 y). Bleeding or blood-tinged discharge was the most common clinical presentation (100%) followed by a protruding vaginal mass (40%) and abdominal mass (20%).Serum alpha-fetoprotein (AFP) was markedly elevated in all patients. All the patients received choledochoscopic examination and tumor biopsy before therapy.

**Results:** The tumor in vagina were identified without uterus involvement by choledochoscopy. Histology was found as YST and patients received cisplatin-based chemotherapy. After 3.5 cycles (range, 2-6) of preoperative chemotherapy, four patients underwent trans-vaginal vaginectomy and the others received trans-abdominal vaginectomy guided by fine choledochoscopy, there is no radical surgery such as hysterectomy or anterior pelvic radiotherapy were performed. No surgical complications included recto-vaginal fistula, vesico-vaginal fistula and urinary injury were found. 29/31 (93.5%) patients remain disease-free with a median follow-up of 5.5 years (range, 1.2-9.5y). Only 2 cases developed local recurrence after 13 and 5 months after initial surgery respectively, and they are cured by redo trans-abdominal vaginectomy with chemotherapy.

**Conclusions:** Partial vaginectomy guided by fine choledochoscopy is an effective and available method on vaginal YST in children, which has

an important role on organ preservation and reduce the recurrence rate.

O069/#422 | IPSO

IPSO: FREE PAPER SESSION 04 - RENAL, SARCOMA, GERM CELL TUMOURS AND FERTILITY

12-10-2023 13:30 - 15:30

### GROWING TERATOMA SYNDROME IN CHILDREN AND ADOLESCENTS: PREVALENCE AND SURGICAL OUTCOME

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**Background and Aims:** Patients affected by metastatic germ cell tumors may occasionally experience enlargement of metastatic lesions with concurrent normalization of tumor markers after chemotherapy. This phenomenon is described as Growing Teratoma Syndrome (GTS). The aim of the present study is to assess the prevalence of GTS in the pediatric population and their implications in terms of surgical outcome.

**Methods:** The clinical notes of patients diagnosed with stage III and IV malignant germ cell tumors from January 2010 until December 2020 were retrospectively reviewed. Patients with residual disease after chemotherapy were studied; the occurrence of GTS, treatment strategies, survival and disease remission were analyzed.

**Results:** Thirty-three patients were diagnosed with stage III (16 patients) and IV (17 patients) malignant germ cell tumors. Eleven patients (34%) had radiologic evidence of enlargement of metastases after chemotherapy; two of them (6%) also had persistently elevated serum markers and eventually died of progressive malignancy. The remaining nine patients (28%) had normal markers after chemotherapy and were classified as GTS patients. All nine patients underwent resection of metastatic lymph nodes and six had surgery on visceral metastases. Six patients had mature teratoma only in the pathology specimen; three patients also had foci of viable malignant tumor in the excised lesions. Six patients had radical surgery on all metastatic sites; five patients are alive and in complete remission while one died

for peri-operative complications. Of the three patients who could not achieve radical excision of the metastases, two died for progressive disease and one is alive with stable disease.

**Conclusions:** Patients affected by GTS have a risk of progression of disease, which is resistant to chemotherapy, and death. Radical surgical excision is essential to achieve disease control and long-term survival; in this setting, even mutilating surgery should be considered.

O070/#144 | IPISO

**IPISO: FREE PAPER SESSION 04 - RENAL, SARCOMA, GERM CELL TUMOURS AND FERTILITY**

12-10-2023 13:30 - 15:30

**IMPACT OF SURGICAL TIMING (UPFRONT, DELAYED, OR SECOND LOOK) IN MALIGNANT GERM CELL TUMOR OF THE OVARY IN CHILDREN**

Sajid Qureshi<sup>1</sup>, Maya Prasad<sup>2</sup>, Badira Parambil<sup>2</sup>, Ram Mohan<sup>2</sup>, Girish Chinnaswamy<sup>3</sup>, Mukta Ramadwar<sup>4</sup>, Poonam Panjwani<sup>5</sup>, Vasundhara Smriti<sup>6</sup>, Akshay Baheti<sup>6</sup>

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**Background and Aims:** Aim: This study aimed to analyze the impact of primary and delayed surgery after chemotherapy on the outcomes of malignant ovarian germ cell tumors in children and to evaluate second-look surgery after inadequate surgical staging. Lastly, the different components of surgical staging were analyzed.

**Methods:** All children below 15 years of age with malignant germ cell tumors of the ovary treated between February 2006 and August 2022 were analyzed. The demographic, clinical, radiological, surgical, and pathological characteristics, treatment details, and outcomes were collected from a prospectively maintained institutional database. Comparison of patients undergoing upfront delayed and second-look surgery after incomplete surgical staging was performed.

**Results:** A total of 110 patients with a median age of 12 years (0.11-15 years) were eligible. Thirty-eight patients underwent upfront surgery, 47 delayed surgery and 24 had second-look surgery. There were 12 patients with stage IV disease and 77% were intermediate-risk. Tumour rupture, blood loss and overall complications were significantly higher in the upfront than the delayed surgery group. Similarly, the second-look surgery conceded more blood loss, longer duration of surgery and complications compared to the delayed surgery. At a median follow-up of 67 months the 5 year event free survival (EFS) and overall (OS) for the entire cohort is 86% and 89% respectively. There was no difference

in the OS and EFS of patients in the upfront, delayed or second look surgery, although the latter had relatively inferior outcomes ( $p=0.11$  and  $0.12$ ). The EFS was significantly low for choriocarcinoma (21%) as compared to other malignant germ cell tumors ( $p=0.0001$ ).

**Conclusions:** Ovarian germ cell tumors have favourable outcomes. Although the outcomes are similar with upfront and delayed surgery, the latter minimize the surgical morbidity associated with resection of large tumours. Optimal surgical staging is essential since second look surgery is associated with significant morbidity.

O071/#555 | IPISO

**IPISO: FREE PAPER SESSION 04 - RENAL, SARCOMA, GERM CELL TUMOURS AND FERTILITY**

12-10-2023 13:30 - 15:30

**OVARIAN TISSUE STORAGE FOR FERTILITY PRESERVATION IN PAEDIATRIC PATIENTS - THE NEED FOR STANDARDISED PRACTICE GUIDANCE**

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**Background and Aims:** Chemo- and/or pelvic radiotherapy in children and young adults treated for cancer can lead to impaired fertility. For prepubertal female patients at high risk of treatment-related infertility, storage of ovarian tissue is recommended by the UK CCLG Fertility Group. No surgical guidelines exist to ensure best practice technique. Thermal damage from surgery close to the dissection margin can affect the quality of ovarian tissue. With the aim to address this problem, we reviewed current UK practice to assess surgical management.

**Methods:** A ten-item, anonymous multiple choice survey was distributed to the lead surgeons in all paediatric centres in England/Wales undertaking ovarian tissue collection surgery for fertility preservation.

**Results:** Responses were received from 94% of invited paediatric surgical oncology centres in England and Wales. 33% of responding centres perform >20 ovarian harvests/year; 42% undertake <10 cases/year. In 57% surgery is performed by a paediatric surgeon with interest in oncology or fertility preservation. Operating surgeon was consultant or senior specialty registrar with consultant supervision in 96%. 70% of respondents stated they gain access to the abdominal cavity using 3-port laparoscopy, 8% with single-port laparoscopy. Most frequently used energy devices for resection were Ligasure™ (42%) and Harmonic Scalpel™ (27%). 96% of respondents perform a total oophorectomy, 1 respondent stated they perform a hemi-oophorectomy. 53% stated



they place the ovary into a retrieval bag only if the ovary was too big for easy removal via the camera port, 27% always place it in a retrieval bag. Most surgeons use the umbilical port site for retrieval (73%). 58% of surgeons place the ovary into the specimen container themselves, 30% hand it to the scrub nurse for further handling.

**Conclusions:** This national survey shows significant heterogeneity in the surgical management of ovarian tissue collection for cryopreservation. To ensure best outcomes a standardised best practice approach should be agreed upon.

O072/#1188 | IPSO

#### IPSO: FREE PAPER SESSION 04 - RENAL, SARCOMA, GERM CELL TUMOURS AND FERTILITY

12-10-2023 13:30 - 15:30

#### SYSTEMATIC REVIEW OF FEMALE FERTILITY CRYOPRESERVATION IN CHILDHOOD CANCER

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**Background and Aims:** As childhood cancer treatment evolves, survival rates have improved drastically. However, patients undergoing chemotherapy and radiation for childhood cancer can experience adverse effects such as gonadotoxicity-related ovarian insufficiency. Ovarian tissue cryopreservation (OTC) is well studied in adults, but has only recently started to be explored as an option to preserve fertility in patients with childhood cancer. This systematic review aims to describe outcomes of cryopreservation in pediatric cancer patients.

**Methods:** A systematic search was conducted in PubMed, Embase, and Web of Science databases to identify English-language full text articles and abstracts published between 2004-2022 describing cryopreservation among female children (0-21 years old) with cancer. Abstracts and full-text articles were screened for inclusion. Subsequently, data from eligible studies was extracted and analyzed. Descriptive statistics were utilized to estimate overall outcomes of cryopreservation.

**Results:** Of the 104 abstracts and 34 full-text articles, 9 studies were included. Data was collected from 7 countries and included 659 patients. Most common cancers included hematologic malignant disease (81%), neurological malignant tumors (56%), and sarcomas (39%). OTC was done in 588 patients, and 1.2% (7/588) of these patients underwent ovarian tissue transplantation (OTT); all 7 had restored menstrual function. After OTT, 6 patients desired pregnancy and 33% (2/6) became pregnant. Both of these patients had live births.

**Conclusions:** Preliminary analysis showed that OTC has been successfully performed but not yet studied thoroughly in pediatric cancer patients in a longitudinal manner. This systematic review revealed that

cryopreservation is largely studied in adult patients in high income countries, demonstrating a need for long-term studies focused on pediatric and premenopausal OTC, subsequent OTT, and potential pregnancy. This work is critical to standardize the recommendation of fertility preservation in childhood cancer patients and inform the use of this procedure to benefit patients in countries of all income levels.

O073/#672 | CCI

#### CCI: SESSION - SURVIVORS - PROJECTS AND TESTIMONIES

12-10-2023 13:30 - 15:30

#### CREATE A SYSTEM TO ENCOURAGE SURVIVORS TO MANAGE THEIR OWN HEALTH AIMING AT REDUCING THE NUMBER OF THOSE WHO END UP BEING "FOLLOW-UP LOSS"

Kohsuke Yamashita

Children's Cancer Association of Japan, Chairman, Tokyo, Japan

**Background and Aims:** Over 2,000 Japanese children are diagnosed with childhood cancer annually and among them nearly 80% are cured resulting rapid increase of childhood cancer survivors. Increased survivors bring the issues of late effects which negatively affect QOL of survivors even more critical. While long-term follow-ups (LTFU) is strongly recommended, unignorable number of survivors do not attend to LTFU on various reasons. (follow-up loss) CCAJ launch a project to encourage survivors to heed their own health management so as to reduce the number of follow-up loss thus better long-term QOL of survivors.

**Methods:** Organize a project team and advisory board comprising doctors, survivors and parents. a. Open a web-site which includes; information about LTFU, health management flowchart and health-check items for survivors, narratives of fellow survivors' experiences and up to date notice/announcement for survivors. b. Deploy PR activities e.g., distributing hand-out, web advertising and awareness-raising activities to attract survivors' attention to the web-site. c. Publish a booklet titled "A Guideline -Promoting Health Management of survivors" which includes a list of hospitals and clinics providing LTFU services.

**Results:** a. Over 80,000 pax visited the web-site and the page containing recommended health-check items were most popular among others. b. Over 5,000 copies of the booklet/guideline were distributed. c. 93,000,000 viewers are counted on web-advertising on a major portal-site. d. Inquiries to CCAJ saying that the web-site and hand-out as a trigger are increasing.

**Conclusions:** The project was commenced without expectation of short-term results. Now that the web-site and other means as effective infrastructures to attract survivors' attention to their own health and necessity of LTFU has been established, the aim of realizing

improvement of QOL of survivors in Japan will surely be achieved by continue the project on a long-term basis.

O074/#28 | CCI

CCI: SESSION - SURVIVORS - PROJECTS AND TESTIMONIES

12-10-2023 13:30 - 15:30

#### IMPLEMENTATION OF COMPREHENSIVE HEALTH CONSULTATION (CHC) FOR CHILDHOOD CANCER PATIENTS AND SURVIVORS BY KOREAN ASSOCIATION FOR CHILDREN WITH LEUKEMIA & CANCER (KACLC)

Jong Jin Seo, Hyun Jung Kim, Jung Eun Seo, In Young Her, Jong Myung Lee

Korean Association for Children with Leukemia & Cancer, Integrated Support Center For Children With Cancer, Seoul, Korea, Republic of

**Background and Aims:** Health literacy of childhood cancer survivors (CCS) is important for successful reintegration of CCS. Although survival rate of childhood cancer patients in Korea is excellent, provision of optimal information on survivorship is not satisfactory. KACLC started CHC service as one of its survivorship advocacy activities 3 years ago to improve health literacy of childhood cancer patients and CCS, and thereby to help their successful reintegration. This study is to review the 3 years' experience of CHC implemented through KACLC.

**Methods:** Individualized comprehensive information on long-term health care of CCS was provided by a dedicated pediatric hematologist. Off-line or on-line consultation was carried out according to request of participants. Feedback survey regarding changes in health literacy of participants was assessed shortly after each CHC. Cumulative data of CHC and feedback survey collected from September 2019 to August 2022 was analyzed retrospectively.

**Results:** 170 cases of CHC were carried out during study period. 54% of the cases was through on-line, and 46% off-line. 62% was from Seoul or vicinity, and the rest from other region. 85% was for survivors, and 15% for patients on-therapy. There were 3 types of participants, parent only (46%), CCS only (44%), and parent together with CCS (10%). The most frequently asked questions were about health care after off-therapy, disease relapse, heritability of suffered malignancy, and post-treatment complications including infertility. Feedback survey revealed improved health literacy in most of the participants leading them to avoid hazardous lifestyle and to adopt advantageous health management such as healthy dietary habits and regular exercise.

**Conclusions:** CHC service of KACLC was able to improve health literacy in most of the participants, and thereby it is expected to help successful reintegration of CCS. Active contribution of major

hospitals treating childhood cancer and health insurance coverage for survivorship care are needed for optimal survivorship care in Korea.

O075/#530 | CCI

CCI: SESSION - SURVIVORS - PROJECTS AND TESTIMONIES

12-10-2023 13:30 - 15:30

#### LUZ DE ESPERANZA: THE IMPORTANCE AND IMPACT OF A CHILDHOOD CANCER SURVIVORS NETWORK IN CHILE

Pablo Allard<sup>1</sup>, Daniela Carvajal<sup>2</sup>, Camila Figueroa<sup>2</sup>, Carla Soto<sup>3</sup>, Valeska Gonzalez<sup>1</sup>, Juan Sepulveda<sup>1</sup>, Scarlett Ponce<sup>2</sup>, Constanza Martinez<sup>2</sup>, Miguel Novoa<sup>2</sup>

<sup>1</sup>Luz De Esperanza, Board And Founder, Santiago, Chile, <sup>2</sup>Luz De Esperanza, Board, Santiago, Chile, <sup>3</sup>Luz de Esperanza, Board, Santiago, Chile

**Background and Aims:** The number of childhood cancer survivors in Chile is increasing, reaching 79%. Despite these figures, survivors still face lack of information, discrimination, stigma, among other difficulties. In 2022, authorities of the National Pediatric Cancer Program together with a group of survivors created a support network to educate, connect, and learn about the needs of this population. **Aims:** - Guarantee healthcare coverage for survivors and their families. - Generate a concrete change at a social and public policy level - Provide socio-emotional support to survivors and families by delivering testimonies of hope - Create awareness and educate about the challenges of survivors - Learn about issues faced by survivors - Creation of networks between local and global organizations.

**Methods:** - Creation of social media to summon and connect survivors from different regions and create awareness in general audience. - Participation as speakers in diverse conferences and congresses about survivorship. - Collaborative work with different cancer stakeholders (ministry, NGOs, hospitals) - Our members have published letters and articles in the most influential newspapers and given radio interviews, creating awareness and recognition of our cause. - Implemented survey to learn about survivors' main challenges.

**Results:** Survivors were invited to participate in the Ministry of Health Committee of Childhood Cancer, to collaborate in the creation and implementation of the *Chilean National Cancer Law*. A representative of Luz de Esperanza is today an active member in this committee. Identified survivor's needs not considered in the current public policies. Active community of over 60 survivors who have implemented activities to support patients and their families in different settings.

**Conclusions:** Survivors face issues that need to be acknowledged by the society: accessibility and quality of follow-up treatments, poor public policies and discrimination and lack of hope. The creation of

survivors networks can make them visible, can unite and help survivors and become a light of hope for those facing cancer.

O076/#918 | CCI

CCI: SESSION - SURVIVORS - PROJECTS AND TESTIMONIES

12-10-2023 13:30 - 15:30

### CASE STUDY ANALYSIS OF YOUNG CANCER SURVIVORS ACHIEVEMENTS AND MILESTONES FROM A SUPPORT GROUP IN LMIC

Preeti Phad<sup>1</sup>, Vandana Dhamankar<sup>1</sup>, Savita Goswami<sup>1</sup>, Maya Prasad<sup>2</sup>, Purna Kurkure<sup>1</sup>

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**Background and Aims:** Childhood Cancer Survivors (CCS) can experience late-effects. They miss school, may develop learning, physical deficits. These affect aspirations, dreams, milestones desired in developmental stages. UGAM, CCS Support Group of Indian Cancer Society (ICS) plays a significant role in helping CCS deal with social stigma, discrimination, creating awareness about curability of childhood cancers. In this context, case study analysis was performed to understand adversities, achievements of CCS.

**Methods:** UGAM members meet once monthly to share their stories of hope & concerns. Struggles and achievements of two survivors have been documented.

**Results: Case-Study 1:** Ms. A, single parent child, diagnosed with Retinoblastoma at 8 years. Due to late diagnosis she had to undergo removal of left eye, received chemotherapy & radiation. After 12th standard she had planned to pursue Hotel Management but couldn't do so due to financial crisis. She had to take a drop of one year due to body image issues. She was introduced to UGAM during Follow up at tertiary cancer centre (Tata Memorial Hospital). UGAM motivated her to complete Graduation and Masters in Social work. She is now employed as a social worker for cancer patients and survivors. Team led by her has replicated the UGAM model in another city in India. **Case-Study 2:** Mr. B, diagnosed with Osteosarcoma left leg below the knee, when he was in 4th standard. He underwent surgery, chemotherapy, & radiation. He Re-joined school after 1.5 years however was experiencing difficulty walking, playing, coping with peers & lack of self confidence. Post his graduation, he was introduced to Ugam where he regained the confidence & started performing in Ugam awareness activities. Now he is a professional artist performing at theatre, TV serials, web-series.

**Conclusions:** Ugam empowered CCS to transform their careers where adversities were turned into opportunities. There are many inspiring stories & these are role models for children undergoing treatment. Support groups are essential component of survivorship care and

should be encouraged to spread the message that Childhood cancer is curable.

O077/#597 | Award Session

HANS-PETER WAGNER PRIZE SESSION

12-10-2023 15:10 - 15:40

### REDUCING CHEMOTHERAPY DOSE INTENSITY BY 25% AND ADDING RITUXIMAB IMPROVES SURVIVAL IN PEDIATRIC MATURE B-CELL NON-HODGKIN'S LYMPHOMA IN LMIC SETTING

Venkatraman Radhakrishnan, Kritthivasan Venkatakrishnan, Tk Balaji, Prasanth Srinivasan, Gargi Das

Cancer Institute (WIA), Medical Oncology And Pediatric Oncology, CHENNAI, India

**Background and Aims:** Pediatric B-cell Non-Hodgkin Lymphomas (NHL) in low and middle-income countries (LMICs) has historically had inferior outcomes compared to high-income countries due to higher treatment-related mortality (TRM). A recent multi-center retrospective study in India reported a 2-year event-free survival (EFS) of 60% and TRM of 15% in B-NHL. To address this issue, we evaluated the impact of reducing chemotherapy dose intensity by 25% and adding rituximab on outcomes in pediatric B-NHL.

**Methods:** Patients, less than 18 years of age with group B and C disease as per the LMB risk stratification were enrolled between Sep 2017-Oct 2022. The LMB-89 protocol with a reduction of all chemotherapy doses by 25% was administered. Rituximab at 375 mg/m<sup>2</sup> was administered on day 1 of the first five cycles of the protocol. The response was assessed using PET/CT after 4 cycles of chemotherapy (interim) and at end of treatment. EFS and overall survival (OS) were calculated using the Kaplan-Meier method.

**Results:** The study included 25 patients with a median age of 6.9 years (2.9-17.9 years), among whom 20 (80%) were males. Twenty patients had group B (stage I: n=1, stage II: n=4, stage III: n=15) and 5 had group C disease (stage IV). Complete metabolic response (CMR) was achieved by 22/25 (88%) patients and 3 (12%) achieved partial metabolic response (PMR) in the interim PET/CT. At the end of treatment, 22/24 (92%) patients achieved CMR, one had PMR, and one had progressive disease. The median follow-up was 32 months (3-66 months). The 3-year EFS and OS were 87.8% and 91.8% respectively. There were 2 deaths, one due to disease progression, and the other due to sepsis.

**Conclusions:** Our study demonstrates a significant improvement in outcomes in pediatric B-NHL compared to previous reports from LMICs, achieved through a 25% reduction in chemotherapy dose intensity and the addition of rituximab.

O078/#1138 | Nursing

**NURSING: QUALITY IMPROVEMENT NURSING ABSTRACT PRESENTATIONS 01**

12-10-2023 16:00 - 16:30

**IMPLEMENTATION OF A NURSE-INITIATED ANTIBIOTIC TIME-OUT (NATO) IN CHILDHOOD CANCER PATIENTS IN CENTRAL AMERICA**

Sergio Licona<sup>1</sup>, Karla Aguilar<sup>2</sup>, Deiby Argüello<sup>3</sup>, Kattia Camacho<sup>3</sup>, Gloria Ceballo-Batista<sup>4</sup>, Alicia Chang<sup>2</sup>, Johanny Contreras<sup>5</sup>, David Duran<sup>6</sup>, Dora Estripeaut<sup>4</sup>, Mario Gamero<sup>6</sup>, Angelica Hernandez<sup>6</sup>, Jacqueline Levy<sup>4</sup>, Marco Luque<sup>7</sup>, Blanca Maradiaga<sup>7</sup>, Mario Melgar<sup>2</sup>, Fernanda Revolorio<sup>2</sup>, Karina Rivera<sup>5</sup>, Yichen Chen<sup>1</sup>, Meenakshi Devidas<sup>1</sup>, Lane Faughnan<sup>1</sup>, Hilmarie Muniz-Talavera<sup>1</sup>, Shane Cross<sup>8</sup>, Ted Morton<sup>9</sup>, Jennifer Pauley<sup>1</sup>, Joshua Wolf<sup>9</sup>, Lorena Segovia-Weber<sup>1</sup>, Monnie Abraham<sup>1</sup>, Sheena Mukkada<sup>1</sup>

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**Background and Aims:** Although essential to care, antibiotic use in children with cancer is associated with significant harms, including toxicity, antimicrobial resistance, and *Clostridioides difficile* infection. Optimizing use of antimicrobials through antimicrobial stewardship (AMS) interventions is key to minimizing adverse effects. A lack of pharmacy and infectious diseases specialists in global settings may impede AMS intervention for this population, but nursing staff are ubiquitous and essential. We report our experience testing a novel intervention, the NATO, in six pediatric oncology units in Central America.

**Methods:** NATO is a scripted conversation between nurses and physicians to reevaluate antibiotic appropriateness after 48 to 72 hours of empiric use for febrile neutropenia. First, we performed a baseline assessment of AMS capacity using the WHO Practical Toolkit for AMS Programmes checklist. Based on these results, a multi-disciplinary team adapted NATO to site. The sites tailored a generic implementation plan emphasizing educational and documentation tools and iterative PDSA (Plan-Do, Study-Act) cycles to improve implementation and effectiveness outcomes.

**Results:** Sites had different baseline AMS capacities but 100% lacked financial support for a facility AMS action plan. Five sites (83%) reported no regular audit and review of prescribing practices and no standard reporting of AMS activities and outcomes to health-care providers. All sites collected antimicrobial use data for patients with febrile neutropenia for a minimum of two months. Three sites then piloted NATO, producing change ideas, including changes to documentation tools, antimicrobial decision categories, communication processes, and times. We produced an electronic tool to graph primary and secondary outcomes. Two sites advanced to implementation maintenance; an additional site has scaled NATO to other hospital units.

**Conclusions:** The change ideas developed by each site differed, however, core resources requirements emerged, which will support AMS in other global settings. Next steps include comparing antimicrobial use pre- and post-intervention and determining a sustainability and scalability plan.

O079/#1799 | Nursing

**NURSING: QUALITY IMPROVEMENT NURSING ABSTRACT PRESENTATIONS 01**

12-10-2023 16:00 - 16:30

**ADAPTATION OF NURSING ACTIVITIES TO IMPLEMENT A NURSE-INITIATED ANTIMICROBIAL TIME-OUT (NATO) IN CENTRAL AMERICA: A QUALITY IMPROVEMENT APPROACH**

Lorena Segovia-Weber<sup>1</sup>, Angelica Hernandez<sup>2</sup>, Karla Aguilar<sup>3</sup>, Blanca Maradiaga<sup>4</sup>, Gloria Ceballo<sup>5</sup>, Evelyn Ramos<sup>6</sup>, Deiby Argüello<sup>7</sup>, Sergio Licona<sup>8</sup>, Sheena Mukkada<sup>8</sup>, Monnie Abraham<sup>9</sup>

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**Background and Aims:** Antimicrobial therapy is common in childhood cancers due to concomitant comorbidities and chemotherapy use. Antimicrobial stewardship is an evidence-based approach to control resistance and minimize toxicity and cost; however, interventions

traditionally rely on pharmacists and infectious diseases professionals, rarely available in many sites globally. The American Nurses Association and pediatric literature highlight the importance of nursing involvement in optimizing antimicrobial use. However, evidence from pediatric oncology settings is lacking. This multidisciplinary collaborative project aims to adapt nursing activities to implement a NATO in pediatric oncology limited-resource settings.

**Methods:** We utilized the improvement model and PDSA cycles to test and improve nursing implementation through a collaborative global nursing approach. We collected baseline data from 6 sites in Central America to understand the essential nursing activities for NATO implementation. An adaptable flowchart was designed to identify when and how the NATO could be performed. Each institution adapted the project and created an implementation plan. Through monthly collaborative meetings, the sites discussed the implementation progress and adjusted as needed.

**Results:** At baseline, three sites had holistic nursing care model and three used functional nursing, and all sites reported availability of more healthcare professionals during morning shifts. In 3 sites, nurses had access to microbiology laboratory results. The NATO flowchart included five steps: triggers for NATO alert at 72 hours, alert initiation, nursing assessment of patient status and documentation, nurses' communication, and physician's response and documentation. Each site adapted nursing activities to implement the flowchart and 1 site shifted to holistic nursing care model. Currently, four sites are implementing NATO and two opted out, citing increased workload and nursing shortage.

**Conclusions:** Implementing the NATO initiative in resource-limited countries is a unique and innovative experience in pediatric oncology. This project showcased antimicrobial use optimization through effective adaptation of nursing interventions despite the resource constraints.

O080/#1467 | CCI

CCI: ADVOCACY MODEL

12-10-2023 16:00 - 16:30

### CHILDHOOD CANCER ADVOCACY HYBRID CUBE

Hedley Lewis

CHOC CHILDHOOD CANCER FOUNDATI, Executive Management, Johannesburg, South Africa

**Background and Aims:** Advocacy used to be two dimensional. The innovative method to be successful in advocating for children with cancer should be the "Childhood Cancer Hybrid Cube"

**Methods:** A cube has equal and balanced sides or planes similarly the approach to advocacy in childhood cancer needs to follow a cube-like approach to be successful. One side of the cube equates to the formal

channel of lobbying policy makers and influencers to prioritise childhood cancer and to continue disseminating information empowering the population with knowledge about the complex challenges faced by and the patients and their families, for example the Siluan Early Warning Signs of childhood cancer. On the opposing side of the cube there is the informal channel which involves onboarding and utilising those passionate about the cause including the medical fraternity, survivors, families, caregivers, civil society. The next two sides of the cube involve digital advocacy and subliminal advocacy. Digital advocacy involves using the right terminology on the correct platforms ensuring the highest level of user engagement which extends into actionable advances for these children and their families. Subliminal advocacy involves enticing people to become lobbyists through connecting to their emotions via sensory stimuli. Often subliminal advocacy is the catalyst in smaller communities to drive the digital advocacy for cancer patients further.

**Results:** The success of the "Childhood Cancer Hybrid Cube" model involves lobbying alongside emotional campaigning which needs to be intertwined with clear messaging. This messaging needs to constantly target various stakeholders using multiple technology tools or media coupled with embedded subliminal messages. Collectively the power of cubed approach will change the mindsets of communities in line with the Cure4All Framework of connecting partners.

**Conclusions:** The only effective solution to advocate for Childhood Cancer is to employ a strategic, hybrid model that addresses the constantly evolving landscape of Childhood Cancer.

O081/#591 | Award Session

SIOP AWARD SESSION

12-10-2023 16:40 - 18:10

### THE EFFECT OF IMMUNOGLOBULIN PROPHYLAXIS ON INFECTIOUS MORBIDITY IN PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA: RESULTS OF A RANDOMIZED CONTROLLED TRIAL

Kirsten Thus<sup>1</sup>, Hester De Groot-Kruseman<sup>1</sup>, Pauline Winkler-Seinstra<sup>1</sup>, Heidi Segers<sup>2</sup>, Marta Fiocco<sup>3</sup>, Cornelis Van Tilburg<sup>4</sup>, Rob Pieters<sup>5</sup>, Marc Bierings<sup>1</sup>

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**Background and Aims:** To investigate whether intravenous immunoglobulin (IVIG) prophylaxis in pediatric patients with acute lymphoblastic leukemia (ALL) prevents admissions for fever.

**Methods:** This randomized controlled trial was a subtrial of the national Dutch multicenter ALL study (ALL-11). Patients aged 1-19 years with medium risk (MR) ALL were randomized into either IVIG prophylaxis (0.7 g/kg IVIG three-weekly) or control group (standard of care). The primary endpoint was number of admissions for fever. Secondary endpoints were antibiotic treatments, adaptation of chemotherapy, ICU admissions, relapse, disease-free survival (DFS), overall survival (OS). To account for possible correlations between episodes within the same patient, generalized estimating equation models were fitted for admissions for fever, therapeutic antibiotics, chemotherapy adaptations and ICU admissions, including age in the models.

**Results:** Between October 2012 until March 2019, 165 patients were enrolled; 82 (50%) patients were randomly assigned to IVIG prophylaxis and 83 (50%) to the control arm. In the IVIG prophylaxis group there were 198 admissions for fever versus 265 in the control group ( $p=0.055$ ). During maintenance treatment of ALL, IVIG prophylaxis was associated with significantly less admissions for fever ( $N=99$  versus 163, for IVIG prophylaxis versus control group,  $p=0.005$ ). IVIG prophylaxis was associated with a significant reduction in admissions for fever with negative blood cultures compared to the control group ( $N=108$  versus 198,  $p=0.009$ ), especially during maintenance treatment ( $N=52$  versus 124,  $p=0.014$ ), and a significant decrease of chemotherapy adaptations ( $N=119$  versus 181,  $p=0.024$ ), especially during maintenance treatment as well ( $N=72$  versus 132,  $p=0.004$ ). There was no significant impact on relapse, DFS or OS.

**Conclusions:** In pediatric patients with MR ALL, IVIG prophylaxis is associated with significantly less admissions for fever during maintenance treatment, resulting in a decreased number of chemotherapy adaptations and antibiotic treatments. Future studies should aim at identifying a subgroup of patients that benefit most from IVIG prophylaxis.

O082/#154 | Award Session

#### SIOP AWARD SESSION

12-10-2023 16:40 - 18:10

#### A COMPARISON OF NEUROCOGNITIVE OUTCOMES AFTER RADIATION THERAPY IN PEDIATRIC EPENDYMOMA WITH OR WITHOUT MAINTENANCE CHEMOTHERAPY: FINDINGS FROM CHILDREN'S ONCOLOGY GROUP CLINICAL TRIAL ACNS0831

Alicia Kunin-Batson<sup>1</sup>, Shelly Lensing<sup>2</sup>, Amy Smith<sup>3</sup>, Arzu Onar-Thomas<sup>2</sup>, Leanne Embry<sup>4</sup>, Sameera Ramjan<sup>5</sup>, Stephen Sands<sup>5</sup>

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**Background and Aims:** To evaluate in a randomized, controlled treatment trial, whether the addition of maintenance chemotherapy post-radiation therapy for children with ependymoma contributes to neurobehavioral morbidity and reduced functional outcomes at 30 months post-diagnosis, compared to treatment with radiation therapy followed by observation.

**Methods:** Children with ependymoma ( $n=325$ ) enrolled on Children's Oncology Group protocol ACNS0831, who had complete or nearly complete resection or complete response after induction chemotherapy, were treated with irradiation therapy (RT) and then randomized to either receive or not receive 4 cycles of post-radiation chemotherapy with vincristine, cisplatin, etoposide, and cyclophosphamide (VCEC). A subset of children ( $n=58$ , 18% of eligible, ages 1-19, 41% female) completed neuropsychological evaluations at 9- and 30-months post diagnosis using gold standard performance measures and parent-report surveys. Change in neurocognitive scores from 9- to 30-months according to randomization group (RT+VCEC or RT alone) was assessed using analysis of covariance (ANCOVA) adjusted for 9-month neurocognitive score, hydrocephalus, and tumor location.

**Results:** Patients with neuropsychological data were similar to those without on demographic, tumor, and treatment characteristics, with the exception of a higher proportion of white and non-Hispanic patients providing data (both  $p<.05$ ). ANCOVA results reveal relatively improved neurocognitive performance at 30-months for children randomized to RT alone compared to RT+VCEC in estimated Full Scale IQ (adjusted mean change, +6.4, -1.0;  $p=0.018$ ), Block Design (+1.4, -0.2;  $p=0.011$ ), and verbal memory for stories (+1.0, -1.3;  $p=0.011$ ). Similar patterns were observed on measures of vocabulary and visual memory but were not significant. There were no significant differences by treatment group on parent-reported measures.

**Conclusions:** Children who received RT alone had higher scores reflecting relatively better functioning on specific neurocognitive measures at 30-month follow-up compared to children treated with RT+VCEC. While the extent of missing data makes it difficult to generalize, these findings suggest that VCEC may confer additional neurocognitive risk.

O083/#926 | Award Session

#### SIOP AWARD SESSION

12-10-2023 16:40 - 18:10

## ALTERED WHITE MATTER CONNECTIVITY IN PEDIATRIC BRAIN TUMOR SURVIVORS DISRUPTS NETWORK NEURAL COMMUNICATION AND COGNITION

Noor Al Dahhan<sup>1</sup>, Arthur Powanwe<sup>2</sup>, Minarose Ismail<sup>1</sup>, Elizabeth Cox<sup>1</sup>, Julie Tseng<sup>1</sup>, Cynthia De Medeiros<sup>1</sup>, Suzanne Laughlin<sup>1</sup>, Eric Bouffet<sup>1</sup>, Jérémie Lefebvre<sup>2</sup>, Donald Mabbott<sup>1</sup>

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**Background and Aims:** Brain tumors are a leading cause of disability and death among children. Surgery and cranial radiotherapy are often required for cure but are damaging to brain tissue – particularly white matter. This damage is related to significant cognitive deficits for pediatric brain tumor survivors (PBTS). White matter tracts are critical for neural communication among brain networks and supports cognition, including information processing speed which underlies higher-order cognitive processes, and is mediated by the brain's default mode (DMN) and executive control (ECN) networks. However, it is unknown how white matter damage results in compromised information processing speed in PBTS. Thus, we address this knowledge gap and hypothesize that white matter damage disrupts neural communication of the DMN and ECN – leading to cognitive impairments.

**Methods:** Forty-one healthy children and fifty-two PBTS were scanned at The Hospital for Sick Children (Toronto, ON). Diffusion tensor imaging (DTI) was combined with magnetoencephalography (MEG) to explore the impact of DMN and ECN structural and functional connectivity on cognition during resting state, a visual-motor task, and through computational modeling. Partial least-squares path modeling statistically described the association of structural and functional connectivity on cognitive performance.

**Results:** DMN and ECN structural connectivity directly influences neural communication and cognition, and PBTS white matter compromise has an indirect adverse impact on cognition via perturbed neural synchrony during both the presence and absence of specific task demands. Further, when our experimentally acquired structural connectomes were used to simulate functional neural activity, not only do the resulting functional simulations confirm our empirical functional results, but they also accurately predict group differences in cognitive performance.

**Conclusions:** Our findings show an important connection between DMN and ECN connectivity that is essential for cognition. Further establishing alterations in DMN and ECN structural and functional connectivity as novel biomarkers of cognitive impairments could facilitate early intervention and monitoring of these deficits following brain tumor treatment.

O084/#596 | Award Session

## SIOP AWARD SESSION

12-10-2023 16:40 - 18:10

## PROGRESS TOWARD LIQUID BIOPSY USING CELL-FREE DNA IN HEPATOBLASTOMA

Eiso Hiyama<sup>1,2</sup>, Masato Kojima<sup>1,2</sup>, Ryo Toge<sup>2</sup>, Sho Kurihara<sup>2</sup>, Isamu Saeki<sup>2</sup>, Genta Nagae<sup>3</sup>, Shohei Honda<sup>4</sup>

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**Background and Aims:** Hepatoblastoma (HB) is the most common malignant liver tumor in children. Our comprehensive genomic analysis revealed 80% or more frequent detection of CTNNB1 mutations. And TERT promoter mutation and hypermethylation of target genes were correlated with poor outcome. For liquid biopsy for detection of these abnormalities in cell-free DNAs (cfDNAs), we designed droplet digital polymerase chain reaction (ddPCR) system and analyzed in JPLT study samples.

**Methods:** Tumor DNAs and cfDNAs were extracted from the tumor and plasma samples obtained before and during treatment in 142 HB patients enrolled in JPLT2 and 3 studies. The CTNNB1 and TERT promoter mutations were analyzed and methylation rates of 5 genes (RASSF1A, PARP6, OCIAD2, MST1R, DLX6AS1) were calculated by ddPCR system. Then, correlation between these abnormalities and clinicopathological factors, overall survival, and event-free survival were retrospectively analyzed.

**Results:** CTNNB1 and TERT promoter mutations were detected 119 (84%) cases and 8 cases (5.6%) in the cfDNA at diagnosis, which were 98% and 100% concordance to the results of tumor DNAs. The tumors with TERT mutations showed poor outcome. The methylation rates of 5 genes in cfDNAs at diagnosis were significantly correlated those of tumor DNAs at diagnosis. Three or more hypermethylated genes were also associated with poorer survival rates. In cfDNAs, CTNNB1 mutations were usually undetectable and the methylation rates of hypermethylated genes were gradually decreased during preoperative chemotherapy then reached at less than 5% after radical resection. In some recurrent/relapse cases, CTNNB1 mutations were detectable and the methylation rates of the hypermethylated genes increased.

**Conclusions:** In liquid biopsy of cfDNA using ddPCR, CTNNB1 mutations might be useful for diagnosis of HB and TERT promoter mutation

might indicate HCN-NOS in elder cases. Methylation assay using ddPCR might also serve for evaluating malignant grade as well as treatment response and early detection of relapse/recurrence in HB.

O085/#1697 | Award Session

## SIOP AWARD SESSION

12-10-2023 16:40 - 18:10

### INTERIM ANALYSIS CHANGES IN ERYTHROCYTE SEDIMENTATION RATE, ALBUMIN AND LACTATE DEHYDROGENASE TO PREDICT PET RESPONSE IN HODGKIN LYMPHOMA

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**Background and Aims:** Response-adapted management of Hodgkin lymphoma (HL) with positron emission tomography-computerised tomography (PET-CT) is gold standard in well-resourced settings, but this is unavailable in most African countries. We aimed to investigate the correlation between changes in PET-CT findings at interim analysis with changes in blood test results in paediatric patients with HL in 17 South African centres.

**Methods:** Changes in ferritin, lactate dehydrogenase (LDH), erythrocyte sedimentation rate (ESR), albumin, white cell count (WCC), absolute lymphocyte count (ALC) and absolute total eosinophil count (AEC) were compared with Deauville scores (DS) on PET-CT assessment after two cycles of ABVD in 132 paediatric patients with HL. Deauville 1-3 denoted rapid early response (RER) while Deauville 4-5 denoted slow early response (SER). Missing values were imputed using the k-nearest neighbour algorithm. The baseline and follow-up blood test values were combined into a single difference variable. Data were split into training and testing sets for analysis using Python scikit-learn 0.23.1 with logistic regression, random forests, neural net, naïve Bayes, and support vector machine classifiers.

**Results:** Random forest analysis achieved a validated test accuracy of 70.0% when predicting RER or SER from blood samples. When applied to the full dataset, the optimal model had a predictive accuracy of 88.3% and a receiver operating characteristic (ROC) area under the curve (AUC) of 95.1%. The most predictive variable was the difference in ESR, which contributed 17% to the model. Differences in LDH and albumin each contributed 12.5%, while differences in WCC, copper, and HGB each contributed around 10-11%. Differences in ferritin, ALC, and AEC each contributed 8%.

**Conclusions:** In settings without access to PET-CT, these results may aid in improving survival in children with HL, a WHO Global Initiative for Childhood Cancer focus cancer. Low-cost, available tests ESR, LDH and albumin may be used to substitute for PET-CT in resource-constrained settings.

O086/#731 | Award Session

## SIOP AWARD SESSION

12-10-2023 16:40 - 18:10



## CHILDHOOD CANCER TREATMENT (CCT) TIME SENSITIVE ADHERENCE TRACKING PROTOCOL (TS-ATP) IN EL SALVADOR: A DECADE OF RESULTS

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**Background and Aims:** In El Salvador, 200 children are diagnosed with cancer yearly. Overall survival (OS) rates are 70%. Abandonment of treatment (AT) prior to 2011 was 13-20%. In 2011, a tracking protocol that allowed for immediate detection and intervention of absences was implemented by the psychosocial team. This study aims to describe the cause of treatment abandonment and the effectiveness of the TS-ATP to promote CCT adherence and prevent treatment abandonment improving the OS rate for children with cancer in the last decade.

**Methods:** This descriptive retrospective study focused on the outcomes of the 11-year implementation of an absence-tracking intervention in pediatric cancer patients from 2011 to 2022. Medical appointments and outpatient treatment absences were registered daily. Patients in treatment were contacted within 24 hours. The interview established a reason for absence and offer support to families. Contact with national entities was also made. When a patient failed to return to treatment, the national law that protects the welfare of children was used.

**Results:** AT was reduced by 76%. The most frequent reasons for absences among pediatric cancer patients in El Salvador are Domestic Needs (caregiver is ill, avoid income loss), Caregiver deciding against Treatment (attending other appointments), Financial Need (lack funds to travel), and Unforeseen Barriers (weather disasters, social/violence issues). The absence reason categories were amplified during COVID with public health system delays. The method of interviewing parents changed from in-person interviews to WhatsApp as telemedicine was implemented. An increase in adolescent population led to an increase in abandonment in 2022 and the addition of the category "Patient Decided against Treatment".

**Conclusions:** After the implementation of the TS-ATP, abandonment rates remain at 1-2%, improving OS. Lessons learned resulted in modifications in the protocol. TS-ATP proved to be an inexpensive and efficient intervention to establish a close relationship with patients and reduce non-adherence and AT.

O087/#766 | Nursing

NURSING: QUALITY IMPROVEMENT NURSING ABSTRACT PRESENTATIONS 02

12-10-2023 16:40 - 18:10

## CAPABILITY BUILDING IN QUALITY IMPROVEMENT FOR PEDIATRIC HEMATOLOGY-ONCOLOGY HEALTHCARE TEAMS AROUND THE GLOBE: THE PROFILE EXPERIENCE

Miriam Gonzalez-Guzman<sup>1</sup>, Alisha Pershad<sup>2</sup>, Melissa Vickers<sup>1</sup>, Alyana Alvarez<sup>1</sup>, Nadya Sullivan<sup>1</sup>, Heather Forrest<sup>1</sup>, Paola Friedrich<sup>1</sup>

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**Background and Aims:** The Pediatric Oncology Facility Integrated Local Evaluation (ProFILE) identifies gaps in pediatric hematology and oncology care delivery and helps care teams and institutions define an improvement strategy. The 9-month implementation process incorporates quality improvement (QI) training opportunities to build healthcare providers' capabilities in QI methods and empower local teams to apply them. We aim to evaluate the ProFILE QI track outcomes.

**Methods:** Three Full ProFILE Beta testing cohorts have participated. The QI track combined two learning methodologies. First, online, self-paced asynchronous learning through the Institute for Healthcare Improvement (IHI) Basic QI Certificate Curriculum for 2-3 team members at each institution. Second, experiential learning through six quality improvement hands-on exercises and a local prioritization workshop, including all assessment team members. Participants completed an 18-question QI knowledge self-assessment (scale 1=No Knowledge, 6=Expert) before and after ProFILE implementation. We used a paired t-test to compare knowledge gain.

**Results:** A total of 35 assessment teams have participated in the QI track since 2019. Median team size was 15 (range 2-32). Institutions were located across five regions and twenty-six countries. The overall IHI Basic QI certificate completion rate was 67%. (66/98) and 69% (24/35)[GM1] of the teams completed all six QI exercises. Prioritization workshop completion rate was 75%. [GM2] Participants reported a statistically significant increase ( $p < 0.001$ ) from general QI knowledge (scale=2) to being able to analyze and apply (scale $\geq$ 4) the following QI tools: IHI Model for improvement, process mapping, fish diagram, task shifting, affinity diagram, and impact-effort matrix.

**Conclusions:** Combining self-paced and experiential learning helped teams to get familiar with QI tools that are part of the ProFILE implementation process. Teams were able to apply QI tools to a clinical process. Additional QI training will be incorporated into the post-ProFILE activities to increase QI capability and help teams to implement their 3-year action plan.

O088/#343 | Nursing

NURSING: QUALITY IMPROVEMENT NURSING ABSTRACT PRESENTATIONS 02

12-10-2023 16:40 - 18:10

## WRAPAROUND CARE: EVALUATION OF THE PEDIATRIC ONCOLOGY GROUP OF ONTARIO INTERLINK NURSING PROGRAM

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**Background and Aims:** Pediatric Oncology Group of Ontario (POGO) Interlink (IL) Nurses are embedded in 5 pediatric cancer centres in Ontario, Canada and practice within a unique patient care model that enables them to move with patients and families across hospital, home, school and community. In alignment with POGO's strategic initiative to provide excellence in pediatric cancer care by strengthening the monitoring and evaluation of programs, a point-in-time evaluation of the IL Nursing Program will be described. The goals of the evaluation were to understand the impact of the program, make evidence-based process improvements, support the sustainability of the program, and confirm and validate the program pathway.

**Methods:** POGO collaborated with an independent evaluation firm to conduct a point-in-time evaluation. Data collection tools included: online family surveys; interviews with key stakeholders including IL Nurses, patients/families, and hospital care teams; artwork created by patients; a review of program data and documentation; and an analysis of data extracted from the POGO Network Information System (POGONIS) database.

**Results:** Family survey response rate was 23% (n=129) with 96% of those surveyed recommending the service to others. Interviews with stakeholders included IL nurses (n=10), hospital team members (n=15), families (n=8), and adolescents and young adults (n=3). Pieces of children's artwork were collected (n=4). Specific areas of impact included health teaching, coordination of services across environments, navigating school support, access to resources, emotional support, and enhancing palliative/bereavement care. Key findings guiding actionable program improvements included strengthening the referral system, expanding coverage in rural areas, and defining geographical catchment areas based on patient population to expand human resources.

**Conclusions:** POGO IL Nurses provide essential wraparound support to children with cancer and their families as evidenced by the evaluation results. Initiatives to further strengthen this vital program and ensure equal access to care include expansion of human resources and continued work on population mapping.

O089/#1065 | Nursing

NURSING: QUALITY IMPROVEMENT NURSING ABSTRACT PRESENTATIONS 02

12-10-2023 16:40 - 18:10

## THE EFFECT OF PARENTAL INVOLVEMENT DURING VENIPUNCTURE ON PAIN AND ANXIETY IN CHILDREN WITH CANCER: A RANDOMIZED CONTROLLED STUDY

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**Background and Aims: Introduction:** Children with cancer often undergo long treatment trajectories that include repeated needle procedures which may cause pain and distress. Venipuncture is one of the most painful and distressing procedures pediatric patients experience. Children with cancer often consider treatment procedures are more painful and traumatic than the cancer itself. **Aim:** This study aims to determine the effect of parental involvement on relieving pain and anxiety in children with cancer during venipuncture.

**Methods: Methods:** This was a randomized controlled trial with parallel groups in which 60 children aged 6-12 diagnosed with cancer were randomly allocated to a parental involvement group (n= 30) and a control group (n = 30). The population of the study consisted of children diagnosed with cancer who were hospitalized in the University Hospital Pediatric Hematology-Oncology Clinic. Data were collected using a Child and Parent Information Form, a Physiological Parameters Form, the Wong-Baker FACES Pain Rating Scale, and the Children's Fear Scale. Ethics committee approval was obtained from the Clinical Research Ethics Committee of the university before starting the study. The children and their parent were informed about the study and their verbal and written consent was obtained. The study was registered in the Clinical Trial Registry (NCT05012904).

**Results: Results:** The parental involvement group had significantly lower pain, anxiety, and heart rates than the control group during venipuncture. However, no significant difference was found in oxygen saturation values between the groups.

**Conclusions:** This study demonstrated that parental involvement during venipuncture reduced pain and anxiety in children with cancer. Parental involvement was found effective in relieving the pain and anxiety of children with cancer during venipuncture. Nurses should use the intervention to reduce children's anxiety and pain during venipuncture. This study contributes to the literature on the use of parental involvement during venipuncture in reducing pain and anxiety related to the procedure.

O090/#170 | Nursing

NURSING: QUALITY IMPROVEMENT NURSING ABSTRACT PRESENTATIONS 02

12-10-2023 16:40 - 18:10

## COMPARISON OF HEPARIN AND SALINE FOR PREVENTION OF CENTRAL VENOUS CATHETER OCCLUSION IN PAEDIATRIC ONCOLOGY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background and Aims:** Central venous catheter (CVCs) occlusion management remains a gap in evidence-based guidelines. Studies show no significant advantage of heparinized solutions over normal saline in reducing catheter dysfunction due to thrombosis, but the levels of evidence from the studies are not strong. This systematic review and meta-analysis aimed to evaluate the effect of heparin and normal saline flushing in preventing CVC occlusion in pediatric cancer patients.

**Methods:** PubMed, Web of Science, Cochrane, MEDLINE, CINAHL, Embase, World Health Organization International Clinical Trials Registry Platform, and ClinicalTrials.gov platform) were searched using keywords until March 2022. Five randomized controlled trials were included.

**Results:** A total of five studies with 316 pediatric cancer patients were included. Studies were found to be heterogeneous due to different types of cancer, heparin concentration, flushing frequency of CVCs, and measurement methods for occlusion. Despite all heterogeneous conditions, there was no significant difference regarding the effect of flushing with heparin and normal saline in preventing CVCs occlusion. It was revealed that normal saline is as effective as heparin in preventing the occlusion of CVCs among pediatric cancer patients.

**Conclusions:** The current systematic review and metanalyses revealed that there is no significant difference in the flushing of heparin and normal saline to prevent the occlusion of CVCs among pediatric cancer patients. Considering the potential risks of heparin, normal saline flushing may be recommended to prevent obstruction in CVCs.

O091/#1391 | Nursing

NURSING: QUALITY IMPROVEMENT NURSING ABSTRACT PRESENTATIONS 02

12-10-2023 16:40 - 18:10

## POSITIONING ETHICS WHEN DIRECT PATIENT CARE IS PRIORITIZED: HEALTHCARE PERSONNELS' EXPERIENCES OF IMPLEMENTING ETHICS CASE REFLECTION ROUNDS IN NORDIC PAEDIATRIC ONCOLOGY

Pernilla Pergert<sup>1</sup>, Bert Molewijk<sup>2</sup>, Cecilia Bartholdson<sup>1</sup>

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**Background and Aims:** To support healthcare personnel in handling ethical dilemmas and to deliberate on what is the right thing to do, ethics case reflections (ECR) rounds can be used. A Nordic working group on ethics has offered a training, in facilitating ECR rounds, to healthcare personnel in paediatric oncology. Trainees implemented ECR rounds at their hospitals. The aim was to explore the trainees' experiences of implementing ECR rounds in paediatric oncology.

**Methods:** All trainees in the first cohort were invited to participate in this study. Three focus group interviews were performed with (n=22/24) trainees from Sweden, Denmark, Finland, Iceland, and Norway, and 27 individual interviews with (n=17/20) trainees from all paediatric oncology centres in Sweden. Data was analysed using grounded theory.

**Results:** In a context where direct *patient care is prioritized*, *positioning* is used to resolve the main concern of doing ethics. *Positioning ethics* is about establishing a position of ethics at the hospital. Taking time for activities that are not the prioritized activities, but still necessary, are considered a luxury. *Allying* is important, while *positioning ethics*, and is done with key actors, including co-facilitators and the management. Strategies for *positioning ethics* can vary in intensity and be more or less successful, and include *promoting ethics*, *scheduling ethics*, *inviting key stakeholders*, and *identifying dilemmas*.

**Conclusions:** A key limitation was that the trainees were working as healthcare personnel, practicing to facilitate, and implementing ECR rounds. The challenging situation with shortage of time and personnel in healthcare is widely recognised. As the trainees implemented ECR rounds in this context, it is not surprising that direct patient care was prioritized. However, the dichotomisation between care and ethics was also questioned, as ECR rounds are viewed as instrumental in handling ethical dilemmas and uncertainties about what *should* be done in treatment/care.

O092/#1292 | Nursing

NURSING: QUALITY IMPROVEMENT NURSING ABSTRACT PRESENTATIONS 02

12-10-2023 16:40 - 18:10

## HOME-ADMINISTERED PARENT-LED LOW-DOSE ARA-C INTERVENTION – A PROSPECTIVE SINGLE-ARM FEASIBILITY STUDY (INTACTATHOME)

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**Background and Aims:** Home-administered treatment is known to reduce time spent at the hospital and mitigate disruption in the everyday lives of children with cancer and their families. Intravenous home chemotherapy services are complex and knowledge on feasibility is limited. This study aims to test the feasibility of a home-administered parent-led low-dose ARA-C (Cytosine Arabinoside) intervention developed previously as part of the INTACTatHome project.

**Methods:** During nine months all families with children 0–17 years of age, diagnosed with Acute Lymphoblastic Leukemia (ALL), Lymphoblastic Lymphoma (LBL), and Philadelphia Positive (ph+) ALL, possessing adequate family care resources were approached. Recruited families were offered a stepwise parent-education program to learn the low-dose ARA-C administration procedure. Feasibility was measured as: 1) demand: Use of the intervention, 2) acceptability: Satisfaction and preferences for delivery place, and 3) safety: Number of severe adverse events. Data were analysed with descriptive statistics.

**Results:** In total 15 of 17 approached families were eligible and enrolled. Two families received all ARA-C treatments at the hospital. The remaining 13 children (ALL=11, LBL= 1, ph+ALL= 1, mean age 5.2 years (range 2–15)) received 174 of 264 (66%) doses ARA-C at home administered by their parents. Mean doses administered at home were 13.4 (range 6–23). Parents evaluated 47 of 66 cycles of ARA-C and thought “good” (11%) or “very good” (89%) about administering the ARA-C at home, were “satisfied” (2%) or “very satisfied” (98%) with the education program and “secure” (6%) or “very secure” (94%) when administering the ARA-C at home. Given the opportunity home administration was preferred in 47(100%) parent surveys. No severe adverse events related to the intervention occurred.

**Conclusions:** The study confirms a substantial demand for the home-administered parent-led low-dose ARA-C intervention. Parents found the home administration highly acceptable. The intervention was safe with no severe adverse events occurring.

O093/#1610 | Nursing

## NURSING: QUALITY IMPROVEMENT NURSING ABSTRACT PRESENTATIONS 02

12-10-2023 16:40 - 18:10

## ONCOLOGY NURSES' KNOWLEDGE ON CARE OF PATIENTS WITH PAIN AT A RURAL DISTRICT HOSPITAL, RWANDA

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**Background and Aims:** Pain is the major symptom that brings patients for consultation and is the most common that has a great impact on quality of life of cancer patients. It is also frequently encountered in post-operative patients in particular. Unrelieved post-operative pain affects the patient, care-taker and/or their families physiologically, psychologically, and socio-economically. We aimed at assessing knowledge of oncology nurses on pain assessment and management at Butaro Cancer Center of Excellence (BCCOE).

**Methods:** A descriptive cross-sectional design with quantitative approach was used to assess knowledge of oncology nurses on pain assessment and management. A sample of 93 nurses was selected from a target population of 122 nurses using non-probability convenience sampling. Data were selected using a questionnaire and analyzed using an SPSS version 20.

**Results:** With regards to oncology nurses' management of pain, according WHO analgesic Ladder; among 93 nurses, 82 (88.17%) knew that there exist 3 steps compared to 5 and 7 steps. For severe pain, as opposed to other categories of mild and moderate pain, 90 (96.77%) knew that they have to start with a strong opioid, like morphine to control pain early. For the treatment principles, 78 (83.87%) knew that it focused by the mouth, 60 (64.51%) by the clock, 49 (52.68%) by the ladder and 80 (86.02%) knew that it focused by the patient. On adjuvants to be used at any step, 67(72.04%) responded they can be used while 26 (27.95%) said they cannot.

**Conclusions:** We found predominant nurses' knowledge on 3 steps of treating pain among cancer patients, this was supported by the study of Geng et al. (2014) in United States but not at same level as him for the appropriate medication the 3 types of pain. Treatment focusing on 4 principle elements by the mouth, clock, ladder and patient is as for studies of WHO, 2014.

O094/#1061 | CCI

## CCI: IMPROVING EARLY DETECTION AND ACCESS TO CARE

12-10-2023 16:40 - 18:10

## ADAPTING NURSING COMMUNICATION TOOLS TO TALK WITH FAMILIES ABOUT PEDIATRIC EARLY WARNING SYSTEMS (PEWS) IN THEIR CARE

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**Background and Aims:** Proyecto EVAT (Escala de Valoración de Alerta Temprana) is a quality improvement collaborative with 83 pediatric oncology centers in 20 Latin America and 2 Europe countries to reduce clinical deterioration in children with cancer through the implementation of a Spanish-language Pediatric Early Warning System (PEWS). Recently, we developed visual tools to guide hospital staff communication with caregivers (family members of children with cancer) about how PEWS will be used in their care. This study aimed to standardize the training process for discussing PEWS with caregivers.

**Methods:** Existing tools include a Spanish infographic and a pamphlet explaining the process of evaluating PEWS in pediatric oncology patients with simple language. To standardize caregiver training, we will additionally create a video to show PEWS use. Communication training will be piloted over two months in five centers. Pre- and post-training surveys will evaluate caregiver understanding of PEWS, supplemented with guided interviews to explore areas to improve the training. This training material will then be adapted based on feedback.

**Results:** Five versions of the tools were created, including local adaptation for inclusive language to allow understanding among caregivers of different socioeconomic and educational levels. Due to regional differences in Spanish, the infographic and pamphlet were made in editable PowerPoint to allow for local adaptation. After the pilot, we will collect feedback from centers to standardize training for use at other hospitals. Adaptation will aim to shorten the time needed for training and allow for personalization based on individual vs. group delivery and the patient's treatment stage.

**Conclusions:** PEWS are effective, low-cost interventions to reduce deterioration mortality in children with cancer; however, few resources exist to explain PEWS to caregivers. The PEWS caregiver

communication tool and training will aid communication between hospital staff and families and improve care for these high-risk patients.

O095/#1169 | CCI

## CCI: IMPROVING EARLY DETECTION AND ACCESS TO CARE

12-10-2023 16:40 - 18:10

## IMPROVING EARLY DETECTION AND REFERRALS OF CHILDHOOD CANCERS AMONG TRADITIONAL AND FAITH-BASED HEALERS IN ASHANTI REGION, GHANA

Comfort Asoogo<sup>1</sup>, Vivian Paintsil<sup>1</sup>, Conrad Batuure<sup>1</sup>, Barnabas Manlokiya<sup>1</sup>, Edward Dassah<sup>2</sup>

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**Background and Aims:** Every year over 1000 children under the age of 15 years develop cancer in Ghana with the number rising each year. Most of these cancers are curable if they are detected early and progressively treated. However, most patients report late with advanced disease partly due to seeking care with traditional and faith-based healers before reporting to health facilities. The study aim was to improve early detection and referral of childhood cancers among traditional and faith-based healers in Kumasi.

**Methods:** A cross sectional and descriptive method was used to involve parents and caregivers of children diagnosed with cancer who report to the paediatric oncology unit of Komfo Anokye Teaching Hospital, who originated from various social and ethnic groups as well as geographically distinct areas of Kumasi. Data of their social and demographic background, as well as knowledge on; early warning signs and treatment of childhood cancer were obtained after seeking their consent. Closed and open-ended questionnaires were used to collect data.

**Results:** 120 filled questionnaires were analysed using SPSS version 12. Majority 45% of the respondents had visited traditional healers, 25% visited faith-based healers before coming to oncology unit and 30% had visited a hospital facility. About 50% were males and 50% females. However, most of the respondents 70% did not have any primary education, 25% had some primary education and 5% had secondary education. Knowledge scores on health seeking behaviour had a marginal positive association with educational level ( $P = 0.055$ ).

**Conclusions:** Generally, the respondents of the present study had some level knowledge of childhood cancer ( $P < 0.05$ ). Barriers to early diagnosis and treatment of cancer can be addressed by training these alternative cancer providers in recognising signs of early childhood cancers and referring such cases promptly to the health facilities for

treatment will improve overall survival rates of childhood cancer in Ghana.

O096/#1459 | CCI

CCI: IMPROVING EARLY DETECTION AND ACCESS TO CARE

12-10-2023 16:40 - 18:10

### SUCCESSFUL PARTNERSHIPS WITH TRADITIONAL HEALTH PRACTITIONERS IN SOUTH AFRICA LEAD TO INCREASED NEW DIAGNOSIS

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CHOC Childhood Cancer Foundation SA, Programme Development, Rivonia, South Africa

**Background and Aims:** In 2010 CHOC Childhood Cancer Foundation in South Africa launched an Awareness Training and Education Programme to train Healthcare Professionals and Healthcare Workers on the Siluan Early Warning Signs of Childhood Cancer. It soon became clear that if we did not include the Traditional Health Practitioners in the Programme, we wouldn't reach the number of new diagnosis that we are supposed to reach.

**Methods:** We reached out to the biggest Traditional Healers Organisation in SA and asked them to connect us with other Traditional Healers Organisations. We got the buy-in from the leaders and started to train Traditional Health Practitioners country-wide. During the first year we reached more than 2000 trainees and at the end of the year we held an open debate between Western and Traditional Medicine with more than 500 participants to see how we could bridge the gap.

**Results:** Through our efforts there is an improvement in the referral pathway from Traditional Health Practitioners to Primary Healthcare Facilities in SA. We used Traditional Health Practitioners to join us on National Television Programmes and on our Webinars to influence their communities and to showcase our partnerships. We were invited back to the Traditional Healers Organisation to train their provincial leads and field workers on a four-day training programme

**Conclusions:** The Traditional Healers praise CHOC for empowering them with knowledge. Through our training they changed their attitudes towards CHOC and childhood cancer and their practices which lead to new referrals.

O097/#1577 | CCI

CCI: IMPROVING EARLY DETECTION AND ACCESS TO CARE

12-10-2023 16:40 - 18:10

### EXPERIENCE IN TRAINING ASHAS (ACCREDITED SOCIAL HEALTH ACTIVISTS) TOWARDS CHILDHOOD CANCER DIAGNOSIS IN INDIA

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**Background and Aims:** Background ASHAs (Accredited Social Health Activists) are trained community health workers (1 million) who are part of India's National Rural Health Mission. India, like most LMICs, does not have a national policy on childhood cancer. In this study, we describe our experience of engaging ASHAs for childhood cancer diagnosis.

**Methods:** We initiated this program in 2 districts of Uttar Pradesh (India's most populous state) viz. Gautam Budh Nagar and Ghaziabad. Between 15 Jan-15 March 2023, four blocks in each district were covered. A flyer and PowerPoint slides prepared in regional language describing the warning signs of childhood cancer were used. A pre-and-post test was conducted to gauge their level of understanding and engagement. The training sessions lasted for 1.5 hours each with time for discussion. The classes were conducted by a team of doctors, social workers and counsellors from PGICH with support from CanKids.

**Results:** Over 8 weeks, 344 ASHAs were trained in batches of 20-30. The same set of questions was administered pre and post-training. The questions assessed myths, facts and early diagnosis of childhood cancer. 99% ASHAs felt that cancer is a fatal illness with no cure. Most were not aware that cancer can occur in children. Among the responders, 68.8% showed an >40% improvement from pre-test value. 10.6% had a score that was less than their pretest value and, in the rest, no or minimal change was noted. The challenges experienced by ASHAs (assessed by interviews of the training team with ASHAs) were inadequate remuneration, overburden due to other health programs and social/cultural barriers.

**Conclusions:** ASHA workers have been instrumental in bringing health-care services to the doorstep of people living in remote and rural areas. Training these grassroot workers and clearing their misconceptions can go a long way in improving cancer outcomes in LMICs.

O098/#214 | Free Paper Session (FPS)

FPS 04: BONE TUMORS (NOLLENBURG AWARD)

13-10-2023 08:40 - 09:40

## A NOVEL DENDRITIC CELL VACCINE TARGETING CD70 FOR OSTEOSARCOMA LUNG METASTASES

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**Background and Aims:** There is an urgent need for identifying new therapies for patients with relapsed and metastatic osteosarcoma (OS) as response and survival rates remain < 20%. Dendritic Cell (DC) vaccines are an emerging focus in immunotherapy. A CD103<sup>+</sup> DC vaccine (cDCV) generated using K7M3 OS cell lysates (K7M3-lysate-cDCV), induced regression of primary tumors and lung metastases, and a systemic immune response in an orthotopic K7M3 mouse model. Identifying a common OS antigen is needed for clinical translation. CD70 is expressed on OS cell lines and patient-derived xenografts (PDX). We determined if a CD70-targeted cDCV (CD70-cDCV) induced tumor regression, prolonged survival, and induced systemic immunity. We compared its activity to K7M3-lysate-cDCV.

**Methods:** cDCVs were generated using K7M3 cell lysates or CD70 protein. Mice were injected with K7M3 cells on the left and right side. On days 4 and 7, right-sided tumors were injected with PBS, K7M3-lysate-cDCV or CD70-cDCV. Tumors on the left were untreated. Left- and right-sided tumors were measured every 3-4 days for 25 days. Prevention of lung metastases was evaluated by pretreating mice with CD70-cDCV or K7M3-lysate-cDCV, injecting labeled-K7M3 cells 5 weeks later, and monitoring for lung metastases by luminescence.

**Results:** CD70-cDCV inhibited the growth of both treated and untreated primary tumors and was equally effective as the K7M3-lysate-cDCV. Fewer metastases were seen in the CD70-cDCV pretreated mice, similar to the K7M3-lysate-cDCV pretreated mice.

**Conclusions:** CD70-cDCV induced tumor regression and systemic immunity resulting in regression of the untreated tumor, and prevention of metastatic spread to the lungs. Therapeutic activity was equal to the K7M3-lysate-cDCV. CD70-cDCV may provide a novel therapeutic approach for relapsed OS patients with metastases in the bone and lung, thereby improving survival for this difficult patient population with few alternative therapies. This approach does not require access to the patient's tumor, simplifying therapy initiation.

O099/#1024 | Free Paper Session (FPS)

FPS 04: BONE TUMORS (NOLLENBURG AWARD)

13-10-2023 08:40 - 09:40

## EIF4A1/2 INHIBITION DOWN-MODULATES THE OXIDATIVE STRESS RESPONSE AND PREVENTS LUNG METASTASIS IN OSTEOSARCOMA

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**Background and Aims:** The presence of systemic (lung) metastases remains to be a major hurdle for improving patient outcomes in osteosarcoma. This underscores the need to develop novel anti-metastatic therapeutics that can be added to the current standard of care. Messenger (m)RNA translation is often dysregulated in many types of cancer. We hypothesize that the overexpression of mRNA translation regulation factors is crucial in the synthesis of cytoprotective/adaptive proteins needed during OS lung colonization.

**Methods:** RNA sequencing datasets of OS cell lines and patient samples were parsed for over-expressed mRNA translation factors. From a panel of small molecule inhibitors (SMIs) against over-expressed targets, a candidate SMI (with the lowest IC<sub>50</sub> activity) was chosen for further in vitro functional characterization using cell-based and mRNA translation assays +/- SMI, +/- *tert*-butylhydroquinone (tBHQ), a chemical inducer of oxidative stress. Translatomics and proteomics were performed on OS cells +/- SMI, +/- tBHQ. The therapeutic effects of the SMI were evaluated in xenograft mouse models of OS.

**Results:** Eukaryotic initiation factor 4A1 (eIF4A1) mRNA levels were found to be overexpressed in OS. CR-1-31B, a SMI of eIF4A1/2, was found to have low nanomolar IC<sub>50</sub> values in a panel of metastatic OS cells. CR-1-31B and tBHQ co-treatment induced higher cellular oxidative stress, reduced cell proliferation, and increased cell death in OS cells versus single agent conditions. CR-1-31B treatment modulated the translation of metastasis-associated mRNA transcripts in OS cells. CR-1-31B-treatment diminished NRF2 translation in OS cells under oxidative stress. Lastly, CR-1-31B treatment delayed primary tumour growth, reduce lung metastases, and increase survival times in xenograft OS mouse models.

**Conclusions:** The current study provides pre-clinical data on the anti-metastatic activity of CR-1-31B, a SMI of eIF4A1/2 in OS. Furthermore, we provide mechanistic insight on how SMIs against mRNA translation factors can down-modulate molecular drivers of the metastatic phenotype in OS, and improve outcomes in mice.

O100/#994 | Free Paper Session (FPS)

## FPS 04: BONE TUMORS (NOLLENBURG AWARD)

13-10-2023 08:40 - 09:40

**OUTCOMES BASED ON HISTOLOGICAL TUMOR NECROSIS AND PREDICTIVE CLINICAL AND LABORATORY PARAMETERS FOR NECROSIS IN CHILDREN WITH OSTEOSARCOMA TREATED ON A NON-HDMTX BASED CHEMOTHERAPY PROTOCOL**

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**Background and Aims:** Histopathological response to neoadjuvant-chemotherapy (NACT) measured as tumor necrosis (TN) compared to residual viable tumor has been reported to be prognostic of outcomes at variable cut-offs of 70%, 90% in studies post HDMTX-based chemotherapy. We studied outcomes based on TN at cut-offs of 70%, 90%, 100% and delineated clinical-laboratory parameters predictive of TN on a non-HDMTX chemotherapy backbone.

**Methods:** Treatment-naïve, biopsy-proven children ≤15years, with osteosarcoma uniformly treated on OGS-2012 chemotherapy protocol and surgery post-NACT from January 2013-December 2020 were retrospectively analyzed. Histopathological-response on post-surgical specimens were reported as percentage necrosis. Kaplan-Meier for survival, log-rank test for comparing survival, Pearson's Chi-square for assessing associations between clinical parameters and necrosis were used.

**Results:** Of 305 patients treated, 258 formed the study cohort. Median age-12years(range,3-15years), M:F-1.7:1, localized-79.8%(n=206), metastatic-20.2%(n=52). Amputation was performed in 20.1%. Median TN was 94%. At a median follow-up of 38months(range,34-45months), 3year Event Free Survival(EFS) and Overall Survival(OS) of the whole cohort were 56.1%(SE,3.3%) and 87.8%(SE,2.4%). For entire cohort, TN at a cut-off of 70%(29.3%vs60.7%), 90%(38.7%vs69.0%), 100%(50.8%vs84.1%), were prognostic for EFS(p=0.0001), while TN 90%(80.3%vs92.9%,p=0.006) and 100%(85.5%vs97.7%,p=0.023) were prognostic for OS. For localized disease, TN at a cut-off of 70%(35.4%vs 66.4%), 90%(41.6%vs77.0%), 100%(54.8%vs96.2%) were prognostic for EFS (p=0.0001), and OS(p=0.0001). Comparison using Cox regression showed 90%TN to be a better predictor for EFS(HR-3.2,95%CI:2.0-4.9,p=0.000) and OS(HR-3.5,95%CI:1.4-8.7,p=0.006) in localised disease, for OS(HR-2.9,95%CI:1.3-6.2,p=0.009) of entire-cohort, and a good predictor

for EFS(HR-2.5,95%CI:1.7-3.6,p=0.000) of entire-cohort compared to 70%TN. For metastatic disease TN 70% was prognostic for EFS(16.6%vs50.1%,p=0.0047). Among clinical and laboratory parameters, male gender(OR:1.9,p=0.01) and amputation(OR:2.1,p=0.014) had a higher risk of <90%TN.

**Conclusions:** Tumor necrosis post-neoadjuvant chemotherapy at a cut-off of 90% is a good prognostic tool on a non-HDMTX based regimen, especially in localised disease, with best outcomes at 100% necrosis, while a lower cut-off of 70% could be used for prognostication in metastatic disease. Male gender and amputation predicts poor histopathological-response.

O101/#957 | Free Paper Session (FPS)

## FPS 04: BONE TUMORS (NOLLENBURG AWARD)

13-10-2023 08:40 - 09:40

**GENOMIC PROFILING ANALYSIS FOR CHILDREN, ADOLESCENTS AND YOUNG ADULTS WITH BONE SARCOMA (BS): SAR-GEN\_ITA, AN ITALIAN MULTICENTRE PROSPECTIVE TRIAL**

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**Background and Aims:** Patients (pts) with bone sarcoma (BS) are underrepresented in genomic profiling trials. The SAR-GEN\_ITA (NCT04621201) trial was set out to gain a comprehensive genomic overview of pediatric BS and to identify matched targeted therapy.

**Methods:** Eleven centres of the Italian Pediatric Onco-Hematology Association collected fresh or formalin-fixed paraffin-embedded (FFPE) tumour and blood samples at BS diagnosis or relapse stage. Whole exome (WES) and RNA sequencing (RNA-seq) were performed, and data were exploited as previously described (Cereda M, 2016).

**Results:** 73 pts were enrolled from 2017 to 2022. Median age was 14 years (range: 2-25 years). 42 pts were male (58%) and 31 (42%) female. 42 pts (58%) had Osteosarcoma and 31 (42%) Ewing sarcoma. Fifty-six samples were fresh (77%) and 17 FFPE (23%). WES was performed for 65 pts (89%), RNA-seq for 52 pts (71%) and 8 (11%) pts were not analysed. Median Tumour Mutational Burden (TMB) was 0.54 muts/Mb (range: 0.1-62), 3 pts with a TMB higher than 10. Most common mutated genes were TP53, RB1. Median Copy Number Alteration Burden was 0.53 (range: 0.002-1). NRAS, PDGFRA and AKT were the genes most frequently amplified. Moreover, the most common deleted genes were CDKN2A, CDKN2B, SMARCB1. 30 pts (46%) had at least one "potentially actionable" genomic alteration, 14 of which with relapsed/progressing disease and the genomic report suggested a matched treatment in 2/14 cases (14%). Moreover, a tyrosine kinase inhibitor (TKI) was used for 4 pts regardless of the genomic report, however their analysis showed a high amplification of specific molecular TKI targets.

**Conclusions:** Sequencing of paediatric BS samples is feasible and might change the treatment strategy in about 50% of pts. A wide and comprehensive genomic characterization is needed to foster biological knowledge of BS, to find new therapeutical approaches and their best timing, and to help clinicians to personalize patient treatment.

O102/#1811 | Nursing

#### NURSING: TOP NURSING ABSTRACTS

13-10-2023 08:40 - 09:40

#### A PILOT STUDY OF IMPLEMENTING A PRECEPTORSHIP PROGRAM IN A PEDIATRIC ONCOLOGY HOSPITAL IN GUATEMALA

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**Background and Aims:** Nursing Preceptorship is an effective strategy to support the orientation of new nurses in pediatric onco-hematology units. A preceptor can provide a supportive and organized clinical edu-

cational experience and improve job satisfaction and retention of new nurses. However, a comprehensive preceptor program is essential to provide the preceptor with the required knowledge, skills, tools, and support. This pilot study aims to implement a comprehensive preceptor program to support the orientation of new nurses at a pediatric oncology hospital in Guatemala.

**Methods:** We collaboratively developed and adapted the preceptor program to the hospital's requirements. The methods included an extensive literature review, creating a comprehensive preceptor program including policies and tools necessary for implementation, preceptor selection criteria, and a two-day preceptor training. The program's outcome was evaluated using a preceptor evaluation tool and a preceptor feedback survey.

**Results:** The program was developed and implemented from August to November 2022 in 5 units of the hospital. Twenty seven nurses met the eligibility criteria and were invited for the training in October 2022. Twenty-six nurses (96%) successfully completed the training, with 92% obtaining more than 80% evaluation score (range 60 - 100%). Through preceptor feedback survey all participants (100%) reported that the program help them acquire the necessary knowledge and skills to perform the role effectively. More than 95% reported that they were confident in carrying out the preceptor role as a result of the training.

**Conclusions:** A comprehensive preceptorship program implemented in Guatemala demonstrated improvement in the preceptor's knowledge, skill, and confidence to support the orientation of new nurses in low- and middle-income countries. The replication of the program in other pediatric oncology settings can both promote the professional growth of preceptors and enhance the integration of new nurses to the clinical settings.

O103/#833 | Nursing

#### NURSING: TOP NURSING ABSTRACTS

13-10-2023 08:40 - 09:40

#### THE MEDIATING ROLE OF RESILIENCE IN THE RELATIONSHIP BETWEEN STRESS AND PSYCHOLOGICAL DISTRESS AMONG PARENTS OF CHILDREN WITH CANCER

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**Background and Aims:** Parents usually report psychological distress in the face of children's cancer diagnosis. Perceived stress has been found highly correlated with the parental psychological distress, while whether resilience could play an indirect effect to stress on the parental psychological distress is unknown. This study aims to explore the mediating role of resilience in the relationship between stress and psychological distress among parents of children with cancer.

**Methods:** A cross-sectional study was conducted in three tertiary hospitals in mainland China, from August 2018 to November 2019. The parents of children (0–19 years old) with cancer were invited to participate in the study. The Perceived Stress Scale (PSS) was used to assess parental stress. Resilience was assessed by the Connor-Davidson Resilience Scale (CD-RISC). The psychological distress, including depressive symptoms and anxiety, were assessed by Self-Rating Depression Scale (SDS) and Self-Rating Anxiety Scale (SAS), respectively. Hierarchical linear regression analyses were conducted to explore the direct effects of stress and resilience on parental psychological distress. The indirect effects of mediation were analysed by structural equation models.

**Results:** A total of 258 parents were recruited in this study. The parents were mostly female (65.9%) and married (95.0%), with a mean age of 33.8 years (SD = 5.5 years). The results indicated that resilience was a significant predictor of psychological distress (depressive symptoms:  $\beta = -0.24$ ,  $P < 0.001$ ; anxiety:  $\beta = -0.16$ ,  $P < 0.001$ ), after controlling for stress. For the relationship between stress and depressive symptoms, the mediating effect of resilience accounted for 23.4% of the total effect; for the relationship between stress and anxiety, the mediating effect ratio was 11.4%.

**Conclusions:** Resilience could be a direct and indirect protective factor for parental psychological distress caused by perceived stress. Interventions to enhance resilience are encouraged to be developed and implemented for parents of children with cancer.

O104/#1111 | Nursing

NURSING: TOP NURSING ABSTRACTS

13-10-2023 08:40 - 09:40

#### ROLE OF NURSING LEADERSHIP IN COORDINATION OF WAR RESPONSE: THE SAFER UKRAINE EXPERIENCE

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**Background and Aims:** The Supporting Action for Emergency Response (SAFER) Ukraine initiative was established to provide safe passage and uninterrupted treatment for pediatric hematology and oncology (PHO) patients from Ukraine affected by the Russian invasion. Referral, triage, and patient allocation were implemented to expeditiously transfer Ukrainian PHO patients to specialized centers across Europe and North America. We describe the role and leadership of nurses at the triage center established in Poland.

**Methods:** A nursing leadership team was formed to manage operations, including conception, piloting, and adaptation of triage systems for medical convoys. Other responsibilities included medical documentation, maintaining emergency supplies, coordination and planning of patient convoys, maintaining daily clinic operations, recruiting and onboarding nurses and volunteers, scheduling to ensure 24/7 safe patient care from arrival to departure, and accompanying patient transport to airports. The leadership team applied transformational nursing leadership traits including authenticity, expertise, vision, flexibility, shared leadership, charisma, and the ability to inspire and motivate others.

**Results:** Between March 3, 2022 – March 3, 2023, the nursing team in Poland facilitated the triage of 512 patients. A core leadership nursing team of one PHO nurse, two intensive care nurses and two local nurses was established early in the operation. This team recruited 40 nurses from approximately 10 Polish institutions. Fifteen nursing policies and procedures were rapidly developed to support safe patient triage and allocation, prioritizing policies for urgent needs (e.g., convoy algorithm).

**Conclusions:** The role of nurses in the SAFER Ukraine initiative demonstrates the impact of nursing leadership in humanitarian emergencies. Nurse leaders were critical as constant elements in this response, navigating complex logistics, multidisciplinary teams, and rapidly changing situations to ensure safe triage for medically complex vulnerable patients. This model of coordination based on an effective nursing leadership style can be replicated to ensure safe and consistent care in future crises.

O105/#612 | Nursing

NURSING: TOP NURSING ABSTRACTS

13-10-2023 08:40 - 09:40

## INITIAL DEVELOPMENT AND PILOT TESTING OF AN INSTRUMENT FOR CONDUCTING A COUNTRY-LEVEL SITUATIONAL ANALYSIS OF PEDIATRIC ONCOLOGY-HEMATOLOGY NURSING

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**Background and Aims:** Within the WHO Global Initiative for Childhood Cancer, Brazil engaged in mobilizing all pediatric oncology workforces, including nursing. To support nurses in this global movement, the Improving Children's Oncology-hematology Nursing (ICON) initiative arose as a collaborative global and local nursing endeavor to co-design improvement strategies at the country level. An instrument was needed for an in-depth understanding of the situation of pediatric oncology-hematology nursing. The purpose of this study was to develop and pilot a new instrument for conducting situational analysis of pediatric oncology-hematology nursing in Brazil.

**Methods:** We used the guidelines for instrument development to create the English version with sections based on the six SIOP baseline Standards for Pediatric Oncology Nursing. The items were newly developed or taken from a previously developed instrument. After content validation by 5 experts and cross-cultural adaptation to Portuguese, we piloted the tool through self-administration among 26 nurses representing hospitals providing pediatric oncology-hematology services in Brazil.

**Results:** The instrument included 62 items covering background information, nursing staffing, orientation program, continuing education, multidisciplinary team meetings, resources for nursing care, and policies/procedures. After experts' review, two bilingual nurses forward translated the tool into Portuguese and agreed on a final version. A third nurse, back translated and checked for equivalence. The pilot study yielded useful data to refine the instrument. The results described the current situation and highlighted improvement areas in Brazil. Ten hospitals (38%) rotate nurses, and 19 (73%) have a nurse-to-patient ratio exceeding 1:5. Half of the hospitals have nurse educators and use structured orientation programs with skills validation. All respondents reported unavailability of chemotherapy-tested personal protective equipment.

**Conclusions:** The new ICON-Situational Analysis Instrument, piloted in Brazil, is a promising tool for examining the pediatric oncology-hematology nursing situation within a country. More evidence on psychometric properties and study replication can promote its use in research and practice.

O106/#620 | IPSO

IPSO: BEST POSTER SESSION

13-10-2023 08:40 - 09:40

## THE USE OF A HIGH FLOW PICC CATHETER FOR STEM CELL AND LYMPHOCYTE APHERESIS: THE INITIAL EXPERIENCE OF A PEDIATRIC ONCOLOGY CENTER IN BRAZIL

Antonella Zanette<sup>1</sup>, Andréia Wasem<sup>1</sup>, Ana Luiza Rodrigues<sup>1</sup>, Andressa Taborda<sup>1</sup>, Julia Dereti<sup>2</sup>, Vilani Kremer<sup>1</sup>

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**Background and Aims:** Autologous hematopoietic stem cell transplants (HSCT), characterized by high intensity chemotherapy followed by the infusion of HSC previously collected from the peripheral blood is a procedure used in the treatment of several malignancies. In pediatrics, the apheresis procedure represents a challenge, due to the need for insertion of a rigid central venous catheter (CVC) in small children. The CVC is usually used for stem cell collection and then removed. Later on, the patient will need a new device for cell infusion. Due to surgical risk and complications that could arise from two catheter insertions, we propose the use of one single catheter for both apheresis and infusion.

**Methods:** We present five children between 1 and 13 years old who underwent apheresis using a high flow PICC catheter surgically inserted under general anesthesia.

**Results:** All patients utilized a double lumen 5fr catheter placed in the brachiocephalic trunk with chest channelization. All catheters were inserted under 24 hours prior to apheresis in order to assure the devices were pervious, with good flow and reflow. Three of the patients were diagnosed with neuroblastoma, one with Ewing's tumor and one was a patient with acute lymphoblastic leukemia (ALL) awaiting Car-T Cell therapy. The four patients who underwent autologous HSCT used the same catheter for cell infusion and remained with the catheter following discharge. The patient who was submitted to apheresis for Car-T Cell still awaits infusion and the catheter was removed.

**Conclusions:** High flow PICC is a viable alternative, with adequate caliber for apheresis in pediatric patients under 20 kg, who are considered difficult patients to access for apheresis. The device is able to maintain an adequate flow of 5ml/s and can be used as a single catheter throughout the HSCT process, reducing the risks from general anesthesia and the catheter insertion procedure.

O107/#1225 | IPSO

IPSO: BEST POSTER SESSION

13-10-2023 08:40 - 09:40

### PERSONALIZED APPROACH TO THE MANAGEMENT OF PAEDIATRIC AGGRESSIVE FIBROMATOSIS: A SINGLE-INSTITUTION EXPERIENCE

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Institute of Mother and Child, Department Of Oncology And Surgical Oncology For Children And Youth, Warsaw, Poland

**Background and Aims:** The management of paediatric aggressive fibromatosis remains still problematic. Aim of the study was to present the possible therapeutic options especially in the case of tumors whose size or anatomically unfavorable location make it impossible for complete surgical resection without mutilation.

**Methods:** A single-center retrospective study was conducted in all patients under the age of 18 years treated from 1992 to 2022. The following clinical factors were analyzed: size, location of the tumor and its relationship to the adjacent structures (favorable and unfavorable factors), surgical margin of resection (microscopically complete-R0, incomplete-R1, macroscopically incomplete-R2), kind of treatment (chemotherapy- CHT, radiotherapy- XRT, personalized treatment- Tamoxifen, Meloxicam), results of treatment (complete remission-CR, stabilization-SD, partial regression-PR, progression-PD, relapse after CR).

**Results:** In the group of 21/22 pts (1-17 years old, mean 11.15 years, mean f-up 6.45 years) the tumor was located in the limb, in 1 pt in the trunk. 15/22 pts were surgically treated: R0-5pt(5CR), R1-10pts(5SD,3CR,2PD). Biopsy had 7/22pts(6SD,1PR). Unfavorable clinical factors were noticed in 10/22 pts (2CR,6SD,2PD). CHT was used in 9/22pts (2CR,5SD,2PD), XRT in 3/22 pts (1CR,2SD), personalized treatment in 5/22pts(5SD). Surgery was performed in 7/22 pts (5-R0:5CR; 2-R1:1CR,1SD); surgery and CHT in 3/22 pts (3-R1:2PD,1CR); surgery, CHT and XRT in 2 pts (2 -R1:1SD, 1-CR); surgery, CHT and personalized treatment in 2 pts (2R1:2SD); surgery, CHT, XRT and personalized treatment in 1pt (R1-1SD). 6/7 pts after biopsy achieved SD (3 pts - biopsy, 1 - biopsy and CHT, 2 - biopsy and personalized treatment), 1 pt PR. 8/22 pts achieved CR,11SD,1PR,2PD. Relapses developed in 10/22 pts (R1:5SD,3CR,2PD).

**Conclusions:** It is crucial to avoid mutilating surgical procedures in children with aggressive fibromatosis. Stabilization of disease (SD) should be classified as a good result of treatment. It is advisable to individualize therapy in patients with progressive tumors.

O108/#1687 | IPSO

IPSO: BEST POSTER SESSION

13-10-2023 08:40 - 09:40

### IS IT WORTH TREATING NONMALIGNANT VASCULAR ANOMALY PATIENTS WITH ONCOTHERAPEUTIC DRUGS?

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**Background and Aims:** Congenital vascular anomalies are the most common congenital diseases under age of 12 months. They have heterogeneous morphology and different clinical behaviour, some of them can cause permanent disfigurement, interference with vital functions, alarming or even life-threatening. These group contains malignant and nonmalignant vascular tumours, as well as vascular malformations, such as lymphangiomas, and arterio-venous malformations. Nowadays we know the genetic defect of almost every vascular disease. With the development of antiangiogenic medicines in recent years we have the abilities of treatment of these, previously untreatable, unresectable, frustrating patients. Our goal was to assess whether it made sense to use oncotherapeutic drugs in these patient group.

**Methods:** In the last 5 years, we retrospectively analysed our nonmalignant vascular patients, treated by any oncological drugs. We have collected data focused on what were the indications of oncotherapeutic treatments and what were the end results of the treatments (patients responded well, moderate or non).

**Results:** 53 patients (0-18 ys, 22, slight female dominance 30/23) were enrolled. Half of the patients (27) gave bleomycin for intralaesional treatment. The other half of the patients gave other, systemic oncological drugs, such as vincristine, bevacizumab, trametinib and sirolimus based on vascular and oncological board's decision. 85 percent of the patients responded well, or moderate, the other, nonresponder patients needed to change treatment, switch to other drugs, or switch to surgical treatments.

**Conclusions:** Non-malignant vascular diseases usually respond well to oncology drugs. This means that in special cases it is worth using such drugs before/after or instead of surgical interventions. Previously untreatable patients can be successfully treated with oncotherapeutic drugs. Some non-responder patients had to switch to another drug, hopefully the broadening of diagnostics (e.g. Next Generation Sequencing) can prevent treatment pitfalls, and in the future we will be able to provide personalized oncotherapy for non-malignant vascular anomaly patients as well.

O109/#101 | IPSO

IPSO: BEST POSTER SESSION

13-10-2023 08:40 - 09:40

**SUMMARY OF THE MULTICENTER APPLICATION OF THE CCCG-NB-2015 CONSENSUS IN NEUROBLASTOMA**Yan Jin, Qiang Zhao, Jie Yan, Jie Li

Tianjin Medical University Cancer Institute and Hospital, Department Of Pediatric Oncology, Tianjin, China

**Background and Aims:** To analyze and summarize the cases of neuroblastoma in children diagnosed and treated by the multi-center application of CCCG-NB-2015 consensus scheme in China.

**Methods:** The clinical and prognostic data of 500 patients with NB diagnosed and treated by the unified and standardized CCCG-NB-2015 program were retrospectively analyzed, and the key factors affecting the prognosis of NB were identified through COX univariate and multivariate regression analysis.

**Results:** A total of 10 potential prognostic factors were identified by COX univariate analysis, and the results showed that the independent prognostic factors closely related to EFS were INPC classification, bone marrow infiltration, NSE and LDH levels at diagnosis, and the independent prognostic factors closely related to OS were NSE, LDH level and INRGSS stage ( $P < 0.05$ ). NSE and LDH can well predict events such as NB bone marrow metastasis and recurrence ( $P < 0.05$ ). After conversion to INRGSS, the 3-year EFS for L1, L2, MS and M were 94.4%, 87.2%, 87.5% and 53.6%, respectively. The EFS at 3 and 5 years in the low-risk, intermediate-risk and high-risk groups were 97.1% and 97.1%, 90.0% and 87.3%, 53.9% and 47.3%, respectively. Among them, patients with stage INSS 3 with UH of INPC were classified as high-risk group in the CCCG-NB-2015 protocol, and their prognosis was poor, with a 5-year EFS of 65.7% ( $P < 0.05$ ), but mostly classified as intermediate-risk in the INRG risk group.

**Conclusions:** NSE and LDH levels are of great value in predicting whether bone marrow metastasis and prognosis evaluation in NB patients. INRGSS staging is an independent prognostic factor and has more clinical significance in assessing prognosis than INSS staging, and the INRGSS staging system is recommended. Under the premise of INRG risk group therapy, the regimen of the intermediate-risk group continued to be CCCG-NB-2015 for the intermediate-risk group.

O110/#592 | IPSO

IPSO: BEST POSTER SESSION

13-10-2023 08:40 - 09:40

**PEDIATRIC ADRENOCORTICAL CARCINOMA: CLINICAL FEATURES AND APPLICATION OF NEOADJUVANT CHEMOTHERAPY**Qin Hong, Lin Yu, Shen Yang, Huanmin Wang

Capital Medical University, Department Of Surgical Oncology, Beijing, China

**Background and Aims:** Objective: To summarize the clinical characteristics of children with adrenocortical carcinoma (ACC) and preliminarily explore the indications for and efficacy of neoadjuvant chemotherapy in certain patients.

**Methods:** The data of 40 children with ACC in the past 15 years were retrospectively analyzed. Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 and three-dimensional (3D) reconstruction of contrast-enhanced computed tomography data were used to evaluate the response to neoadjuvant chemotherapy.

**Results:** Forty patients (17 males, 23 females) were enrolled. Abnormal hormone levels were common in children with ACC ( $n=31$ ), and in terms of clinical presentation, sexual precocity was the most common (14 cases, 35.0%), followed by Cushing's syndrome (12 cases, 30%). Seven of 40 children received neoadjuvant chemotherapy because of a maximum lesion diameter greater than 10 cm ( $n=4$ ), invasion of surrounding tissues ( $n=2$ ), intravenous tumor thrombus ( $n=2$ ), and distant metastasis ( $n=2$ ); 2 patients achieved a partial response, and 5 had stable disease according to the RECIST 1.1 standard. Furthermore, 3D tumor volume reconstruction was performed in 5 children before and after neoadjuvant chemotherapy. The tumor volumes were significantly reduced in all 5 children, with a mean reduction of  $221.68 \pm 152.39$  mL, and the most significant change was a decrease from 55.71 mL to 6.59 mL. After surgery with/without chemotherapy, the 5-year overall survival rate for all children was 82.5% (73.7%, 91.3%), and the 5-year progression-free survival rate was 74.6% (64.5%, 84.7%).

**Conclusions:** Conclusion: In the diagnosis and treatment of pediatric ACC, a comprehensive endocrine evaluation is necessary to facilitate early diagnosis. Surgery and chemotherapy are important components of ACC treatment, and neoadjuvant chemotherapy may be tried in children with ACC who meet certain criteria.

O111/#754 | IPSO

IPSO: BEST POSTER SESSION

13-10-2023 08:40 - 09:40

### CLINICAL FEATURES AND DETERMINANTS OF OUTCOMES OF EWING SARCOMA AMONG CHILDREN $\leq$ 5 YEARS: A RETROSPECTIVE SINGLE INSTITUTION ANALYSIS OF 86 PATIENTS

Chitrakshi Nagpal<sup>1</sup>, Archana Sasi<sup>1</sup>, Shuvadeep Ganguly<sup>1</sup>, Sandeep Agarwala<sup>2</sup>, Vishesh Jain<sup>2</sup>, Anjan Dhua<sup>2</sup>, Devendra Yadav<sup>2</sup>, Shah Khan<sup>3</sup>, Adarsh Barwad<sup>4</sup>, Asit Mirdha<sup>4</sup>, Ahitagni Biswas<sup>5</sup>, Deepam Pushpam<sup>1</sup>, Sameer Bakhshi<sup>1</sup>

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**Background and Aims:** Ewing sarcoma (ES)  $<$ 5 years accounts for 10-15% of all cases and have distinct clinical presentations and survival outcomes. Data in this age group is scarce. We evaluated clinical features, outcomes, and prognostic factors of ES among children  $\leq$  5 years.

**Methods:** The study included consecutive patients with ES registered at our centre between 2003-18. Baseline clinical presentation, treatment details, and outcomes were retrieved from the hospital database. Prognostic factors for survival were identified using multivariable Cox regression. The clinical features and survival outcomes of children  $\leq$  5 years were compared with those  $>$ 5 years by chi-square and log-rank tests.

**Results:** Of the 859 ES patients included, 86 (10%) were  $\leq$  5 years of age [median age 4 years, 60 males (69%), and median symptom duration 3 months]. Twenty-five children (29%) had extra-osseous primary tumours, and baseline metastases was observed in 24 patients (28%). Extremity tumours were most common [33/86 (37.5%)], followed by thorax [23/86 (26.7%)] and head and neck [19/86 (22.09%)]. 57/86 children (66.3%) received local treatment (surgery alone 21/86 (24.4%), radiation alone 25/86 (29.1%), or both 11/86 (12.8%)). Median event-free-survival (EFS) and overall-survival (OS) 25.6 months and 68.7 months respectively. Metastatic disease independently predicted inferior OS (HR=2.61,  $p=0.024$ ) and EFS (HR=2.46,  $p=0.009$ ), and symptom duration  $\leq$  3 months (HR=2.26,  $p=0.047$ ) predicted inferior OS. Compared to age  $>$ 5 years ( $n=773$ ), younger children have more head and neck and less pelvic primaries ( $p=0.021$ ), are less likely to have baseline metastases ( $p=0.030$ ) and have superior OS (68.7m vs 29.2m,  $p=0.032$ ). Age  $\leq$  5 years predicted superior OS (HR=0.57,  $p=0.018$ ) independent of tumor size or metastases in the entire cohort.

**Conclusions:** Patients  $\leq$  5 years have more localised disease, and better outcomes than those  $>$ 5 years, even when adjusted for upfront metastasis and tumor size, likely due to differences in tumor biology.

O112/#825 | IPSO

IPSO: BEST POSTER SESSION

13-10-2023 08:40 - 09:40

### APPLICATION EXPERIENCE OF DA VINCI ROBOT IN ADRENAL TUMOR RESECTION IN CHILDREN

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**Background and Aims:** This paper summarizes and analyzes the application experience of da Vinci surgical robot in children's adrenal tumor surgery, and discusses the safety and feasibility of da Vinci surgical robot in children's adrenal tumor surgery.

**Methods:** From April 2020 to August 2022, 28 children with adrenal tumors who were hospitalized in the Department of Oncology, Children's Hospital, Zhejiang University, School of Medicine, and underwent da Vinci robot-assisted laparoscopic adrenal tumor resection were collected. Among them, there were 13 males and 15 females, with an average age of (6.11 $\pm$ 4.18) years old. The perioperative period and follow-up status of tumor pathological type, size, operation time, intraoperative bleeding, and postoperative hospital stay were summarized and analyzed.

**Results:** 28 children with adrenal tumors underwent surgical interventions, with 3 cases of adrenalectomy and 25 cases of partial adrenalectomy being performed. No operative deaths were reported. The distribution of tumors was 14 left and 14 right adrenal tumors, with a mean longest tumor diameter of (3.7 $\pm$ 1.5) cm. The mean operation time was (126.8 $\pm$ 56.7) min, the mean blood loss during the operation was (7.3 $\pm$ 4.7) ml. There were no postoperative complications, all patients were successfully discharged from the hospital. Seven patients with larger tumors and longer operation times required postoperative monitoring and treatment in SICU, all recovered well. The average cost of treatment was 74303.4 $\pm$ 6058.2 CNY. Pathological assessments revealed a predominance of neurogenic tumors, including neuroblastoma, ganglioneuroblastoma, and ganglioneuroma, as well as adrenal hyperplasia and adrenal cortical tumor. After a follow-up period of 2-24 months, all patients showed no recurrence.

**Conclusions:** The da Vinci robot has shown to be a safe and feasible option for children with adrenal tumors, with appropriate patient

selection criteria. The robot-assisted approach enables the preservation of adrenal gland tissue in most cases. Nevertheless, the cost associated with this technology remains relatively high in the current clinical setting.

O113/#860 | IPSO

IPSO: BEST POSTER SESSION

13-10-2023 08:40 - 09:40

### CYTOREDUCTIVE SURGERY (CRS) AND HYPERTHERMIC INTRAPERITONEAL CHEMOTHERAPY (HIPEC) FOR PERITONEAL MALIGNANT TUMORS IN CHILDREN: INITIAL EXPERIENCE IN A SINGLE INSTITUTION

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**Background and Aims:** Peritoneal malignant tumors in children are rare but commonly associated with disease progression and poor outcome. The successful treatment experience of cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) in adult peritoneal carcinoma has been applied to pediatric peritoneal malignancy in recent years. However, patients with desmoplastic small round cell tumor (DSRCT) accounted for the majority of patients treated with CRS and HIPEC in previous studies with unclear outcomes. The role of CRS and HIPEC remains controversial due to the rarity of the disease and the limited sample size of studies. We present our experience in the treatment of pediatric peritoneal malignancies using CRS and HIPEC, with more emphasis on the safety, feasibility, and short-term outcome.

**Methods:** A retrospective query from December 2019 to February 2022 identified 19 children with peritoneal malignancies who underwent CRS and HIPEC in our institution. Clinical characteristics, therapies, and outcomes were summarized and analyzed.

**Results:** The median age was 6.4 years (range, 0.7–13.9 years). The histologic types included rhabdomyosarcoma (7), Wilms tumor (2), clear cell sarcoma of the kidney (2), undifferentiated sarcoma (2), immature teratoma (1), peritoneal serous carcinoma (1), malignant rhabdoid of the kidney (1), malignant germ cell tumor (1), neuroblastoma (1), and epithelioid inflammatory myofibroblast sarcoma (1). The median peritoneal carcinomatosis index was 5 (range, 2–21). There were no perioperative deaths or life-threatening complications of CRS and HIPEC. Two patients had grade 3 complications of wound infection and wound dehiscence. With

a median follow-up time of 14 months (range, 1.5–31 months), 14 patients were alive, and 5 died of tumor recurrence.

**Conclusions:** CRS and HIPEC are safe and feasible in children, without increasing serious complications in the peri- and postoperative periods. The short-term outcome shows possible effectiveness in pediatric peritoneal malignant tumors. The long-term effectiveness needs to be verified by additional cases and long-term follow-ups.

O114/#497 | IPSO

IPSO: BEST POSTER SESSION

13-10-2023 08:40 - 09:40

### SATISFACTION OF PAEDIATRIC ONCOLOGY PATIENTS, SURVIVORS AND NURSES WITH THE LOCATION OF TOTALLY IMPLANTABLE VENOUS ACCESS PORTS (SPACE-STUDY)

Ceder Van Den Bosch<sup>1</sup>, Cornelus Van De Ven<sup>2</sup>, Caroline Hulsker<sup>1</sup>, Guus Bökkerink<sup>1</sup>, Sheila Terwisscha Van Scheltinga<sup>1</sup>, Marianne De Wetering<sup>3</sup>, Maria Koopman<sup>4</sup>, Heleen Van Der Pal<sup>5</sup>, Marc Wijnen<sup>1</sup>, Alida Van Der Steeg<sup>1</sup>

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**Background and Aims:** This study was performed to compare totally implantable venous access ports inserted for paediatric oncologic treatment at the anterior thoracic wall, above the breast ("high"), to ports at the lateral thoracic wall, below the breast ("low"), in terms of satisfaction.

**Methods:** Paediatric oncology patients (≥8 yrs.), parents (patient <8 yrs.), survivors and nurses of the Princess Máxima Centre for paediatric oncology, the Netherlands, completed a survey from 05-2022 until 03-2023. Participants were equally distributed in terms of sex and port position (excl. survivors who only received high ports). The survey consisted of questions regarding scar-related symptoms and preferred port position. Patients, parents and nurses were additionally asked questions regarding port-related hindrance during daily life. For survivors, scar appearance was assessed using the Patient and Observer Scar Assessment Scale (POSAS 2.0); a high score (i.e. very different compared to normal skin) was defined as a score of >75<sup>th</sup> percentile.

**Results:** In total, 146 participants were included; 42 patients, 41 parents, 31 survivors, and 32 nurses. All participants experienced minimal scar-related symptoms or port-related hindrance, slightly more hindrance was experienced when the port was connected. Regarding scar appearance, a high score for 8 (22%) of 36 high scars was reported by

survivors. The surface of all scars was expanded, which was very extensive for 5 (14%) of 35 high scars as reported by the researcher. No difference in median scores between a high versus low port position, and observer versus survivor was observed. A high position was preferred due to increased mobility. A low position due to less visible scars and easier access to the port.

**Conclusions:** Satisfaction did not differ between a high and low port position. The port position should be chosen by patients/parents based on the (dis-)advantages of each position, as identified by this study.

O115/#1174 | IPSO

IPSO: BEST POSTER SESSION

13-10-2023 08:40 - 09:40

#### IRINOTECAN AS SALVAGE THERAPY FOR RECURRENT HEPATOBLASTOMA(HB): OUTCOME FROM A TERTIARY CARE CENTRE IN A LOW AND MIDDLE INCOME COUNTRY OVER A 15 YEAR PERIOD

Sampreeti Mukherjee<sup>1</sup>, Apoorv Singh<sup>1</sup>, Anjan Dhua<sup>2</sup>, Vishesh Jain<sup>2</sup>, Sameer Bakhshi<sup>3</sup>, Devasenathipathy Kandasamy<sup>4</sup>, Manisha Jana<sup>5</sup>, M. Srinivas<sup>1</sup>, Veereshwar Bhatnagar<sup>6</sup>, Sandeep Agarwala<sup>2</sup>

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**Background and Aims:** There is no consensus on best salvage therapy for recurrent hepatoblastoma (HB) and the survival for these patients is dismal. This study aims to evaluate the outcome of children with recurrent hepatoblastoma (HB) treated with Irinotecan, a semi-synthetic camptothecin analogue topoisomerase-I inhibitor.

**Methods:** A Retrospective review from records of children with recurrent HB from 2007-2022, treated with irinotecan. Overall response to Irinotecan treatment and the outcome of patients was evaluated. Kaplan Meier survival estimates for a 2-year overall survival (OS), Median survival time (MST) and event free survival (EFS) was calculated. Events being re-recurrence, progression, or death.

**Results:** Seventeen children with age range of 6-60 months (median 16) were enrolled. They were 2(11.7%), 3(17.6%), 11(64.7%) and 1(5.8%) patients of PRETEXT 1,2,3 and 4 groups respectively. Five (30%) were standard risk while 12(70%) were high risk at initial presentation. Recurrence occurred during adjuvant chemotherapy in 4(23.5%) and after completion of chemotherapy in 13 (76.4%). Median time to recurrence from diagnosis was 11months (range 2-36m). The recurrences were local in 9 (52.9%), pulmonary in 7 (41.1%) and both in 1 (5.8%).

After salvage chemotherapy, 3 (17.6%) good response, 4 (23.5%) partial response, 10 (59%) progressive disease. One achieved complete response on chemotherapy. Nine (53%) underwent resection of recurrence of whom, 3 are alive and disease free while 3 died on therapy; 3 alive with progressive disease. Remaining 7 could not be resected (2 died on therapy; 5 progressive disease). 2-year EFS was 27.8% (95 CI:1.8-53.8); 2-year OS 57.8% (95 CI:27.6-88.0), with Median Survival Time from diagnosis at 16 months (6-185). At last follow up, 4 (23.5%) were alive and disease free.

**Conclusions:** Irinotecan salvage therapy for recurrent HB resulted in good or partial response in 42% cases and disease-free survival in 23.5% of cases.

O116/#1550 | IPSO

IPSO: BEST POSTER SESSION

13-10-2023 08:40 - 09:40

#### MANAGEMENT OF RESIDUAL PAEDIATRIC PANCREATIC NEUROENDOCRINE TUMOUR WITH PEPTIDE RECEPTOR RADIONUCLIDE THERAPY

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**Background and Aims:** Zollinger-Ellison Syndrome (ZES) in children is reported as only 1% of all cases. Metastatic neuroendocrine tumours are even more rare in childhood and present diagnostic and therapeutic challenges. This report aims to discuss the role of peptide receptor radionuclide therapy (PRRT) in the management of gastrinoma.

**Methods:** A thirteen-year-old male presented with symptoms of abdominal pain, diarrhoea, vomiting and upper gastrointestinal (UGI) bleeds due to multiple ulcers in duodenum and stomach diagnosed on UGI endoscopy. CECT showed a localised mass in the head and neck of pancreas with somatostatin receptor (SSTR) positivity on 68Ga-DOTA-NOC PET-CT. No metastatic deposits were identified on imaging. There was no syndromic association like Multiple Endocrine Neoplasia (MEN) syndrome. Serum gastrin and chromogranin levels were raised while exocrine pancreatic functions were normal. Image guided FNAC showed malignant pancreatic neuroendocrine tumour (PNET). The mass was enucleated along with lymphadenectomy of clinically enlarged nodes identified along middle colic artery and gastrohepatic ligament. Histopathology confirmed a WHO grade 2 PNET with involved lymph nodes. Post operatively the patient was



asymptomatic however, the gastrin levels remained high and 68Ga-DOTA-NOC PET-CT scan was suggestive of SSTR positive residual disease in peripancreatic nodes. The child was administered 1 cycle of 150mCi Lu-117 DOTATATE therapy as PRRT and post procedure scan showed no residual disease. The serum gastrin levels showed a serial decline, with no brunt on the renal function. The child is asymptomatic on follow up with no residual disease and normal serum gastrin levels.

**Results:** This case highlights the role of 68Ga-DOTA-NOC PET-CT for the diagnosis of pancreatic neuroendocrine tumours and of Lu-117 DOTATATE based PRRT for the management of residual or recurrent deposits in these tumours. PRRT showed a desirable outcome in a single cycle with good tolerance.

**Conclusions:** PRRT is a safe and effective management strategy for neuroendocrine tumours in paediatric population.

O117/#312 | Free Paper Session (FPS)

FPS 05: SUPPORTIVE CARE - MANAGING INFECTION

13-10-2023 08:40 - 09:40

#### EXAMINING THE IMPACT OF MULTI-DRUG RESISTANT BACTERIA COLONIZATION ON INDUCTION CHEMOTHERAPY OUTCOMES IN ACUTE LEUKEMIA PATIENTS: A PROSPECTIVE STUDY

Venkatraman Radhakrishnan<sup>1</sup>, Perraju Bhaskar Bhuvan Lagudu<sup>1</sup>, Varalakshmi Vijaykumar<sup>2</sup>, Jayachandran Perumal Kalaiyarasi<sup>1</sup>  
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**Background and Aims:** Patients with acute leukemia receiving induction chemotherapy are at high risk of developing infections due to immunosuppression. Multi-drug resistant (MDR) bacteria have been associated with increased morbidity and mortality in these patients. The purpose of this prospective study was to assess the prevalence of MDR bacteria in stool cultures of patients with acute leukemia during induction chemotherapy and correlate it with patient outcomes.

**Methods:** The study included 200 patients aged between 1-60 years with newly diagnosed acute lymphoblastic leukemia (ALL) or acute myeloid leukemia (AML) planned for intensive induction chemotherapy. Stool cultures were collected on day 1 and day 15 of induction. The routine bacterial culture method was used for culture and sensitivity.

**Results:** Of the 200 patients enrolled between January-2018 and March-2020, 193 patients could provide stool samples on day 1 and 185 on day 15. The median age was 13 years, 61% were males, 81% had ALL, and 19% had AML. Day 1 stool cultures were positive in 35.7% of patients, and all grew MDR bacteria. Day 15 stool cultures were positive in 36.7% of patients, and all grew MDR bacteria. MDR E.coli and MDR Enterococcus faecium were the most common organ-

isms isolated. Positive day 15 stool cultures but not positive day 1 stool cultures were significantly associated with positive blood cultures, mortality, infections, febrile neutropenia, hypoalbuminemia, inotropic support, not attaining remission, and AML. Day 1 and day 15 stool culture positivity did not significantly correlate with age, sex, nutritional status, diet (neutropenic vs. regular), and induction duration.

**Conclusions:** Colonization with MDR bacteria in stools on day 15 of acute leukemia induction is associated with an increased incidence of infections, intensive-care admissions, and mortality. These findings suggest that surveillance of stool colonization with MDR bacteria during induction chemotherapy could help identify patients at high-risk of poor outcomes and guide antimicrobial therapy.

O118/#671 | Free Paper Session (FPS)

FPS 05: SUPPORTIVE CARE - MANAGING INFECTION

13-10-2023 08:40 - 09:40

#### IMMUNE RESPONSE TO SARS-COV-2 VACCINATION IN CHILDREN AND ADOLESCENTS WITH CANCER

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**Background and Aims:** Community precautions for COVID-19 have been reduced following vaccination and lower morbidity in the general population. Children with cancer are a vulnerable population where information regarding vaccine induced protection is important.

**Methods:** Children and adolescents with cancer aged 5 to 19 years of age were recruited to a prospective study of SARS-CoV-2 vaccine response (SerOzNET) prior to BNT162b2 vaccination given as 2-3 priming doses +/- booster. Serial blood samples were analysed for neutralising antibody (NAb) and T cell response. Patients were followed until 6 months post 2<sup>nd</sup> dose or 3 months post final dose, whichever was later.

**Results:** Participants: 114 enrolled, the median age was 13 years (range 5-19), 69% have haematological and 31% solid cancers. Chemotherapy was received within 28 days of first vaccination in 70%. NAb: Detectable NAb responses increased over time: 62% and 84% at 1- and 3-months post 2<sup>nd</sup> dose respectively and 82% and 100% at 1- and 3-months post third dose, respectively. Receipt of chemotherapy within

28 days of enrolment reduced response rate compared to non-receipt (54 vs. 81% post dose 2 ( $p=0.04$ ), 79 vs. 100% post dose 3 (n.s.)). NAB response to Omicron was tested in 54 patients and detected in 13% at baseline, then 18%, 48%, and 67% at 1 month post 1<sup>st</sup>, 2<sup>nd</sup>, and 3<sup>rd</sup> dose respectively. T cell response: The proportion of children with detectable IFN- $\gamma$  response to Spike antigen increased with each dose, from 38% at baseline to 57% post dose 1, 68% post dose 2 and 75% post dose 3.

**Conclusions:** Immunocompromised children with intensive chemotherapy treatment develop likely protective immune responses with 3 doses of standard BNT162b2 vaccination. Chemotherapy within 4 weeks of first vaccination reduces likelihood of response, children on active chemotherapy may benefit from additional vaccine doses. Acknowledgements: Katie Lineburg and Anouschka Akerman.

O119/#662 | Free Paper Session (FPS)

#### FPS 06: BASIC AND TRANSLATIONAL RESEARCH IN NEUROBLASTOMA

13-10-2023 08:40 - 09:40

#### WHOLE EXOME SEQUENCING AND MORE TARGETED APPROACHES IN LIQUID BIOPSY FOR DIAGNOSTIC, PROGNOSTIC AND MINIMAL RESIDUAL DISEASE DETECTION IN NEUROBLASTOMA

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**Background and Aims:** Liquid biopsies allow detailed analysis of the genomic tumor profile in body fluids. We showed previously, the prognostic relevance in high-risk neuroblastoma of minimal residual disease (MRD) detection by combining real-time quantitative PCR (qPCR) mRNA and cell-free DNA (cfDNA) by droplet digital PCR (ddPCR). We now investigated the potential application of Whole-Exome Sequencing to detect copy-number and single-nucleotide variants in liquid biopsies in comparison with qPCR and ddPCR.

**Methods:** In  $n=29$  peripheral blood (PB) and bone marrow (BM) samples from 20 patients with high-risk neuroblastoma, both cfDNA and mRNA were analyzed: ctDNA by both WES and methylated *RASSF1A* (*RASFFA-M*) ddPCR; mRNA by the adrenergic (ADRN) NB-mRNA qPCR panel (*PHOX2B*, *TH*, *DDC*, *CHRNA3* and *GAP43* and *DBH* for BM and PB), and mesenchymal (MES) NB-mRNA panel (*FMO3*, *PRRX1* and *POSTN*).

**Results:** cfDNA sequencing results mimic the paired tumor DNA for almost all recurrent aberrations (e.g. *MYCN* and *ALK* amplification, 1p

loss, 11q loss and 17q gain). However, additional copy-number aberrations were detected in the plasma. Moreover, cfDNA sequencing of paired PB and BM plasma ( $n=12$ ) were concordant in 11/12 samples. The ADRN mRNA-panel (24/29) and MES mRNA-panel (2/29) was detected in paired samples. High BM ADRN mRNA-levels correlated with MES mRNA-positivity and high BM ctDNA levels. Lastly, the level of *RASSF1A-M* detected by ddPCR mimicked the aggressiveness of the tumor as analyzed by WES.

**Conclusions:** We demonstrate the feasibility to study liquid biopsy approaches in paired samples at diagnosis and for MRD testing by WES, ddPCR and mRNA qPCR. To establish the optimal liquid biopsy panel, this is an important outcome, which will be further studied in the ongoing SIOPEN HR-NBL2 study. This will also help determining the exact clonal and (sub)clonal compositions of the neuroblastoma tumor and to develop both tumor and patient-specific evolutionary trajectories.

O120/#680 | Free Paper Session (FPS)

#### FPS 06: BASIC AND TRANSLATIONAL RESEARCH IN NEUROBLASTOMA

13-10-2023 08:40 - 09:40

#### A NOVEL AMINO ACID METABOLISM-RELATED AND IMMUNE-ASSOCIATED GENE RISK SIGNATURE FOR PREDICTING PROGNOSIS IN NEUROBLASTOMA

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**Background and Aims:** The metabolic changes of amino acids have significant effects on cancer cells, and their immune-microenvironment. However, the features of the amino acid metabolism-related and immune-associated gene set have not been systematically described in neuroblastoma.

**Methods:** RNA expression and clinical data were downloaded from the Gene Expression Omnibus (GEO) and the Therapeutically Applicable Research to Generate Effective Treatments (TARGET) database, which was used as a training set and validation set, respectively. Different bioinformatics and statistical methods were combined to construct a robust amino metabolism-related and immune-associated risk signature for distinguishing prognosis and clinical pathology features. Furthermore, external validation of C19orf48 expression was conducted in 69 patients with neuroblastoma at our hospital.

**Results:** The amino acid metabolism-related genes had significant correlations with prognosis. The patients in Cluster A demonstrated better survival, higher immune scores, and higher microenvironment scores. Amino acid metabolism-related genes with prognostic values were also used to construct a risk model and patients in the

low-risk group were associated with improved outcomes. Sankey diagram showed that the different clusters demonstrated closer correlations with live status compared with different risk groups. The GSEA results demonstrated that Cluster A and Cluster B participated in different pathways. The patients with higher immune scores had better survival. WGCNA identified three gene modules correlated with the amino acid metabolism-related genes and the immune cell infiltrations. Among those hub genes, we found that C19orf48 was upregulated in tumors of patients with worse outcomes and was an independent risk factor ( $P=0.049$ ). In validation, Patients with high expression of C19orf48 had lower five-year event-free survival (EFS) ( $P=0.030$ ).

**Conclusions:** A novel amino acid metabolism-related and immune-associated risk signature for predicting prognosis in neuroblastoma has been constructed and identified as a potential novel biomarker.

O121/#1183 | Free Paper Session (FPS)

#### FPS 06: BASIC AND TRANSLATIONAL RESEARCH IN NEUROBLASTOMA

13-10-2023 08:40 - 09:40

#### MTHFD1 REGULATES NADPH REDOX HOMEOSTASIS IN MYCN AMPLIFIED NEUROBLASTOMA

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**Background and Aims:** MYCN amplification is an independent risk factor for patients with neuroblastoma (NB). The  $\alpha$ -helical structure of MYCN protein makes it difficult to pharmacologically target, and cause a lack of effective therapies for targeting MYCN. Investigation into the exact molecular mechanism of MYCN amplified NB tumorigenesis will pave the way for novel therapy.

**Methods:** Differentially expressed genes in MYCN amplified and non-amplified NB were identified based on TARGET database, among which MTHFD1 was highly expressed and correlated with poor prognosis of patients. Both functional experiments and animal experiments demonstrated the tumor-promoting role of MTHFD1. CHIP-qPCR and double luciferase reporter gene assay were conducted to illustrate the interaction between MYCN and MTHFD1. Regulation of MTHFD1 on NADPH redox homeostasis was explored by detecting nadp+/nadph, gsh/gssg ratio and reactive oxygen species; The synergistic inhibitory effect of folic acid cycle inhibitor methotrexate (MTX) and JQ1, an inhibitor of bromodomain and extraterminal domain, were also evaluated in MYCN amplified NB cells.

**Results:** MTHFD1 was highly expressed in NB tumor tissues and MYCN amplified cell, and correlated with poor prognosis of patients with MYCN-amplified NB. MTHFD1 promoted NB cell proliferation,

migration, and inhibited apoptosis, and it promoted tumorigenesis in NCG mice; Besides, MYCN specifically bound to the promoter of MTHFD1 to regulate its expression, and led to the imbalance of redox homeostasis and reduction of cell apoptosis by producing NADPH. The folic acid cycle inhibitor MTX synergistically combined with JQ1 to inhibit the proliferation of MYCN-amplified NB both in vitro and in vivo.

**Conclusions:** MTHFD1 is an oncogene in NB and is transcriptionally regulated by MYCN, causing the imbalance of NADPH redox homeostasis. MTX and JQ1 can jointly inhibit tumor growth in MYCN amplified NB; MTHFD1 may be a promising therapeutic target for MYCN-amplified NB, and the combination of MTX and JQ1 has clinical translational significance.

O122/#729 | Free Paper Session (FPS)

#### FPS 06: BASIC AND TRANSLATIONAL RESEARCH IN NEUROBLASTOMA

13-10-2023 08:40 - 09:40

#### A MYCN-INDEPENDENT MECHANISM MEDIATING SECRETOME REPROGRAMMING AND METASTASIS IN MYCN-AMPLIFIED NEUROBLASTOMA

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**Background and Aims:** MYCN amplification (MNA) is a defining feature of high-risk neuroblastoma (NB) that predicts dismal prognosis. However, whether genes within or in close proximity to the MYCN amplicon also contribute to aggressiveness in MNA+ NB remains poorly understood. GREB1 (Growth Regulating Estrogen receptor Binding 1) is a transcription factor-encoding gene neighboring the MYCN locus, which is a crucial estrogen receptor (ER) regulatory factor and oncoprotein in multiple hormone-dependent cancers. In support of a proto-oncogenic function of GREB1, multiple fusion genes involving GREB1 have been identified in cancer.

**Methods:** We probed the co-amplification and co-expression of various genes neighboring the MYCN locus, including GREB1, in multiple genomic and transcriptomic datasets of NB. We evaluated the oncogenic function of GREB1 in MNA- and MNA+ NB cells in 2D and 3D conditions. We integrated various transcriptomic, ChIP-seq, and proteomic datasets to identify effector genes controlled by GREB1 that are highly expressed in MNA+ NB but independently of MYCN

regulation. We evaluated NB cell extravasation and metastasis using a chick chorioallantoic membranes metastasis model. For secretome profiling, we employed pSILAC-Click to specifically label and purify cell-derived proteins in conditioned media.

**Results:** We uncover that *GREB1* is frequently co-expressed with *MYCN*, and promotes cell survival in *MNA+* NB. *GREB1* controls gene expression independently of *MYCN* in *MNA+* NB, among which we identify Myosin 1B (*MYO1B*) as being highly expressed in *MNA+* NB. *MYO1B* promotes aggressive features, including NB cell invasion and metastasis. Global secretome and proteome profiling further delineate *MYO1B* as a major regulator of secretome reprogramming in *MNA+* NB cells. Moreover, we identify the cytokine MIF as an important pro-invasive and pro-metastatic mediator of *MYO1B* activity.

**Conclusions:** Therefore, we have identified *GREB1* as a previously uncharacterized proto-oncogene in *MNA+* NB that functions independently of *MYCN*, and delineated the *GREB1-MYO1B-MIF* axis as a crucial pro-metastatic in this aggressive malignancy.

O123/#1546 | PROS

PROS: FREE PAPER SESSION 02

13-10-2023 08:40 - 10:20

#### TEXTURE ANALYSIS FOR PROGNOSTICATION OF PEDIATRIC NASOPHARYNGEAL CARCINOMA TREATED WITH INTENSITY MODULATED RADIATION THERAPY (IMRT) & CHEMOTHERAPY

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**Background and Aims:** Pediatric Nasopharyngeal carcinoma is treated with a combination of Radiation Therapy (RTh) and Chemotherapy (CTh). Despite optimum treatment, a significant proportion of patients develop regional and distant metastasis. Similar

patient groups treated with identical protocols have different outcomes. This could be attributed to intra-tumoural heterogeneity. Texture analysis of pre-treatment PET-CT scan may help identify patients at higher risk of locoregional and distant relapse.

**Methods:** Patients <18 years, treated with RTh & CTh between January 2005 & January 2019 were accrued for evaluation. First order radiomic features of primary tumour and metastatic nodes were extracted using the TexRAD software for texture analysis using pre-treatment PET-CT images and were correlated with locoregional control (LRC), progression free survival (PFS), distant metastasis free survival (DMFS) and overall survival (OS).

**Results:** Fifty-eight patients were analysed. For primary tumour, at spatial scale filter (SSF2), standard deviation (SD) of pixel intensities > -29.9 resulted in inferior PFS (p=0.02) & OS (p=0.01). DMFS was superior at the median < -29.9 (p=0.02). Similarly at SSF3, skewness > -2.6 correlated with superior OS, PFS and DMFS (p= 0.03, 0.05 and 0.01 respectively). Kurtosis < 1.96 at SSF5, resulted in superior 5year OS (p= 0.07). At SSF2 and 3, higher values of entropy correlated with higher DMFS (p=0.07). For nodal disease, the SD of pixel intensities at SSF 6, values > 80.6 correlated with higher LRC (p=0.05). In the absence of any filter, nodal kurtosis < 3.1 resulted in superior median PFS, OS and DMFS (p=0.047, 0.03 and 0.002 respectively). On multivariate analysis, kurtosis retained the statistically significant correlation with PFS (p=0.002, 95% CI=1.022-1.104) and OS (p=0.03, 95% CI=1.005-1.062).

**Conclusions:** Pre-treatment CT based texture features correlated with intra-tumour heterogeneity. First order radiomic features correlated with LC, PFS, DMFS, & OS both for primary & nodal disease.

O124/#185 | PROS

PROS: FREE PAPER SESSION 02

13-10-2023 08:40 - 10:20

#### REDUCING DOSE TO DENTOFACIAL STRUCTURES: A PENCIL-BEAM SCANNING PROTON THERAPY AND VOLUMETRIC-ARC THERAPY PHOTON TREATMENT PLANNING COMPARISON STUDY

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**Background and Aims:** In children, radiation to dentofacial structures (DFS) can result in long-term functional and psychological sequelae. We report on a proton and photon planning comparison study to explore the feasibility of dose reduction to DFS.

**Methods:** Five rhabdomyosarcoma cases with dentofacial sequelae post passive-scattered proton therapy were included: three (mandible/paranasal sinus/parotid), treated sequentially in two-phases (36Gy+14.4Gy); two (orbital/soft palate), in single-phase (41.4Gy). Eleven DFS were retrospectively delineated using an in-house atlas. All cases were replanned with pencil-beam scanning (PBS) and volumetric-arc therapy (VMAT). The two-dose level cases were planned using simultaneous-integrated boost (SIB)-PBS and SIB-VMAT with current standard-of-care doses (42.5Gy/50.4Gy). Dose constraints from a separate study (under publication) of 34 patients with dentofacial effects (mean dose in GyEQD<sub>2</sub>) were used: ethmoid 26, mandible 41, maxilla\_left/right 34, nasal bone 31, orbits\_L/R 36, sphenoid\_L/R 27, temporomandibular joints (TMJs) 29, dentition 20. Target coverage was prioritised. Mean doses to DFS were compared between techniques.

**Results:** For the soft palate case, constraints for all DFS were met with either PBS or VMAT. For the orbital case, PBS enabled greater sparing of TMJs (0.2Gy vs. 5.7Gy) and sphenoid\_R (4.2Gy vs. 9.5Gy), whilst the nasal bone constraint was exceeded (PBS and VMAT). For the large midline paranasal sinus case, minimal differences were observed across all techniques. For the mandible case, SIB-PBS permitted more sparing, particularly when compared to SIB-VMAT. SIB-PBS maxilla\_R dose was 20.0Gy vs. 24.8Gy and orbit\_R 13.4Gy vs. 15.2Gy. For the parotid, where a range shifter was applied for PBS, doses to sphenoid\_L (14.8Gy vs. 13.0Gy), sphenoid\_R (42.5Gy vs. 38.3Gy) and orbit\_R (22.6Gy vs. 18.2Gy) were higher compared to VMAT. SIB in both modalities allowed better structure sparing.

**Conclusions:** Contouring and use of constraints for DFS facilitates individualised planning. SIB allowed better dose-sparing of DFS whilst PBS potentially offers further sparing in most cases. Further work is ongoing.

O125/#982 | PROS

PROS: FREE PAPER SESSION 02

13-10-2023 08:40 - 10:20

## INHIBITION OF ATM KINASE BY THE CNS-PENETRANT AZD1390 ENHANCED RADIOTHERAPY IN NEUROBLASTOMA AND RHABDOMYOSARCOMA PRECLINICAL MODELS

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**Background and Aims:** **Background:** Most cancers use telomerase (TA+) to maintain replicative immortality, while ~10% use alternative lengthening of telomeres (ALT). Approximately 22.5% of high-risk neuroblastomas (NB) are ALT, which confers a poor prognosis, most likely due to ataxia-telangiectasia mutated kinase (ATM)-mediated chemotherapy resistance, which is reversible with ATM inhibition. Some pediatric sarcomas utilize ALT and manifest elevated ATM activation; thus, we hypothesized ATM inhibition could enhance radiotherapy (RT) in ALT pediatric solid tumors. **Aim:** Evaluate RT response in combination with AZD1390 in pediatric solid tumor patient derived cell lines (PDCLs) and xenografts (PDXs).

**Methods:** PDCLs, cultured in physiological hypoxia (pO<sub>2</sub> = 5%), were dosed with AZD1390 24 hours before 2.5 Gy irradiation. Cytotoxicity was assessed 7 days thereafter by DIMSCAN. PDXs were grown subcutaneously in nu/nu mice. Shielded mice received 10 mg/kg AZD1390 gavage 1 hour prior to 2.5 Gy, for 3 cycles (5 days on, 2 days off), totaling 37.5 Gy.

**Results:** *in vitro*, 6/9 NB and 8/9 rhabdomyosarcoma (RMS) PDCLs had a significant (p < 0.05) cytotoxic enhancement of RT by AZD1390. *In vivo* ALT (NB = 2, RMS = 2) and TA+ RMS (N = 2) xenografts showed a significant (p < 0.05) increase in event-free survival (EFS) at 100 days. CHLA-90 NB ALT PDCL-derived xenograft AZD1390 + RT mice had 2/7 maintained complete responses (MCR) and 5/7 complete responses (CR), while 0/7 RT reached CR. The ALT RMS PDX Rh41x had 4/4 AZD1390 + RT mice in MCR at 100 days, compared to 9/9 RT mice progressing at < 40 days. All models combined resulted in median overall EFS of 66 days for RT vs 112 days for AZD1390 + RT.

**Conclusions:** AZD1390 enhanced RT in ALT and non-ALT NB and RMS preclinical models. A phase I trial of AZD1390 + RT is warranted in pediatric solid tumors.

O126/#305 | PROS

PROS: FREE PAPER SESSION 02

13-10-2023 08:40 - 10:20

**LOCOREGIONAL FAILURE IN HIGH-RISK ABDOMINAL NEUROBLASTOMA USING HIGHLY CONFORMAL IMAGE-GUIDED RADIOTHERAPY – OUTCOME AFTER CENTRALIZATION OF CARE IN THE NETHERLANDS**

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**Background and Aims:** Advanced radiotherapy modalities to irradiate neuroblastoma have stepwise replaced 2D-conventional and 3D-conformal techniques. The aim of this study was to investigate locoregional failure rate and pattern of failure after highly-conformal image-guided radiotherapy, applied since centralization of neuroblastoma care in the Netherlands (2014).

**Methods:** All patients with high-risk abdominal neuroblastoma treated with curative intent between 01-2015 and 03-2022 were eligible. Edited gross tumor volumes were defined by pre-operative imaging, endorsed by input from surgeons and radiologists, and adjusted for post-operative anatomical shifts. For clinical, internal, and planning target volume (CTV, ITV, and PTV), 0.5 cm, 4DCT-based, and 0.3–0.5 cm margins were added, respectively. Prescription dose was 21.6/1.8 Gy after complete macroscopic excision (CME), followed by 14.4/1.8 Gy in case of residual tumor  $\geq 1$  cm<sup>3</sup> (IME; incomplete macroscopic excision). Intensity-modulated arc therapy combined with daily 3D online position verification/correction was applied. Three-year cumulative incidence of locoregional failure, event-free survival (EFS), and overall survival (OS) were calculated.

**Results:** A total of 81 patients were included (median age: 4.1 years, IQR 2.7–5.9), 46 (57%) with CME and 35 (43%) with IME (median residual volume: 10.1 cm<sup>3</sup>, IQR 4.5–34.5). Mean follow-up was 5.9 years. Three-year cumulative incidence of locoregional failure was 9.9% (95% CI 3.4–16.5) and did not differ significantly between CME (8.8%, 95% CI 0.5–17.2) and IME (11.4%, 95% CI 0.7–22.1),  $P=0.71$ . Three-year EFS was 52.9% (95% CI 64.1–41.6) and three-year OS was 67.8% (95% CI 58.1–79.1). Eight patients presented with locoregional failure (three isolated and five combined), all of which occurred within two years from diagnosis.

**Conclusions:** In a setting of nationally centralized neuroblastoma care, highly-conformal target volumes using CTV margins of 0.5 cm com-

bined with image-guided radiotherapy, results in excellent locoregional control compared to current literature. A 14.4 Gy boost dose to any residual tumor  $\geq 1$  cm<sup>3</sup> may compensate for a higher risk of locoregional failure.

O127/#1385 | PROS

PROS: FREE PAPER SESSION 02

13-10-2023 08:40 - 10:20

**EVALUATING THE IMPACT OF RADIOTHERAPY TIMING AFTER PRE-OPERATIVE CHEMOTHERAPY AND SURGERY FOR PATIENTS WITH NON-METASTATIC WILMS TUMOUR IN THE UNITED KINGDOM**

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**Background and Aims:** The impact of time to radiotherapy (RT) after nephrectomy for children with Wilms' tumour (WT) following the International Society of Paediatric Oncology (SIOP) pre-operative treatment paradigm has not been evaluated. This study aims to assess whether the time to start RT has an adverse impact on the outcome of patients with non-metastatic WT enrolled in a national UK study, IMPORT, that followed the SIOP approach.

**Methods:** Patients aged  $\leq 15$  years with non-metastatic WT treated with flank RT or whole abdominal RT (WART) between 1 April 2012 and 30 June 2018 were identified from IMPORT database. Time to relapse and overall survival were investigated.

**Results:** A total of 152 patients had flank RT or WART after nephrectomy. Seventy-one out of 152 patients had non-metastatic disease. Of these, 42 patients had flank RT and 29 had WART. Median age was 3 years (range, 0–13). Most patients had intermediate risk histology (83%). The median time from surgery to RT was 40 days (range, 18–189). Median follow-up time was 50 months (range, 7–100). There were 9 relapses and 5 deaths, and no deaths where RT commenced  $< 35$  days post-surgery. Using a threshold of 40.5 days, identified through ROC analysis, logistic regression analysis highlighted a possible relationship between time to RT and survival ( $p=0.19$ ). Patients with  $\geq 40.5$  days

from surgery to flank RT had 6.6 greater relative risk compared to those who started <40.5 days ( $p=0.10$ ). Patients with  $\geq 62.5$  days from surgery to abdominal RT (flank RT or WART) had 58 greater relative risk of relapse, compared to those with <62.5 days ( $p=0.002$ ).

**Conclusions:** This study suggests a relationship between RT timing and disease outcomes in the setting of pre-operative chemotherapy for WT. The optimal timing of RT requires urgent evaluation in a larger cohort. A study looking at patients in the international SIOP RTSG database is in planning.

O128/#750 | PROS

PROS: FREE PAPER SESSION 02

13-10-2023 08:40 - 10:20

#### MULTI-SITE SBRT FOR PEDIATRIC, ADOLESCENT, AND YOUNG ADULT PATIENTS WITH OSTEOSARCOMA: LOCAL CONTROL OUTCOMES AND OPTIMAL BIOLOGIC EFFECTIVE SBRT DOSE

Jenna Kocsis<sup>1</sup>, Eashwar Somasundaram<sup>1</sup>, Timothy Smile<sup>2</sup>, Shireen Parsai<sup>3</sup>, Jake Scott<sup>1</sup>, Lilyana Angelov<sup>4</sup>, Matteo Trucco<sup>5</sup>, Peter Anderson<sup>5</sup>, Stacey Zahler<sup>5</sup>, Shauna Campbell<sup>1</sup>, Peng Qi<sup>1</sup>, Anthony Magnelli<sup>1</sup>, Erin Murphy<sup>1</sup>

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**Background and Aims:** Osteosarcoma is a radioresistant tumor that may benefit from SBRT- a non-invasive high dose highly conformal ablative radiation treatment. Data for sarcoma SBRT includes a heterogeneous population and the ideal SBRT dose strategy is not known. We aim to understand osteosarcoma specific SBRT outcomes and to find the optimal biologic effective SBRT dose for osteosarcoma.

**Methods:** We queried an IRB- approved registry of patients treated with SBRT for recurrent/metastatic osteosarcoma between 2015-2022. Patients were assessed for local control, survival, and toxicity. Rates of local control were estimated from the time of SBRT completion for each lesion treated. Survival ROC analysis at 8 months was used to determine BED cut off that maximized local control. The toxicities were graded according to CTCAE v4.0.

**Results:** Twenty-three patients with 66 lesions met eligibility criteria. Median age was 19.5 years. Forty-five lesions were osseous, 13 parenchymal and 8 soft tissue. Median dose was 40 Gy in 5 fractions (range 18-60 Gy in 1-5 fractions). Median BED was 120 Gy (range 56-323 Gy). Thirty (45.5%) lesions received concurrent therapy. Median follow-up was 9.8 months (mos). Median time from development of local recurrence/metastatic disease to SBRT was 13.7 mos. No acute

grade  $\geq 3$  toxicity was observed. Six- and 12-month local control was 89% (95% CI 0.8-0.99) and 78% (CI 66%-92%) respectively. A dose cut-off for improved local control was found at a BED of 120 Gy. Local control at one year was 89% (CI 77%-100%) for lesions that received  $\geq 120$  Gy BED versus 61% (CI 40%-91%) for those that received <120 Gy BED ( $p=0.034$ ).

**Conclusions:** Our large osteosarcoma SBRT series demonstrates that local control for recurrent and metastatic disease is possible with minimal toxicity. Local control was significantly improved with a biologically effective dose of at least 120 Gy. This approach should be further investigated on prospective trials.

O129/#824 | PROS

PROS: FREE PAPER SESSION 02

13-10-2023 08:40 - 10:20

#### EFFICACY AND TOXICITY OUTCOMES OF STEREOTACTIC ABLATIVE RADIATION THERAPY (LIGHT-SABR) FOR METASTATIC AND/OR RECURRENT PEDIATRIC CANCERS

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**Background and Aims:** Pediatric and adolescent/young adult (AYA) patients with metastatic and/or recurrent solid tumors have poor outcomes. Systemic therapy is the mainstay of treatment, with palliative radiotherapy (RT) reserved for symptom control. Stereotactic ablative radiation therapy (SABR) allows delivery of ablative doses of RT in 1-5 fractions, which may provide more durable disease control of metastatic lesions. We report our institutional local control, survival, and toxicity outcomes with the use of SABR in this patient population.

**Methods:** All pediatric and AYA patients treated with SABR from 2016 to 2022 at our institution were included in this study. Primary endpoint was local failure. Secondary endpoints were progression-free survival (PFS), overall survival (OS) and toxicity. Survival analysis was performed using Kaplan-Meier estimates in R version 4.2.3.

**Results:** Our cohort included 44 patients who received 102 SABR courses. Median age at SABR was 15.6y (range, 3.2-31.8y). Median total RT dose was 30Gy and dose per fraction was 6Gy (range 5-20Gy).

The most common histologies were Ewing's sarcoma(23%), Rhabdomyosarcoma(18%), Osteosarcoma(14%) and gliomas(14%). The most common SABR sites were spine(28.4%) followed by extraspinal osseous metastases(32.4%), lung(21.6%) and CNS(9.8%). About 59% patients had oligo-metastatic disease ( $\leq 5$  lesions) at presentation, 64% patients had prior RT, and 94% patients had received prior systemic therapy. Median follow-up was 7.5m (10.9m for surviving patients). Nine patients(8.8%) had a local failure (7 were in-field and 2 were marginal). The median PFS was 4.2m (95%CI, 3.5-5.2), while the median OS was 14.2m (95%CI, 6.7-17.1); with 1-yr PFS and OS rates of 17.3%, and 51.1%, respectively. The rate of all grade 1, 2 and 3 toxicities were 11.8%, 2.9% and 1.9% respectively, most commonly grade 1 dermatitis. No grade 4 or higher toxicities were observed.

**Conclusions:** SABR is well tolerated in pediatric patients with local failure rates of <10% and >50% 1-year survival. Further studies are needed to evaluate its role in combination with systemic therapy.

O130/#1705 | PROS

PROS: FREE PAPER SESSION 02

13-10-2023 08:40 - 10:20

#### PATTERNS OF SECONDARY MALIGNANCIES AND TUMOR RECURRENCES IN CHILDREN WITH LI-FRAUMENI SYNDROME TREATED WITH RADIATION THERAPY

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**Background and Aims:** For tumor histologies associated with Li-Fraumeni syndrome (LFS) in children, radiation therapy (RT) is an important modality for optimal local control. The risk of an in-field radiation-induced secondary malignant neoplasm (SMN) in children with LFS treated with modern RT is unknown.

**Methods:** To determine the risk of an in-field radiation-induced SMN in children with LFS, the Pediatric Proton/Photon Consortium Registry (PPCR) was queried for patient, disease, and treatment characteristics. SMN location was defined as in the RT field, on the margin of the RT field, or outside of the RT field.

**Results:** Seventeen patients with LFS treated with RT were identified. Prior to RT, one patient developed a second primary tumor (medulloblastoma after rhabdomyosarcoma [RMS]); all others received RT for their primary tumor (n=4 RMS, n=4 medulloblastoma/PNET, n=4 choroid plexus carcinoma, n=2 glioma, n=2 non-RMS sarcoma, n=1 AT/RT). Nine patients had tumor recurrence prior to RT. Median age at RT was 7.1y (range, 1.5 - 21.9y). Fourteen patients were treated with protons, two with photons, and one with combined protons/photons. Median follow-up for all patients was 21 months. Three patients (18%) developed SMN after RT. No SMN occurred in the RT field; one was a soft tissue sarcoma out of the RT field 6.4y after RT, one was a leukemia/MDS 1.9y after RT, and one was a bone sarcoma on the margin of the RT field 1.5y after RT. Four patients had tumor recurrence after RT: two local, one regional, and one distant. Median overall survival was 32 months.

**Conclusions:** In children with LFS, early results suggest that there is not an increased risk of SMN in the RT field. Primary tumor recurrence remains a risk for these patients. Longer follow up will be needed to observe patterns of SMN development and primary tumor progression over time.

O131/#1481 | PROS

PROS: FREE PAPER SESSION 02

13-10-2023 08:40 - 10:20

#### FIRST YEAR EXPERIENCE OF PAKISTAN PEDIATRIC RADIOTHERAPY PEER REVIEW NETWORK MEETINGS

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**Background and Aims:** Pakistan Pediatric Radiotherapy Peer Review Network was established to bridge the gaps in radiation therapy being offered to pediatric patients as part of their treatment plan. We aim to share our experience of peer review meetings conducted virtually at national level every month to discuss radiation therapy plans.

**Methods:** Participants from radiotherapy centers across Pakistan, invited via flyer every month to virtually discuss pediatric cases for peer review of radiation treatment plans starting June 2022. Total



number of participants in meeting, their institutes, cases discussed, their demographic details, changes suggested and treatment protocols discussed for evidence were documented in a password protected sheet.

**Results:** A total of nine meetings have been conducted to date starting June 2022 for 60 minutes each. The meetings were attended by a median of 14 participants (10-18), from thirteen institutes in Pakistan and abroad. Total (n=26) cases were discussed in 9 meetings which included Rhabdomyosarcoma (n=8), CNS tumors (n=7), Wilms (n=4), Ewing's sarcoma (n=3), Hodgkin's (n=2), osteosarcoma and paraspinal myoepithelial neoplasm, one each. Majority were male patients (n=16). The median age of patients discussed in meeting was 8 years (2-17). Changes were suggested in almost 2/3<sup>rd</sup> (n=18) of the cases discussed, which included recommendations on total radiation dose, volumes, technique, fractionation, staging, risk stratification, histopathology review, overall management plan and outcome. Moreover, treatment protocols for each tumor diagnosis were discussed for evidence and academic purposes.

**Conclusions:** Our national initiative serves as a forum to exchange knowledge, promote education and support practices in cost-constrained setting. It will help to create a meaningful impact on the outcomes of childhood malignancies in Pakistan.

O132/#1628 | PROS

PROS: FREE PAPER SESSION 02

13-10-2023 08:40 - 10:20

#### DELIVERING CENTRALISED PEER-REVIEW IN PAEDIATRIC CLINICAL TRIALS – RESULTS FOR TREATMENT PLAN REVIEWS PERFORMED BY SIOP EUROPE'S QUARTET PROJECT

Sarah Kelly<sup>1,2,3</sup>, Andrada Turcas<sup>2,3</sup>, Coreen Corning<sup>3</sup>, Tom Boterberg<sup>4</sup>, Mark Gaze<sup>5</sup>, Gail Horan<sup>6</sup>, Henry Mandeville<sup>7</sup>

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**Background and Aims:** QUARTET is a SIOP Europe project to provide centralised radiotherapy quality assurance (RTQA) for European paediatric clinical trials in order to standardise and improve the quality of radiotherapy across institutions. Prospective individual case review (ICR) of planning data allows error correction prior to treatment deliv-

ery. The aim of this study is to provide a descriptive report of the ICR outcomes since QUARTET launched in May 2016.

**Methods:** Data for all ICR submissions between 01/05/2016 and 31/10/2022 were collated and analysed. Planning and ICR submission requirements are defined per trial, within the associated RTQA guidelines. Expert clinicians and physicists perform a plan evaluation using the uploaded DICOM imaging, structure sets, and plan/dose files according to protocol requirements. Evaluation outcomes are: Per Protocol, Acceptable Variation, Unacceptable Variation, or Justified Variation.

**Results:** In total, 263 cases from 56 institutions across 15 countries were submitted for ICR for six QUARTET-affiliated trials. ICRs were completed for 252/263 cases at the time of analysis; 52.4% were performed prospectively (133/252). ICRs were accepted at first submission for 62.4% of cases, with the remainder taking an average of 1.4 submissions until approval by reviewers (average range 1-1.75). Although the initial plan rejection rate is similar between prospective and retrospective ICRs (38.4% vs. 41.3%), unacceptable variations were corrected in 92% (47/51) of prospective cases. The three main causes of unacceptable variation were target delineation (n=53), organ-at-risk dose (n=31), and target dose (n=28).

**Conclusions:** Despite availability of comprehensive RTQA guidelines, variations in planning persist in paediatric radiation oncology. This report highlights the need for prospective plan review within this cohort of patients. QUARTET will continue to provide RTQA for European clinical trials including children and adolescents with cancer. Education and practice-sharing initiatives will better support institutions to produce high-quality treatment plans and meet protocol requirements.

O133/#45 | PROS

PROS: FREE PAPER SESSION 02

13-10-2023 08:40 - 10:20

#### INITIAL REPORT OF THE SIOP EUROPE QUARTET PROJECT ON THE PROFILE OF CENTRES PARTICIPATING IN PAEDIATRIC RADIOTHERAPY CLINICAL TRIALS

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**Background and Aims:** QUARTET is a SIOPE-EORTC collaborative project for radiotherapy quality assurance (RTQA) in paediatric clinical trials. Each participating centre must undergo site RTQA approval procedures, which are streamlined across all EORTC and QUARTET trials. The process includes a Facility Questionnaire (FQ) containing multiple choice and open-ended questions detailing site infrastructure, personnel, workload, radiotherapy techniques and RTQA methods used, as well as paediatric-specific facilities. The aim of this work was to evaluate the profiles of radiotherapy centres participating in QUARTET RTQA.

**Methods:** We performed a descriptive analysis of the data collected via the QUARTET FQs. Sites that were approved for patient enrolment in EPSSG-FaR-RMS (EUDRACT 2018-000515-24), SIOPEN-VERITAS (EUDRACT 2015-003130-27) SIOPEN-HRNBL2 (EUDRACT 001068-31), SIOP-HRMB (EUDRACT 2018-004250-17) trials between October 2020- October 2022 were included.

**Results:** Currently 66 centres (59 photon and 7 proton) from 20 countries are approved to participate in QUARTET trials. Most sites are in the UK (18), France (10) and Australia (7). Molecular radiotherapy and brachytherapy are available in 12 and 19 centres, respectively. The majority (61) are paediatric referral centres, with 50 centres having designated paediatric radiation oncologists. Paediatric MDTs take place in 49 sites, with 40 having access to resources for advice on unusual or rare cases. All centres use advanced techniques and all proton centres have pencil beam scanning and IMPT. Deep sedation/general anaesthesia facilities are present in 55 sites. Forty-nine sites have paediatric-adapted protocols for CT simulation and 36 for MRI scanning.

**Conclusions:** This early data shows variability in terms of resources among sites participating in QUARTET-affiliated paediatric radiotherapy clinical trials. Most participants are reference centres for paediatric radiotherapy with the majority having paediatric-specific facilities such as designated clinicians, paediatric MDTs, and adapted imaging protocols. This is the first report from the QUARTET project, and we expect more mature data as trial recruitment increases and new trials open.

O134/#1171 | Free Paper Session (FPS)

FPS 07: EPIDEMIOLOGY I

13-10-2023 10:50 - 12:20

## IMCICA+: OPTIMIZATION OF THE "INTEGRATED MANAGEMENT FOR CHILDHOOD ILLNESSES-CANCER (IMCICA)" TO DECREASE TIME TO CANCER DIAGNOSIS IN CHILDREN BY TAILORED TRAINING OF PRIMARY HEALTHCARE PROVIDERS

Oscar Ramirez<sup>1,2,3</sup>, Jesus Ardila<sup>1,2</sup>, Romel Segura<sup>1,4</sup>, David Maldonado<sup>1,4</sup>, Karen Salinas<sup>1</sup>, Alexandra Mendoza<sup>1</sup>, Paula Aristizabal<sup>5,6</sup>

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**Background and Aims:** In low-and-middle-income countries (LMIC), delayed cancer diagnosis impacts survival. In 2013, the Pan-American Health Organization (PAHO) launched the "Integrated-Management-for-Childhood-Illnesses-CANcer" (IMCICA) module in Colombia and Honduras. After IMCICA launching, we found in Cali, Colombia's third largest city, that only 3% of primary care providers (PCP) knew IMCICA. Therefore, supported by Foundation-S, we developed and pilot-tested IMCICA+ to decrease time-to-diagnosis by adapting the IMCICA module and providing targeted training to PCP. We describe the impact of IMCICA+ on time-to-cancer-diagnosis.

**Methods:** We developed IMCICA+ by conducting focus groups with PCP to inform our training approach, adapting IMCICA to the local context, and developing a mobile app (PohemaApp) to increase uptake and use of the IMCICA decision-making tool. We measured PCP knowledge gain (pre-and post-tests), referral time to a pediatric oncology unit, and number of medical visits pre-cancer diagnosis in three time periods: 1) pre-IMCICA+ implementation (2015-2016; n patients=71), 2) during IMCICA+ implementation (2017-2018; n=240), and 3) post-IMCICA+ implementation (2019-2021; n=338). We used Kruskal-Wallis and  $\chi^2$  tests to compare median referral times and proportions of medical visits.

**Results:** During IMCICA+ implementation, we trained 1590 PCP (699 physicians, 351 nurses, 158 medical students, and 382 allied professionals) in Cali and surrounding cities. Knowledge gain was >60%. Pre-IMCICA+ implementation median referral time was 15 days, during IMCICA+ implementation was 13 days, and post-IMCICA+ implementation was 10 days ( $p=0.005$ ). The percentage of patients with >3 visits pre-IMCICA+ implementation was 16%, during IMCICA+ implementation was 7%, and post-IMCICA+ implementation was 6% ( $p<0.001$ ).

**Conclusions:** We successfully pilot-tested IMCICA+ (targeted training, local adaptation, and app development). We trained a large number of PCP on IMCICA with significant knowledge gain. IMCICA+ improved

the median referral time and decreased the number of medical visits pre-cancer diagnosis. The next steps include validating and expanding IMCICA+ in Colombia and further adaptation and testing in other LMIC.

O135/#1127 | Free Paper Session (FPS)

FPS 07: EPIDEMIOLOGY I

13-10-2023 10:50 - 12:20

#### USING QUALITY IMPROVEMENT COLLABORATIVES TO IMPROVE TIME TO ANTIBIOTIC THERAPY AMONG FEBRILE HEMATOLOGY-ONCOLOGY PATIENTS: EXPERIENCE FROM LATIN AMERICA

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**Background and Aims:** Building on the success of the 1<sup>st</sup> Mexico in Alliance with St. Jude (MAS) Collaborative, in November 2021, we launched the 2<sup>nd</sup> MAS Collaborative to increase the proportion of febrile pediatric hematology-oncology patients (fPHOP) presenting to the emergency department who receive the first dose of antibiotics in  $\leq 60$  min from a baseline of 46% to  $\geq 70\%$  across 85 hospitals from six countries (Brazil, Haiti, Mexico, Panama, Paraguay, and Peru) by May 2023.

**Methods:** This 18-month quality improvement collaborative (QIC) followed the Institute for Healthcare Improvement's Breakthrough Series Model (BTS) coupled with two certified improvement science capability-building programs. The QIC was organized around three 2-day learning sessions (LS) and three action periods (AP). During the AP, teams tested change ideas using Plan-Do-Study-Act (PDSA) cycles, attended monthly learning calls, received coaching, and reported PDSAs and data into a shared repository.

**Results:** Three LS (two virtual and one in-person), 14 learning calls, and 1,693 coaching sessions were provided to teams, and 782 PDSA cycles were documented. Participating teams reported 5,075 fPHOP visits (baseline period (BP)=986; implementation period (IP)=4,089). The median time to antibiotic administration decreased from 70 minutes (RIQ: 40-150) during the BP to 45 minutes (RIQ: 30-75) during the IP. The mean proportion of fPHOP receiving the first dose of antibiotics

in  $\leq 60$ min increased from 46.1% during the BP to 68.1% during the IP ( $p < 0.001$ ). The percentage of patients who developed sepsis decreased from 13.5% to 8.6% during the IP ( $p < 0.001$ ).

**Conclusions:** QICs are an effective method to promote the adoption of best practices, promote collaboration and shared learning across teams, and improve clinical outcomes for PHOP in Latin America.

O136/#1533 | Free Paper Session (FPS)

FPS 07: EPIDEMIOLOGY I

13-10-2023 10:50 - 12:20

#### RETROSPECTIVE COMPARATIVE ANALYSIS OF TWO INTERNATIONAL REFERRAL PATHWAYS FOR UKRAINIAN PEDIATRIC HEMATOLOGY AND ONCOLOGY PATIENTS AFFECTED BY WAR

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**Background and Aims:** The war in Ukraine significantly compromises the healthcare infrastructure and affects all aspects of patient-centered cancer care. The Supporting Action For Emergency Response (SAFER) in Ukraine initiative launched in February 2022 to address the needs of pediatric hematology-oncology (PHO) patients. In parallel, the European Union Emergency Response Coordination Center (ERCC) started a governmental evacuation process for all Ukrainians facing illness. This study describes comparative analysis of both evacuation pathways in preparation of a joint evacuation effort.

**Methods:** For SAFER, an international referral network of country coordinators was established to organize timely patient transfer by

identifying participating hospital capacity and appropriate expertise. ERCC facilitates evacuations via the Common Emergency Communication and Information System (CECIS). Using data from respective evacuation registries, a retrospective data analysis described timing and outcomes of PHO patients referred between February 24 and December 24, 2022.

**Results:** SAFER assisted 1,281 PHO patients (median age: 9 [0-22] years). Scope of support ranged from medical record translation to evacuation from Ukraine and international referral based on individual patient need. During the study period, 545 (42.54%) patients were evacuated from Ukraine through a Polish triage center to 14 European and North American countries, among those 80.55% received active cancer-directed treatment. ERCC evacuated 1,438 patients (median age: 36 [0-85] years), mostly trauma patients (81.71%) to 16 European countries. Of 498 civilian patients evacuated by ERCC, 103 were children, including 14 PHO patients. The average duration from evacuation request to final destination arrival was 8.34 days for SAFER and 9.33 days for ERCC ( $P=0.03$ ), respectively.

**Conclusions:** Both SAFER Ukraine and ERCC developed successful evacuation pathways to meet the needs of Ukrainian patients affected by war. There is a need to harmonize both efforts to sustain a collaborative, effective long-term humanitarian response and deliver safe and timely medical treatment to patients.

O137/#1249 | Free Paper Session (FPS)

FPS 07: EPIDEMIOLOGY I

13-10-2023 10:50 - 12:20

#### ESTABLISHING A SUSTAINABLE PUBLIC-PRIVATE PARTNERSHIP (PPP) MODEL FOR THE DELIVERY OF SPECIALIZED MULTIMODALITY PAEDIATRIC CANCER CARE

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**Background and Aims:** Specialised treatments such as HSCT and Orthotopic Liver Transplant(OLT) have substantially improved survival in paediatric high-risk malignancies. High quality infrastructure/expertise available for such therapies in private sector, is often underutilized, while public-sector centres are unable to meet the demand. We report our experience of setting up a PPP model for advanced therapies, to offset the waiting list at Tata Memorial Centre(TMC), Mumbai- a government funded oncology centre

**Methods:** TMC, a referral centre for high risk paediatric malignancies, on average, needs to perform 120 HSCTs(allogeneic/autologous) and 10 OLTs annually. Starting 2018, TMC established collaboration with three centres for HSCT and one for OLT. To offset costs of services, pre-transplant workup, pre/post-transplant procedures, medications required were provided from TMC. Comprehensive joint-funding mechanism(crowdfunding, NGOs, corporate/governmental grants) was established to completely obviate out-of-pocket-expenditure(OOPE). A central waitlist was maintained and virtual meetings conducted for coordination and data transfer. The number of patients treated, pre- and post-establishment of the collaborative PPP model were analyzed.

**Results:** Between 2014-2017, prior to the PPP collaboration, only about 10% of eligible patients(37/360) underwent HSCT at TMC. Post-collaboration, a total of 228 HSCTs(47% of eligible children) were performed between 2018-2022. These included 100 allogeneic and 128 autologous HSCTs. None of the eligible hepatoblastomas( $n=19$ ), between 2014-2017 underwent OLT and since PPP collaboration, 75%(18/24) of pretext IV cases underwent OLT. Transplant(HSCT) related mortality varied between 1.2-2% for autologous and 5-8% for allogeneic HSCT between centres. 3/18 OLT patients died (1-disease progression and 2-operative complications). The patients' families incurred no medical expenses in this model.

**Conclusions:** The establishment of a sustainable Public-Private collaboration in the city of Mumbai gave children with advanced malignancies a chance at cure. This model, which used the infrastructure of the private sector to cater to the high volumes in the public sector, with no OOPE, can be replicated in similar settings.

O138/#1450 | Free Paper Session (FPS)

FPS 07: EPIDEMIOLOGY I

13-10-2023 10:50 - 12:20

#### DOSE ROUNDING OF PARENTERAL CHEMOTHERAPY: A STRATEGY FOR MINIMIZING THE COST OF PEDIATRIC CANCER TREATMENT AT MBARARA REGIONAL REFERRAL HOSPITAL, UGANDA

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**Background and Aims:** The growth rate of chemotherapy expenditure surpasses that of new cancer cases; with a global market of approximately \$200 billion in 2022. The increasing burden of pediatric cancers with over 150 new cases registered annually at the pediatric unit of Mbarara Regional Referral Hospital (MRRH), increases the need for anti-cancer drugs. However, with a limited budget, the risk of drug stockout increases, interrupting treatment schedules hence disease progression and poor quality of life for children with cancer. The 5% dose-rounding of parenteral chemotherapy is a strategy that can minimize treatment cost without compromising treatment outcomes. This study aimed at determining if dose-rounding of chemotherapy is a feasible cost-saving strategy at a limited resource pediatric cancer unit.

**Methods:** The registry of MRRH Pediatric cancer unit was reviewed to identify all patients who received at least one cycle of parenteral chemotherapy between January 2022 and December 2022. Chemotherapy doses were rounded down within 5% of the prescribed dose to the nearest vial and evaluated for a potential decrease in number of vials needed to prepare the dose. The cost was represented as the shilling per vial of the drug, and based on the acquisition price. Data was analyzed using SPSS version 25.

**Results:** A total of 1221 doses of parenteral chemotherapy were prescribed for 146 patients during the study period. 147(12.0%) doses qualified for a decrease in number of vials (from 624 to 477 vials). The potential for cost-savings was Uganda shillings 20 million ( $p = 0.002$ ). A total of 12 different drugs qualified for the 5% dose rounding, mostly Ifosphamide (56/147, 38.1%), Cytarabine (30/147, 20.4 %) and Methotrexate (23/147, 15.6%).

**Conclusions:** The 5% dose rounding of parenteral chemotherapy is an effective cost-saving strategy for treating pediatric cancers in a limited resource setting. Additional studies that evaluate the impact of dose rounding on patient outcome are warranted.

O139/#598 | Free Paper Session (FPS)

FPS 07: EPIDEMIOLOGY I

13-10-2023 10:50 - 12:20

#### CREATING A RESOURCE FOR PEDIATRIC CANCER RESEARCH: US NATIONAL CHILDHOOD CANCER REGISTRY

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**Background and Aims:** The aim of this presentation is to describe the establishment of a US National Childhood Cancer Registry for the US that will serve as a resource for cancer research and discovery.

**Methods:** The US Congress has initiated a Childhood Cancer Data Initiative, with the intention of learning from every child with cancer. A cornerstone of this initiative is the establishment of a National Childhood Cancer Registry (NCCR). The NCCR builds on surveillance data collected by SEER registries supplemented by additional population based state cancer registries. Traditional cancer surveillance data will be enriched by matching to other data sources critical to pediatric cancer research such as clinical trial participation, pharmacy data, genomics, and residential histories. We will present information on the unique methods utilized to establish this resource, pitfalls encountered, plans for the future, and implications for global pediatric cancer research.

**Results:** Data from the NCCR are currently available online, and will be demonstrated during the presentation. See <https://nccrexplorer.ccdi.cancer.gov/> Additional data will be presented describing the attributes of the NCCR and underlying data.

**Conclusions:** Creating a national childhood cancer registry to serve as a research resource is essential to the understanding of pediatric cancer. Surveillance data need to be supplemented with other rich and reliable data sources to provide a meaningful resource for research. While many hurdles have presented themselves, great progress has been made which can provide lessons learned for other countries and researchers around the world. We look forward to sharing our experiences.

O140/#1089 | Free Paper Session (FPS)

FPS 08: PALLIATIVE AND SUPPORTIVE CARE

13-10-2023 10:50 - 12:20

#### THE GLOBAL NEED FOR PEDIATRIC PALLIATIVE CARE EDUCATION AND HOLISTIC MANAGEMENT OF PEDIATRIC CANCER PATIENTS: THE CREATION OF AN EDUCATION PROGRAM

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**Background and Aims:** Education in Pediatric Palliative Care (PPC) is in high demand worldwide. Lack of healthcare professional training, as well as misperceptions of families with children with cancer, have been cited as major barriers to accessing skilled PPC. Our aim is to provide knowledge and tools to health professionals who care for children with cancer in all clinical settings.

**Methods:** Based on Kern's 6-step approach for curriculum development, we developed an online education program on PPC for healthcare professionals caring for children with cancer and other catastrophic illnesses. We conducted a literature review and surveyed key subject matter experts.

**Results:** An initial literature review and environmental scan of available courses showed 14 PPC Virtual curricula available with various durations and price ranges (only 2 with free access). Most available courses were medium complexity courses for specialized training. After deliberation with an expert panel of global PPC experts and based on a needs assessment, it was decided that a shorter program would better meet the need and be more feasible and attractive for participants. Based on surveys to subject matter experts, topics were prioritized. After multiple meetings evaluating the high demand and needs of an accessible course, 7 essential modules were decided upon which include, 1)Key Concepts in PPC, 2)Integration of PPC, 3)Evaluation and Management of Symptoms, 4)Communication and Goals of Care, 5)Pain Management, 6)End-of-Life Care, and 7)Grief and Bereavement support. The course will be free of charge and have a multidisciplinary approach. The modules include different interactive activities, available resources for further reading, pre-test activity and an evaluation after completion of each module.

**Conclusions:** High quality, accessible PPC education programs are key to ensure all healthcare personnel around the globe who care for children with cancer have the knowledge and tools to address the needs of their patients and families in a holistic way.

O141/#397 | Free Paper Session (FPS)

#### FPS 08: PALLIATIVE AND SUPPORTIVE CARE

13-10-2023 10:50 - 12:20

#### QUALITY OF INTERDISCIPLINARY COMMUNICATION IS RELATED TO CLINICIAN BURNOUT AND INTENTION TO LEAVE: A MULTISITE CROSS-SECTIONAL ANALYSIS

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**Background and Aims:** Periods of patient deterioration create needs for decision-making and care coordination that can often result in periods of high stress for clinicians of many different

disciplines and professions. However, there has been little focus on how team communication quality during episodes of deterioration impacts overall clinician outcomes. We use a new measure, CritCom, to evaluate the relationship between communication quality and clinician outcomes, including burnout and job satisfaction.

**Methods:** CritCom is a valid, reliable measure to assess the quality of interdisciplinary communication around patient deterioration using 30 questions ranked on a Likert scale of 1 (low quality) to 5 (high quality) across 6 domains (actionable, clarity, tone, empowerment, collaboration and teamwork, leadership). CritCom was administered to a global sample of clinicians who care for patients at risk of deterioration via an anonymous electronic survey. Results were calculated by averaging items within each domain and an overall average. Participants also answered questions about burnout, job satisfaction, and intention to leave. The analysis included descriptive statistics and bivariate analyses.

**Results:** We received 1,086 responses (63 institutions, 24 countries) from participants in a mix of clinical roles working across ward, Intensive Care Unit (ICU), and other care settings. Overall, communication quality was rated at 4.09 (range 1 to 5), with the lowest scoring domain being tone (3.81, range 1-5). Individuals with higher burnout (H(5) = 90.39,  $p < 0.01$ ) and greater intention to leave (H(3) = 14.06,  $p = 0.002$ ) report lower communication quality in their setting (lower CritCom scores).

**Conclusions:** We describe an association between interdisciplinary communication quality and clinician burnout and intent to leave. Future work will leverage a multidisciplinary team to explore findings and develop targeted interventions to address identified communication challenges and improve clinician outcomes. This work further validates CritCom, which is a reliable and pragmatic tool to assess team communication.

O142/#1667 | Free Paper Session (FPS)

#### FPS 08: PALLIATIVE AND SUPPORTIVE CARE

13-10-2023 10:50 - 12:20

#### PROCEDURAL SEDATION ANALGESIA AMONG PEDIATRIC ONCOLOGY PATIENTS USING KETAMINE: DO WE NEED MIDAZOLAM?

Narendra Chaudhary<sup>1</sup>, K Krishna Kumar<sup>2</sup>, Kundavaram Rajkumar<sup>3</sup>, Anuj Jain<sup>4</sup>, Shikha Malik<sup>3</sup>

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**Background and Aims:** If given before ketamine, midazolam helps in lowering the dose and adverse effect profile of ketamine but some studies have shown no benefit of adding it to ketamine alone. We compared the efficacy and safety of ketamine alone versus midazolam and ketamine used for procedural sedation.

**Methods:** We conducted a single center prospective non-randomized controlled trial in a tertiary care center in Central India among pediatric hematology oncology patients upto 18 years of age undergoing painful procedures (bone marrow aspiration/biopsy and intrathecal chemotherapy) under sedation over a period of 13 months (June 2021 to July 2022). The dose of midazolam was 0.1 mg/kg intravenous (IV) while ketamine was used in graded doses of 0.2 mg/kg IV till adequate sedation is attained. Statistical analysis was done using SPSSv23.

**Results:** A total of 41 patients aged 1-17 years with median age 8 years (IQR 5.25-10.00) undergoing 82 painful procedures were enrolled. Procedures included 26 (31.7%) bone marrow aspiration/biopsy and 56 (68.3%) intrathecal chemotherapy. The mean dose of ketamine was  $1.25 \pm 0.6$  mg/kg in ketamine alone group (n=37) vs  $1.05 \pm 0.6$  mg/kg in midazolam + ketamine group (n=45; p=0.039). Nine (11%) patients had non-serious adverse events similar among both the groups. Midazolam did not decrease the incidence of recovery agitation among our study cohort. Mean recovery time was  $26.35 \pm 5.5$  min in ketamine alone group and  $27.8 \pm 11.4$  min in ketamine + midazolam group (p>0.05). Frequency of amnesia, analgesia and overall patient satisfaction were 100% among both study groups (p=1.0).

**Conclusions:** Use of graded dosing of ketamine as per requirement is feasible, safe and effective way to optimize dosing in an individual case. Use of midazolam in addition to ketamine reduces the dose of ketamine required to achieve adequate sedation, but does not affect side effect profile and overall patient satisfaction.

O143/#1380 | Free Paper Session (FPS)

FPS 08: PALLIATIVE AND SUPPORTIVE CARE

13-10-2023 10:50 - 12:20

**SINGLE-DAY INTRAVENOUS FOSAPREPITANT VERSUS THREE-DAY ORAL APREPITANT BASED ANTI-EMETIC REGIMEN IN PEDIATRIC PATIENTS RECEIVING HIGHLY-EMETOGENIC CHEMOTHERAPY: AN INVESTIGATOR-INITIATED, RANDOMIZED, OPEN-LABEL, NON-INFERIORITY TRIAL**

Azgar Abdul Rasheed, Shuvadeep Ganguly, Priya Sharma, Anu Theresa Joison, Ashwati S Pillai, Swetambri Sharma, Deepam Pushpam, Sameer Bakhshi

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**Background and Aims:** Fosaprepitant is non-inferior to oral aprepitant among adults receiving highly-emetogenic chemotherapy (HEC).

Metabolism of fosaprepitant is different in children where it has not been evaluated. We aimed to investigate the non-inferiority of fosaprepitant in children receiving HEC as compared to aprepitant.

**Methods:** This was an investigator-initiated, randomized, open-label, non-inferiority trial, which included chemotherapy-naïve children aged 5-18 years (weight  $\geq 15$ kg), planned for the first cycle of HEC. Patients randomized to fosaprepitant arm received single-dose intravenous fosaprepitant 4mg/kg (maximum 150mg) on day1. Patients on aprepitant arm received oral aprepitant capsules (weight  $15 \leq 30$ kg: Aprepitant 80mg days 1-3, weight  $\geq 30$ kg or age  $\geq 12$  years: Aprepitant 125mg day1, 80mg days 2,3). All patients additionally received ondansetron and dexamethasone during and till 3 days after completion of last chemotherapy dose with daily follow-up. The primary outcome was complete response (CR) rate (no vomiting/retching or need for rescue medications) in the acute phase (AP) with a non-inferiority margin of 15%. Secondary outcomes included CR rates in the delayed (DP) and overall phases (OP), grade of vomiting, incidence and severity of nausea, and adverse effects in two arms.

**Results:** Out of 290 randomized patients, 279 were included for modified intention-to-treat analysis (Fosaprepitant arm: 140; Aprepitant arm: 139). In AP, the difference of CR rate between fosaprepitant [76(54.3%)] and aprepitant arm [84(60.4%)] was -6.1%[90% CI: -15.7% to +3.6%] with lower limit of CI exceeding 15%, thus failing to establish non-inferiority of fosaprepitant. In DP, the difference in CR rate was -3.4%[Fosaprepitant: 87(62.1%) vs Aprepitant: 91(65.5%); 90% CI of difference: -12.7% to +6.1%], while in OP, the difference was -6.7%[Fosaprepitant: 60(42.9%) vs Aprepitant: 69(49.6%); 90% CI of difference: -16.5% to +3.1%]. Grade of vomiting, incidence and severity of nausea, and adverse effects were not different between two arms.

**Conclusions:** Non-inferiority of single-dose intravenous fosaprepitant compared to oral aprepitant in children receiving HEC was not established.

O144/#1207 | Free Paper Session (FPS)

FPS 08: PALLIATIVE AND SUPPORTIVE CARE

13-10-2023 10:50 - 12:20

**A RANDOMIZED, DOUBLE-BLIND STUDY COMPARING SINGLE VERSUS TWO DOSES OF PALONESETRON FOR PREVENTION OF CHEMOTHERAPY-INDUCED NAUSEA AND VOMITING IN CHILDREN RECEIVING MULTIPLE DAY CHEMOTHERAPY**

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**Background and Aims:** Chemotherapy induced nausea and vomiting (CINV) is a common adverse effect of cancer treatment. There is paucity of data regarding optimum regime for CINV prevention in

children receiving multiple day drug protocols. Present study prospectively demonstrate efficacy of single versus two doses of palonosetron for CINV prophylaxis in children receiving multiple-day chemotherapy 2- 18 year of age.

**Methods:** In this single centre, double blinded, randomized study, wherein children receiving moderate and high emetogenic multiple-day chemotherapy were assigned to get either single (Day-1) or two (Day-1 and Day-4) doses of palonosetron in addition to other similar anti-emetic prophylaxis. We assessed number of events on D-1 (phase 1), D2- 24 hour till last dose of chemotherapy (phase 2), 24 hour from last dose of chemotherapy to next 5 days (phase 3). The primary efficacy endpoint was proportion of children with complete response during the acute and delayed phase of the first on-study chemotherapy cycle. Risk factors for suboptimal response were also analysed by univariate analysis.

**Results:** During the study period, 100 patients were randomly enrolled to receive either placebo or additional second dose of palonosetron on D-4. Distribution of all variables in two groups was essentially balanced. These 100 patients received 307 blocks of chemotherapy (median 3; range 1-7). On evaluating the first on-study chemotherapy cycle during the phase 2, CR was recorded in 76% (32/42) and 53.8% (21/39) patients receiving D-4 palonosetron and placebo respectively (p value 0.04). There was no difference in CINV between two groups in phase-1 and phase-2. Emetogenicity potential, age, gender, diagnosis and chemotherapy protocol did not influence response rate.

**Conclusions:** Two doses of palonosetron (D-1 and D-4) is effective for prevention of chemotherapy-induced nausea and vomiting in children with cancer receiving multiple-day moderate or high emetogenic chemotherapy in phase-2 (acute and delayed overlap phase).

O145/#200 | Free Paper Session (FPS)

#### FPS 08: PALLIATIVE AND SUPPORTIVE CARE

13-10-2023 10:50 - 12:20

#### CONNECTING CLINICAL CAPACITY AND SUSTAINABILITY OF PEDIATRIC EARLY WARNING SYSTEMS (PEWS) IN RESOURCE-VARIABLE PEDIATRIC ONCOLOGY CENTERS IN LATIN AMERICA

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**Background and Aims:** Clinical capacity for sustainability describes organizational resources needed to sustain an evidence-based intervention after implementation. We examine the relationship between clinical capacity for sustainability and sustainment of Pediatric Early Warning Systems (PEWS), an evidence-based intervention to improve early identification of clinical deterioration in pediatric oncology patients in variably resourced hospitals in Latin America.

**Methods:** We conducted a cross-sectional survey in March 2022 among pediatric oncology centers participating in Proyecto EVAT, a collaborative to implement PEWS. Eligible hospitals had implemented and were currently sustaining PEWS. Clinicians were eligible to participate if they were involved in PEWS implementation or used PEWS in their clinical work. The Spanish-language survey consisted of 56 close and open-ended questions about the respondent, the hospital, the participants assessment of clinical capacity to sustain PEWS using the clinical sustainability assessment tool (CSAT), and perceptions about PEWS. PEWS sustainment was defined by respondent report of frequency of PEWS use in clinical care at their center. Results were analyzed using multi-level modeling to examine the relationship between individual, hospital, intervention, and clinical capacity determinants to PEWS sustainment.

**Results:** A total of 797 responses from 37 centers in 13 countries were included. Eighty seven percent of participants reported PEWS sustainment (PEWS use at all times during clinical care). After controlling for individual, hospital, and intervention factors, clinical capacity was significantly associated with PEWS sustainment (OR 3.27,  $p < 0.0001$ , Figure). Other significant factors included respondent profession, length of work at the hospital, and perceived importance of PEWS. Hospital factors, such as available resources or structure, were not significant predictors of PEWS sustainment.

**Conclusions:** This study demonstrated a strong relationship between capacity and PEWS sustainment and identified multiple potential modifiable capacity factors important for sustainability. PEWS are a highly sustainable intervention and should be scaled up to reduce global disparities in childhood cancer survival.

O146/#1285 | Free Paper Session (FPS)

## FPS 09: RENAL TUMORS

13-10-2023 10:50 - 12:20

### DOES THE ROUTE TO DIAGNOSIS OF NEPHROBLASTOMA CORRELATE WITH OUTCOME?

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**Background and Aims:** The route to diagnosis in nephroblastoma very much depends on the health care system of a given country. In countries with childhood preventive check-up programs an earlier diagnosis is possible in asymptomatic children. This raises the question if different routes to diagnosis have an impact on outcome.

**Methods:** The analysis is based on data of 2,998 patients diagnosed between 1994-2020 in Germany and Austria where the route to diagnosis is known from SIOP93-01/GPOH and SIOP2001/GPOH studies.

**Results:** Only 2,066 (68.9%) patients were diagnosed with tumor related symptoms, 257 (8.6%) during mandatory preventive medical check-ups in children, 586 (19.5%) incidentally due to non-tumor related symptoms, 43 (1.4%) prenatally and 46 (1.5%) during screening in case of an underlying cancer predisposition syndrome. The mean tumor volume at diagnosis was 534±428ml, 271±290ml, 333±331ml, 103±116ml and 110±312ml for the different groups, respectively ( $p < 0.001$ ). Accordingly, the number of patients with metastasis was also significantly ( $p < 0.001$ ) different: 420 (20.3%), 13 (5.1%), 61 (10.4%), 0 (0%) and 2 (4.3%). Altogether 384 relapses were diagnosed with corresponding 285 (13.8%), 21 (8.2%), 67 (11.4%), 2 (4.7%) and 9 (19.5%) per group. Out of 71 deceased patients, 61 (86.0%) patients had tumor related and 8 (11.3%) other symptoms compared to 2 (2.8%) patients diagnosed during mandatory preventive check-ups and none after prenatal diagnosis or syndrome-triggered screening.

**Conclusions:** The route to diagnosis in patients with nephroblastoma has an impact on initial tumor volume and rate of metastasis. The outcome of patients must be interpreted differentially as the relapse

rate in patients diagnosed by screening is not lower than in patients diagnosed due to tumor related symptoms.

O147/#1262 | Free Paper Session (FPS)

FPS 09: RENAL TUMORS

13-10-2023 10:50 - 12:20

### IS THE ABSOLUTE BLASTEMAL VOLUME AFTER PRE-OPERATIVE CHEMOTHERAPY A RISK FACTOR IN PATIENTS WITH NEPHROBLASTOMA?

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**Background and Aims:** In SIOP risk stratification of nephroblastoma after preoperative chemotherapy is mainly based on staging and histology. High-risk blastemal type is defined by the percentage of surviving blastema. We hypothesize that the absolute blastemal volume (ABV) after preoperative chemotherapy may be more specific as a prognostic marker.

**Methods:** Only unilateral nephroblastoma patients' are included in this analysis. Clinical data and detailed histologic data have been collected prospectively from the SIOP2001 Nephroblastoma Trial. ABV after preoperative chemotherapy was calculated based on tumor volume, percentage of necrosis and of viable blastema.

**Results:** Of 3,421 patients enrolled in SIOP2001 1,787 (52%) have available volume measures including 295 (53%) of 559 stage IV patients. 39 (2%) have low, 1445 (81%) intermediate and 303 (17%) high-risk histology with a median ABV of 0ml, 5.1ml and 62.4ml respectively. Martingale residual plots revealed a cut-off of 20ml for localized intermediate risk histology. 5y-EFS for patients having <20ml ABV was 93% (95%CI:91.3-94.8) and >20ml 82% (95%CI:77.7-86.4) (p<0.0001). Similar significant findings for a cut-off of 20ml ABV were found for regressive and mixed subtypes. Patients with stage IV receiving six weeks of AVD show a threshold at 10ml ABV with a 5y-EFS of 88.1% (95%CI:83.7-92.8) compared to 44.2% (95%CI:35.1-55.7) (p<0.0001). In a COX model adjusted for established risk factors (age, metastasis, local stage, risk-group, tumor-volume at surgery and ABV) stage IV (HR:3.4), diffuse anaplasia (HR:2.13) and age>48m (HR:1.80) remain significant for relapse.

**Conclusions:** In addition to established independent risk factors like stage IV, diffuse anaplasia and age ABV after preoperative chemotherapy ≥20ml for localized and ≥10ml for metastatic tumors can be defined as a threshold distinguishing between good and poor outcome for patients with unilateral nephroblastoma. This prognostic marker could be considered to be used for risk stratification of treatment after tumor resection.

O148/#906 | Free Paper Session (FPS)

FPS 09: RENAL TUMORS

13-10-2023 10:50 - 12:20

### PROGRESS BY TRANSATLANTIC COLLABORATION FOR PEDIATRIC RENAL TUMORS BY HARMONISATION AND COLLABORATION OF COG-RTC AND SIOP-RTSG, THE HARMONICA INITIATIVE

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**Background and Aims:** Transatlantic collaboration for children with renal tumors, has been challenging due to substantial differences in upfront therapeutic approaches. However, further progress needs intensive international collaboration.

**Methods:** Therefore, the HARMONisation and Collaboration (HARMONICA) joint venture was envisioned, which represents the efforts of the Children's Oncology Group Renal Tumor Committee (COG-RTC) and the International Society of Pediatric Oncology Renal Tumor Study Group (SIOP-RTSG) to formally collaborate, with the purpose to enhance knowledge in childhood kidney tumors, particularly rare tumors, and to further improve survival rates while concurrently minimizing long-term toxicity. The creation of HARMONICA builds on years of informal collaboration and leverages two key components. First, HARMONICA brings together a rich multidisciplinary intellectual reservoir of combined input from the two largest pediatric oncology clinical trial cooperative groups in the world. Second, each cooperative group has conducted a series of renal tumor studies and trials with systematic prospective data collection available for combined further exploration. Our driving principle to collaborate is rooted in the fact that many research questions cannot be answered successfully by either cooperative group separately.

**Results:** Real advances mandate networking among global clinical, translational and basic science experts. This is reflected by the 2023, special Open Access issue on pediatric renal tumors (Pediatric Blood and Cancer), in which over 100 authors participated, including young investigators and colleagues from Low/Middle income countries. This issue explores and recommends research priorities for the key challenges that face both the fundamental science and clinical care of pediatric renal cancer, highlighting opportunities for advancement of potential through such international collaboration.

**Conclusions:** HARMONICA, has already and will reinforce progress for children with renal tumors by international, collaboration on common well-defined global care and research targets.

O149/#941 | Free Paper Session (FPS)

FPS 09: RENAL TUMORS

13-10-2023 10:50 - 12:20

## IMPACT OF THE COVID-19 PANDEMIC ON PAEDIATRIC RENAL TUMOUR PRESENTATION AND MANAGEMENT, A SIOP-RTSG RENAL TUMOUR STUDY GROUP STUDY

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**Background and Aims:** The COVID-19 pandemic had a global catastrophic effect on management of non-communicable diseases including paediatric cancer. Despite efforts of the World Health Organization, restrictions in the first months of 2020 imposed challenges for timely referrals of patients to specialized paediatric cancer centres. We aimed to evaluate the pandemic's impact on the number of new diagnoses, disease characteristics, treatment delays and management of patients with Wilms tumour included in SIOP-RTSG-UMBRELLA, across European countries and Brazil.

**Methods:** The number of intensive care admissions, national restrictions and national mobility rates were used as proxies of the severity of the pandemic and its impact on societies. Disease characteristics and number of new diagnoses were collected from the UMBRELLA registry (2019-2020) and compared with historical SIOP2001 registry data (2005-2009).

**Results:** During the first lockdown and population immobilisation in Europe, we observed a decrease in newly diagnosed Wilms tumour patients. There was a significantly higher proportion of metastatic disease (36%, versus 16% and 17%,  $p < 0.001$ ) and larger tumour volume ( $563\text{cm}^3$ , versus  $377\text{cm}^3$  and  $431\text{cm}^3$ ,  $p < 0.001$ ) compared to before and after lockdown period, respectively. In Brazil, where restrictions regionally varied in time, the national immobilisation period (already in March-April) followed a similar pattern (metastases in 50% and 24% of patients, versus 10% and 14% before and after,  $p < 0.001$ ). Overall, we did not observe significant delays in referral nor in time to start treatment.

**Conclusions:** COVID-19 led to a short-term impact on number of newly diagnosed patients and higher stages and larger tumour volumes were

observed. This followed the COVID-19 restrictions, but more strikingly the population immobilisation. No delay in referral times or start of treatment were observed, probably reflected by the rapid response of the paediatric oncology community to aiming to continue excellent care despite the restrictions. The longer-term impact on clinical outcomes will be kept under review.

O150/#1100 | Free Paper Session (FPS)

FPS 09: RENAL TUMORS

13-10-2023 10:50 - 12:20

#### COMPARING ROUTINELY COLLECTED POPULATION LEVEL HEALTH DATA TO A PROSPECTIVE CLINICAL STUDY OF WILMS TUMOUR IN ENGLAND

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**Background and Aims:** The English National Disease Registration Service publishes anonymised statistics derived from routine healthcare data through its Get Data Out (GDO) programme. These include incidence, treatment modalities and overall survival for cancers in standard groups of patients with about 100 cases/year. We assessed the concordance between GDO and comparable data from IMPORT, a prospective observational study of childhood renal tumours across the UK and Ireland, to test the utility of GDO datasets for prospective continuous monitoring of treatment burden and overall survival at a population-level.

**Methods:** We identified English-resident children diagnosed with WT between 1/1/2014-31/12/2018 enrolled in the IMPORT study. Data were extracted from study CRFs and checked for consistency and completeness. Summary statistics were generated from the IMPORT cohort and compared to publicly available GDO data.

**Results:** IMPORT registered 344 patients (age 0-19) and GDO published 440 patients (all ages, 98% 0-19yr) in the same 5yr time period (2014-2018). Use of combined treatment modalities was similar between IMPORT and GDO: chemotherapy and surgery without radiotherapy in 57.8% vs 49.5%; chemotherapy, surgery and radiotherapy 41.0% vs 42.0% respectively. 0.9% had chemotherapy and radiotherapy (without surgery) in GDO but none in IMPORT. 4yr overall survival rates 2014-2016 were 93.4% [95%CI: 89.7-95.8%] for GDO and 92.0% [95%CI 88.3-95.5%] for IMPORT. IMPORT enrolled 80% (344/431) of all children diagnosed with WT in England (2014-2018), lower than the national trials in preceding decades, SIOP2001 (92%) and UKW3

(94%). Radiotherapy use for non-anaplastic WT was higher in IMPORT than in UKW3 (39% vs 27%).

**Conclusions:** The GDO and IMPORT data are remarkably similar, with minor differences likely due to age inclusion criteria and data fidelity. This supports using routinely collected healthcare data to characterise treatment burden and outcomes at a population level across a wider range of paediatric cancers.

O151/#1048 | Free Paper Session (FPS)

FPS 09: RENAL TUMORS

13-10-2023 10:50 - 12:20

#### RELAPSED WILMS TUMOR MANAGEMENT AND OUTCOMES IN CANADA

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**Background and Aims:** Wilms tumor (WT) is the most common renal tumor among children. While relapse of Wilms tumor occurs in up to 15% of cases, its management is not well characterized, with various approaches taken internationally. We aimed to describe the Canadian experience in relapsed WT and the effect of surgical intervention as part of multimodal therapy on survival.

**Methods:** We identified a cohort of patients with relapsed WT between 2001-2020 from the Cancer in Young People in Canada program (CYP-C), a population-based surveillance program. Demographic and treatment-related characteristics were summarized using descriptive statistics. Event-free survival (EFS) and overall survival (OS) were estimated using the Kaplan-Meier method. Effect of surgical intervention on EFS/OS was evaluated via a Cox proportional hazards model (which included number of upfront chemotherapy agents).

**Results:** 97 patients with relapsed WT were identified; one with insufficient data was excluded. Median age at relapse was 5.3 years (range 0.4-16.0 years), with 52% male. Median time to relapse from initial diagnosis was 13.0 months (range 3.0-73.0 months). 28.9% of relapses occurred after initial upfront treatment with two chemotherapy agents (standard risk) versus 62.9% with three or more agents (high risk). 2-year EFS and OS from time of relapse were 57.0% and 64.8%, respectively. 68 patients with relapsed WT had surgery included as part of a multimodal therapeutic approach. The hazard ratio associated with

surgical intervention in multiple regression was 0.49 for EFS (95% CI, 0.26-0.92;  $p = 0.03$ ) and 0.35 for OS (95% CI, 0.18-0.69;  $p = 0.004$ ).

**Conclusions:** In this large cohort of patients treated in Canada, outcomes compare favorably to those reported by international cooperative groups. More favourable survival was observed in patients amenable to surgical intervention at relapse. The relative impact of surgery and other clinico-pathological variables on outcome should be further investigated.

O152/#1669 | CCI

### CCI: PROVIDING PSYCHOSOCIAL SUPPORT 01

13-10-2023 10:50 - 12:20

#### A PSYCHOLOGICAL THERAPY PROGRAM „MY LOGBOOK – I KNOW MY WAY AROUND“ TO NAVIGATE CHILDREN BECOMING EXPERTS OF THEIR OWN HEALTH AND DISEASE

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**Background and Aims:** The Quality Improvement Project “My Logbook” presents a method for the development of a consensus-based and patient-oriented tool to systematically translate standards of psychosocial care into clinical practice and subsequently make psychosocial services and underlying processes measurable and transparent for patients.

**Methods:** Feasibility was fostered through an iterative process (PDSA-Cycles) of constant evaluation and adaptation of the tool by health care experts and a multi-centered pilot in the D-A-Ch Region (N=29 sites; ClinicalTrials.gov Identifier: NCT04474678). 16 booklets and a supplementary handbook for professionals provides practical materials with enhanced stimulating elements to encourage the child to explore actively health related issues from diagnosis to follow-up care. Each booklet is structured in two face-to-face sessions covering psychoeducational, activity & practice and reflective aspects and accompanied by a processoriented screening at four time points to evaluate perceived emotional state and level of knowledge; analysis involved Poisson regression, a generalized linear mixed model and Wilcoxon rank-sum/signed-rank test and Wilcoxon signed-rank test.

**Results:** N = 145 patients represented by children (cancer and/or NF1) at standard risk, according to the Pediatric Psychosocial Preventative Health Model showed a significant decrease in neutral (slope = -0.210,  $p < .001$ ) and negative (slope = -0.293,  $p < .001$ ) emotions, while positive emotions remained stable (slope = -0.018,  $p = .431$ ). However, typical processes for differentiated topics (e.g. building trust compared to concrete medical treatment methods) could be illustrated. In general, perceived knowledge of patients improved significantly ( $z = 883.5$ ,  $p < .001$ ,  $r = 0.32$ ). Specific facilitators and barriers could be detected, apart from a highly rated attractiveness of booklets.

**Conclusions:** This standardized psychological therapy tool identifies persisting gaps between evidence-based standards and clinical practice. Moreover, it illustrates needs of patients considering their active role in disease management. Subsequently, patients benefit from targeted individualized practical implications.

O153/#383 | CCI

### CCI: PROVIDING PSYCHOSOCIAL SUPPORT 01

13-10-2023 10:50 - 12:20

#### THE ROLE OF PLAY THERAPY FOR CHILDREN WITH CANCER. A VOLUNTEER'S EXPERIENCE

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**Background and Aims:** **BACKGROUND** Children with cancer undergo tremendous suffering both physically and psychologically since they spend long days on the wards, as they undergo intense treatment and traumatic procedures. This can sometimes be overwhelming to their emotion and psychological being requiring them to have a safe space to escape all the negative effects that come with suffering a chronic illness and stress of treatment. Playing can help children relax and is very crucial in reducing stress and anxiety. It also helps children with cancer to express their thoughts and feelings about their diagnosis and treatments. **OBJECTIVE** To describe the importance of play therapy and its contribution in management of children with cancer.

**Methods:** Volunteering two days a week, at the Uganda Cancer Institute pediatric ward in the playroom. Used various forms of play therapy to interact with children including drawing and painting. Role plays where children got to act as nurses or doctors, listening to music, and watching television. Also encouraged to express their feelings and emotions through play and art.

**Results:** Children were much happier in the playroom than on the wards. They were able to express emotions and feelings that they were going through. Parents got to spend an hour or two away from the children, they found this so helpful. There was a beautiful bond

between the volunteers and the children that encouraged sharing of experiences.

**Conclusions:** The benefits of play therapy include but not limited to a safe place for expression of unacceptable feelings and fantasies but also facilitate communication between child and staff. It is therefore a necessary consideration to incorporate a children play center in the areas where pediatrics cancer treatments are offered to improve on the quality of life of these children.

O154/#1367 | Free Paper Session (FPS)

#### FPS 10: MYELOID LEUKEMIA AND STEM CELL TRANSPLANT

13-10-2023 10:50 - 12:20

##### ARE DAILY PATIENT REPORTED OUTCOME MEASURES BENEFICIAL IN HAEMATOPOIETIC STEM CELL TRANSPLANT?

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**Background and Aims:** Validated patient-reported outcome measures (PROMs) are emerging as an additional clinical resource for healthcare decision making in haemato-oncology patients with positive impact on long-term survival. To date, there are no data on the efficacy and utility of daily PROMs in patients undergoing hematopoietic stem cell transplantation (HSCT). The aim of this study is to determine the clinical value of daily PROMs during the conditioning phase until engraftment in HSCT recipients.

**Methods:** In this prospective longitudinal, single-arm utility study, we used our unique App - ePROtect - to record daily symptoms related to pain, nausea and appetite loss, physical impairment and sleep disturbance. The association of these PROMs with adverse events (by CTCAE standards) and laboratory values were examined.

**Results:** Twenty children underwent HSCT (nine autologous, eleven allogeneic; median age at transplantation 10.2 years) and complete engraftment was achieved in all patients at median time of 15.0 days (IQR, 13.0-23.0). From conditioning to engraftment, patients or proxies completed 354 PROMs daily, corresponding to an overall completion rate of 70.9% (IQR, 58.2-84.0). Patients were routinely examined according to a standardized procedure, which primarily identified mucositis (95% of all patients), febrile neutropenia (70%) and graft-versus-host-disease (35%). The most severe deterioration in health status with severe symptoms such as pain, nausea and loss of appetite, were noted six to 11 days (median 8.5 days) after transplantation. At the same time, increasing values of IL-6 and CRP were measured. Inter-

estingly the peak value of these laboratory parameters was associated with the degree of self-reported pain. During the neutropenic phase, self-reported pain preceded the increase in laboratory parameters for 24 hours.

**Conclusions:** This study found that PROMs accurately reflect daily symptoms in children undergoing HSCT. The implementation of PROMs might improve early detection and management of adverse events and enhance patient satisfaction.

O155/#1247 | Free Paper Session (FPS)

#### FPS 10: MYELOID LEUKEMIA AND STEM CELL TRANSPLANT

13-10-2023 10:50 - 12:20

##### HAPLOIDENTICAL TRANSPLANTATION FOR PATIENTS WITH FANCONI ANEMIA

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**Background and Aims:** Fanconi anemia (FA) is a heterogeneous bone marrow failure disorder characterized by, progressive marrow failure, and predisposition to leukemia and epithelial malignancies. Allogeneic stem cell transplantation (alloHSCT) is the only therapy that can correct the hematological manifestations of FA patients. Haploidentical transplantation has increased the pool of donors.

**Methods:** Retrospective analysis of FA patients, who underwent haploidentical allogeneic HSCT at King Hussein Cancer Center (KHCC) from Jan, 2005 until Jun, 2022.

**Results:** We are reporting the outcome of haploidentical alloHSCT for 8 FA patients, with overall survival 75%(95% CI: 31.5-93.1). Five patients underwent upfront T-cell repleted with post-transplant cyclophosphamide (PT-CY). The preparative regimen included Fludarabine and single fraction total body irradiation (TBI), one patient has received cyclophosphamide which was omitted later due to toxicity, rabbit antithymocyte globulin was added to the last 2 patients to decrease the graft vs host disease (GVHD). All patients received calcineurin inhibitors and Mycophenolate mofetil starting from day 5 post-transplant. The timing of immunosuppressants was adjusted for the last patient from day zero and 1 post-transplant, respectively. Three patients were rescued after primary graft failure, one after related donor transplant using PT-CY, two patients after unrelated cord blood transplantation, Alemtuzumab in the stem cells bag was used for T-cell depletion. Seven (90%) patients developed acute GVHD, six (75%) developed CMV reactivation (one had CMV colitis), six (75%) patients developed chronic GVHD, three patients are still receiving immunosuppressants more than 4 years post-transplant. We report 3 deaths, one due to chemotherapy toxicity before engraftment, the second patient died 8 months post-transplant due to extensive

chronic GVHD, and the third death was in the rescue group due to squamous cell carcinoma 5 years post-transplant.

**Conclusions:** T-cell repleted haploidentical donor transplantation with PT-CY is feasible for FA patients without a matched related, with increased risk of post-transplant complications, and requires extensive supportive care. Modification of the timing of r-ATG and the GVHD prophylaxis may decrease the toxicity.

O156/#1753 | Free Paper Session (FPS)

#### FPS 10: MYELOID LEUKEMIA AND STEM CELL TRANSPLANT

13-10-2023 10:50 - 12:20

#### EVOLVING CLINICAL SIGNIFICANCE OF TREATMENT-RELATED ACUTE MYELOID LEUKEMIA IN PEDIATRICS: PATHOBIOLOGICAL AND CLINICAL IMPLICATIONS

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**Background and Aims:** Treatment-related acute myeloid leukemia (tAML) secondary to primary malignancies is rare in pediatrics but still associated with an extremely poor prognosis. However, the implication of prior treatment and malignancies for therapeutic decision, clinical management, and prognosis in tAML remain unclear.

**Methods:** Here we retrospectively studied available data of 119 patients, aged between 2 and 29 years, who were diagnosed with tAML between 1993 and 2019. All patients were enrolled into either the multicenter AML-BFM study 93 (n=30), 98 (n=28), 2004 (n=35) or the registry 2012 and 2017 (R12/17) (n=26).

**Results:** Distribution of primary malignancies did not reveal significant differences aside from less central nervous system tumors (13%), whilst the largest proportion was allocated as acute lymphoblastic leukemias or myelodysplastic syndromes (31%). In tAML, previous radiotherapy was associated with worse 10-year overall survival (10y.OS, 5.6±5% vs. 32±5%,  $p=0.003$ ). Outcome in patients with an interval of less than 1.2 years between 1<sup>st</sup> malignancy and tAML was significantly decreased (10y.OS, 7.1±6.9% vs. 29±4.7%,  $p=0.01$ ). Over the past 30 years, survival in pediatric tAML continuously improved from the AML-BFM study in 93 to the register 2012/2017 (10y.OS, 10±5.5% to 50±9.8%,  $p<0.001$ ). A major change after the AML-BFM 2004 study was the recommendation to perform Hematopoietic stem cell transplantation (HSCT) following two induction regimens. Accordingly time to HSCT (<120d) is significantly associated with improved outcome in tAML (10y.OS, 66±8.1 vs. 22±9.8,  $p<0.001$ ). Moreover, waiting for complete hematopoietic recovery before proceeding to

HSCT did not convey prognostic benefit over HSCT in no evidence of leukemia (NEL, <5% blasts) (53±8.4 vs. 47±12.3).

**Conclusions:** In conclusion, prognosis in pediatric tAML has significantly improved in the past decades. Our data suggest that pediatric patients with tAML benefit from earlier HSCT, without waiting for complete hematopoietic recovery.

O157/#1224 | Free Paper Session (FPS)

#### FPS 10: MYELOID LEUKEMIA AND STEM CELL TRANSPLANT

13-10-2023 10:50 - 12:20

#### HISTONE HYPOACETYLATION-DRIVEN CD9 REPRESSION ARRESTS DIFFERENTIATION AND EVADES IMMUNOSURVEILLANCE IN PEDIATRIC ACUTE MYELOID LEUKEMIA

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**Background and Aims:** Despite intensive treatment regimes, the clinical outcomes of pediatric AML remain suboptimal, underscoring the need to decipher the underlying pathology and translate into therapeutic interventions. In this study, we pursued to deconvolute the functional, mechanistic and therapeutic relevance of tetraspanin CD9 in pediatric AML.

**Methods:** Patients were stratified based on CD9 status for comparison of long-term survival. Epigenetic control of CD9 was investigated by ChIP-sequencing and confirmed by HDACi treatment. Impact of CD9 on leukemia aggressiveness was measured by competition and colony formation assays, coupled with disease evaluation in xenograft models. The underlying mechanisms were dissected by bulk and single-cell transcriptomics, followed by proof-of-function experiments on myeloblasts and in immune-reconstituted mouse models.

**Results:** CD9 was absent in two-thirds of patients where low expression correlated with a dismal survival. At the CD9 locus, we observed low occupancies by acetylated histones (H3K9/27Ac), thereby suppressing its transcription but reversible by the HDAC inhibitor panobinostat. Overexpression of CD9 not only inhibited myeloblast proliferation, but also blocked their dissemination in NOD/SCID mice. Mechanistically, transcriptome profiling of pediatric AML samples revealed decreased stemness and increased monocyte gene signatures in CD9<sup>high</sup> cases. Concordantly, we detected a profound upregulation of CD9 preceding appearance of lineage

markers in monocyte/macrophage-biased differentiation cultures. CD9 alone primed myeloblast maturation but was insufficient to drive terminal differentiation. Further, CD9 promoted basal and cytokine-induced MHC expression through the JAK2/STAT5 axis, and regulated their intracellular trafficking by physical binding. In NSG mice, co-transplantation of allogeneic PBMCs mounted an effective immunity against CD9+ but not CD9- AML, concomitant with a robust infiltration of cytotoxic T cells.

**Conclusions:** Our data provided molecular, cellular and clinical evidence showing the definitive function of CD9 as a key driver intertwining differentiation and immunosurveillance in pediatric AML, and inspired a new combinatorial epigenetic/immunotherapy for managing this rare but aggressive malignancy.

O158/#923 | Free Paper Session (FPS)

#### FPS 10: MYELOID LEUKEMIA AND STEM CELL TRANSPLANT

13-10-2023 10:50 - 12:20

#### CENTRAL AMERICAN ASSOCIATION OF PEDIATRIC HEMATOLOGY AND ONCOLOGY (AHOPCA) APL-AHOPCA III TREATMENT GUIDELINES FOR ACUTE PROMYELOCYTIC LEUKEMIA (APL): 14-YEAR EXPERIENCE IN CENTRAL AMERICA

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**Background and Aims:** AHOPCA established the APL-AHOPCA III treatment guidelines for pediatric APL with the mentorship of experts from Italy and the United States in 2008. Complex cases were consulted in weekly virtual meetings.

**Methods:** Previously untreated patients greater than 12 months and up to 18 years of age with morphological APL diagnosis were treated. Patients were stratified into two risk groups according to initial WBC. Induction therapy consisted of all-trans retinoic acid (ATRA) and doxorubicin (2 doses for standard-risk and 3 for high-risk) followed by three consolidation courses including ATRA+doxorubicin±cytarabine. Intrathecal methotrexate was administered to all patients before each

consolidation course. At the end of consolidation, patients in hematological remission (HCR) proceeded to standard maintenance therapy with 15 days ATRA every three months for a total of 2 years.

**Results:** From January 2008 to June 30, 2022, 222 children entered the protocol; 220 were evaluable. The cytogenetic and/or molecular studies were available in 43% of patients and resulted in positive in 41%. Forty-five (22%) children died during induction (62.3% bleeding, 33.3% infection, 4.4% other), 6 (3%) from resistant disease, three abandoned the treatment, and 146 (73%) achieved HCR. The relapse rate was 29%, and 11 patients in HCR abandoned the treatment. With a median follow-up of 4.8 years, considering abandonment as an event, the 5-year EFS and OS are 34% and 44%, respectively.

**Conclusions:** Induction death, mainly due to inadequate access to blood products, remains a significant cause of failure. Molecular diagnosis is not available in all countries, and there is no access to arsenic trioxide (ATO). Advocacy and more resources are needed to improve the cure of children with APL in AHOPCA, considering that the overall incidence in Central America seems relatively high. In Guatemala, APL represents 17% of all pediatric acute myeloid leukemia.

O159/#1353 | Free Paper Session (FPS)

#### FPS 10: MYELOID LEUKEMIA AND STEM CELL TRANSPLANT

13-10-2023 10:50 - 12:20

#### PROFILE OF CHRONIC MYELOID LEUKEMIA-CHRONIC PHASE (CML-CP) IN CHILDREN UNDER 5-YEARS AGE AT DIAGNOSIS: EXPERIENCE FROM THE TATA MEMORIAL HOSPITAL PAEDIATRIC-CML (PCML) COHORT

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**Background and Aims:** pCML is a rare malignancy comprising 2-3% of paediatric leukemias and literature in children < 5-years age is extremely scarce. The younger age at diagnosis presents more challenges in management including long-term off-target toxicities of tyrosine kinase inhibitors (TKIs). We report our experience of managing pCML below 5-yrs age in the TKI era.

**Methods:** Retrospectively and prospectively collected data pertaining to children diagnosed with CML < 5-years age between 2002 and 2022 from the pCML cohort of our hospital is presented. Conventional statistics has been used for analysis.

**Results:** Twenty-seven of 185 children were eligible. Median age at diagnosis was 4 years(1-5years). At presentation mean (SD)



Hb, WBC, platelet counts were 8.5(1.7)g/dl, 161970(142218)/cmm, 567(374)X10<sup>9</sup>/cmm respectively, mean (SD) liver and spleen size (from costal margins) were 2(1.4)cm and 5.9(4.3)cm respectively. All children were started on imatinib (dose:250-300 mg/m<sup>2</sup>) at presentation. Mean (SD) time to attainment of CHR(n=23), CCyR(n=24), MMR(n=22) and DMR(n=13) were 3.7(3.12), 10.2(8.7), 45.9(32.0) and 85.7(61.2) months respectively. Time to attainment of CHR was significantly higher than in children over 5 years (3.05-2.1 months) (P=0.005). At a median follow up of 122 months, growth deceleration and reduced bone density were seen in 8 (30%) and 3 (12%) patients respectively. Endocrinopathies like hypogonadism, hypothyroidism and delayed puberty was seen in 10 (43%) patients. Incidence of endocrine issues were more common in children <5-years when compared to the over-5 cohort (43% vs. 18%, p=0.009). Growth issues (30% in under-5 Vs 14% in >5 yrs) were commoner in the under-5 patients but the difference was not statistically significant.

**Conclusions:** Management of pCML in very young children is challenging due to very early exposure to TKIs during active growth and organ maturation. Under 5 children are at a higher risk of long term toxicities of TKIs and need structured monitoring for early detection and management.

O160/#329 | Free Paper Session (FPS)

## FPS 11: NEW TREATMENTS AND CLINICAL STUDIES IN NEUROBLASTOMA

13-10-2023 14:10 - 15:40

### HIGH RISK NEUROBLASTOMA (HR-NB) WITH MNA AND AGE

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**Background and Aims:** The poor overall survival (OS) of 30% (SE, 0.08) at 2 years in INES 99.4 (JCO 2009,27(7):1014-9) for MYCN amplified (MNA) infants.

**Methods:** Patients <18 months with MNA INSS stages >1 were eligible in HR-NBL1/SIOPEN. All infants received Rapid Cojec induction, eventually 2 TVDs, Busulfan-Melphalan and ASCR and could receive Dinutuximab- beta immunotherapy. Toddlers (12-18 months) followed the HR-NBL1/SIOPEN respective eligibility criteria.

**Results:** Of 414 patients (median follow up 7 years): 56% were male; 75% stage 4; 6.8% stage 4S; 18.6% had localised tumours. Predominant primary tumour site was abdominal (85%). Rapid Cojec was used in 85%, BUMEL in 89% and 26% received Dinutuximab-beta. Multiple metastatic compartments were reported in 82% of stage 4. 5year-event free (EFS) and overall survival (5y-OS) was 0.46±0.03 and 0.51±0.03. Stage 2,3&4S patients had a 5y-EFS of 0.64±0.03 (p<0.005) (5y-OS:0.66±0.06), compared to stage 4 with 0.41±0.03 (OS:0.46±0.03). Infants' 5y-EFS was superior with 0.53±0.04 (5y-OS:0.57±0.04) (p=0.015) over toddlers with 5y-EFS 0.42±0.03 (5y-OS:0.46±0.03). Patients with bone marrow (BM) and skeletal metastases ± other sites (MS) did worse (p< 0.005) with a 5y-EFS of 0.31±0.04 (5y-OS:0.36±0.04) whilst other metastatic combinations revealed outcomes above 0.50 ±0.03. LDH (2x>normal) predicted a worse 5y-EFS of 0.43±0.03 (5y-OS:0.46±0.03) (p< 0.001) versus normal LDH (5y-EFS 0.71±0.07; 5y-OS:0.80±0.06). EFS multivariable analysis at diagnosis (MVA) showed independent significance for stage 4 (p-value 0.0139; HR: 1.608) and LDH (p-value 0.0042; HR: 2,237), but not for age. In stage 4 patients MVA on EFS found LDH (p-value 0.0098; HR: 2,567) and BM/skeleton involvement (p-value 0.0024; HR: 1,693) as independent risk predictors. In maintenance Dinutuximab-beta had a major impact on 5y-EFS in stage 4 patients with 0.69±0.05(5y-OS:0.71±0.05) vs. 0.41±0.07 (0.46±0.07) for those treated with 13-cis retinoic acid (p=0.002 & p=0.001), but not on others.

**Conclusions:** The HR-NBL1/SIOPEN strategy improved 5year- EFS/OS with only few late events.

O161/#1243 | Free Paper Session (FPS)

**FPS 11: NEW TREATMENTS AND CLINICAL STUDIES IN NEUROBLASTOMA**

13-10-2023 14:10 - 15:40

**APATINIB COMBINED WITH IRINOTECAN AND TEMOZOLOMIDE IN CHILDREN AND ADULT WITH REFRACTORY/PROGRESSIVE/RELAPSED NEUROBLASTOMA (APTIN-01): A PHASE 2, SINGLE-ARM, PROSPECTIVE STUDY**

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**Background and Aims:** Outcomes for children and adult with relapsed/progressive/refractory neuroblastoma (R/R NB) are dismal. Irinotecan combined with temozolomide (IT) is an effective salvage treatment for R/R NB with tolerable toxicity. We aimed to investigate the efficacy and safety of apatinib combined with IT regimen in children and adult with R/R NB.

**Methods:** Patients with evaluable lesions received irinotecan (50 mg/m<sup>2</sup>/dose, d1-5) and temozolomide (150 mg/m<sup>2</sup>/dose, d1-5) every 3 weeks for a maximum of eight cycles, and apatinib (0.125g, weight <20 Kg; 0.25g, 20 Kg≤weight<40Kg; 0.5g, 40 Kg≤weight<50 Kg) once daily on a continuous basis until disease progression, patient withdrawal, or unacceptable toxic effects. Response was assessed after two and four and six courses using International Neuroblastoma Response Criteria. The primary endpoint was the proportion of patients achieving a best objective (complete or partial) response after six cycles of treatment.

**Results:** Between Aug 17, 2021, and Feb 7, 2023, 31 patients (20 first relapsed, 11 primary refractory/progressive disease) were enrolled, including 29 children and 2 adults, with median age at enrollment of 86.3 months (32.2-542.1 months) and median courses of 5 cycles (1-8 cycles). The objective response rate (ORR) was 67.7% (8 CR, 13 PR, 3 MR, 5 SD, 2 PD). The ORR of first relapsed and primary refractory/progressive disease were 90% (7 CR, 11 PR, 1 MR, 1 SD) and 27.3% (1 CR, 2 PR, 2 MR, 4 SD, 2 PD), respectively. The most common grade 3 or worse adverse events were leukopenia (14.7%), neutropenia (5.9%), fatigue (5.9%), epistaxis (5.0%), thrombocytopenia (2.2%), anemia (2.0%), hypertension (1.8%), nausea (1.9%). No deaths attributed to protocol therapy occurred.

**Conclusions:** The combination of apatinib with IT regimen shows promising efficacy and manageable toxicities in children and adult patients with R/R NB, especially in first relapsed patients, and continuing to expand the sample size is warranted.

O162/#1198 | Free Paper Session (FPS)

**FPS 11: NEW TREATMENTS AND CLINICAL STUDIES IN NEUROBLASTOMA**

13-10-2023 14:10 - 15:40

**SENSITIVITY ANALYSES OF EVENT FREE AND OVERALL SURVIVAL IN HIGH-RISK NEUROBLASTOMA PATIENTS RECEIVING DFMO MAINTENANCE TREATMENT WITH MATCHED EXTERNAL CONTROLS INCLUDING MYCN**

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**Background and Aims:** We reported previously the relapse rate for HRNB patients in remission after upfront dinutuximab treated with DFMO was approximately half that of matched control patients from

the COG trial, ANBL0032. We further interrogate these survival outcomes using multiple sensitivity analyses.

**Methods:** Our phase 2 trial enrolled N=141 HRNB patients in remission treated with continuous DFMO for 2 years. ANBL0032 enrolled N=1328 HRNB patients assigned to dinutuximab. Selection rules identified like-groups of patients eligible for matching. Propensity-score matching (PSM) balanced cohorts on risk characteristics including MYCN. Inferential analyses compared EFS and OS. Sensitivity analyses, including modifying the PSM ratio to 1:2 and 1:1, removing patients with partial response [PR] or with events <123 days post immunotherapy from the control group, and evaluation of contemporaneous population.

**Results:** Complete covariate data for analysis was available in n=91 treated patients and n=516 control patients. PSM ratio to 1:2 and 1:1 confirmed improved EFS: HR 0.39[0.22,0.70], p-value=0.0016), HR 0.39[0.21,0.74], p-value=0.0038) and OS: HR 0.0.26[0.12,0.57], p-value=0.00009), HR 0.22[0.10,0.52], p-value=0.0005). Excluding NO-DFMO patients with PR, events <123 days, or contemporaneous comparison, all significantly improved EFS: HR 0.49[0.28,0.85], p-value=0.012), HR 0.54[0.30,0.98], p-value=0.044), HR 0.57[0.33,1.00], p-value=0.050) respectively as well as OS: HR 0.44[0.20,0.87], p-value=0.0208), HR 0.43[0.19,0.96], p-value=0.0395), HR 0.39[0.18,0.84], p-value=0.0319). MYCN amplified patients treated with DFMO relative to NO-DFMO show an EFS of 90% and 75.2% (HR 0.37[0.14,1.02]) and OS of 97.5% and 84.1%, (HR 0.13[0.02,0.92]) respectively. MYCN non-amplified patients treated with DFMO relative to NO-DFMO show an EFS of 78.4% and 67.8% (HR 0.60 [0.33, 1.12]) and OS of 86.3% and 79.7% (HR 0.57 [0.26,1.25]) respectively.

**Conclusions:** EFS/OS findings were consistent across all sensitivity analyses and reproducibly confirmed the statistically significant EFS/OS improvements with DFMO treatment pre- and post-PSM, regardless of MYCN status. These results further support DFMO as maintenance treatment for HRNB.

O163/#1149 | Free Paper Session (FPS)

#### FPS 11: NEW TREATMENTS AND CLINICAL STUDIES IN NEUROBLASTOMA

13-10-2023 14:10 - 15:40

#### BONE MARROW INFILTRATION BY SENSITIVE RT-QPCR CORRELATES WITH POOR OUTCOME IN NEUROBLASTOMA WITH POST-INDUCTION SIOPEN SCORE ≤3

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**Background and Aims:** Reverse transcriptase-quantitative PCR (RT-qPCR) is a sensitive method for detecting submicroscopic bone marrow (BM) infiltration in neuroblastoma. The aim was to investigate the added diagnostic yield and prognostic value of RT-qPCR compared to conventional methods in patients with high-risk neuroblastoma.

**Methods:** Patients with high-risk neuroblastoma who were enrolled in the prospective Minimal Residual Disease study (2008–2022) at diagnosis and/or post-induction, were included. Iliac crest BM samples were analysed by immunohistochemistry plus cytomorphology (IHC+CM) and RT-qPCR (mRNA panel: *PHOX2B*, *TH CHRNA2*, and *GAP43*). SIOPEN scores were collected from paired (≤15 days interval) meta-[<sup>123</sup>I]iodobenzylguanidine (MIBG) scans. After excluding paired examinations with missing results, diagnostic yield of the three methods was analysed at diagnosis and post-induction. After single imputation of missing post-induction results, five-year recurrence-free survival (5y-RFS) was calculated, for patients with the following conditions: SIOPEN score ≤3 vs. >3 and RT-qPCR positive vs. negative.

**Results:** Of the 164 patients in the total cohort (95% stage 4), 157 were included at diagnosis and 134 at post-induction. At diagnosis and post-induction, 137 and 67 patients had complete results with additional cases of BM involvement being detected by RT-qPCR-only in 10 (7%) and 8 (12%), respectively. In total, there were nine cases with BM involvement by MIBG-only, all concerning MIBG uptake outside the iliac crests. In patients with a post-induction SIOPEN score ≤3 (n=92), a RT-qPCR-positive result was associated with a significantly reduced 5y-RFS (28%) compared to a negative result (60%), P<0.01. A similar association was seen in patients with a SIOPEN score >3 (n=42): 14% vs. 43%, respectively, however not statistically significant in this small number of patients.

**Conclusions:** RT-qPCR detected additional cases of BM-involvement in high-risk neuroblastoma, both at diagnosis and post-induction. Addition of RT-qPCR showed significant prognostic value in patients with a post-induction SIOPEN score ≤3, which may improve risk classification within high-risk neuroblastoma.

O164/#349 | Free Paper Session (FPS)

#### FPS 11: NEW TREATMENTS AND CLINICAL STUDIES IN NEUROBLASTOMA

13-10-2023 14:10 - 15:40

## 18F-MFBG PET IMAGING IN PATIENTS WITH NEUROBLASTOMA: LESION TARGETING AND COMPARISON WITH MIBG

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**Background and Aims:** <sup>123</sup>I-MIBG gamma camera scans (MIBG) are routinely used for imaging neuroblastoma. Limitations include need for two-day imaging and lack of quantitative uptake measurements. Phase I study showed that <sup>18</sup>F-MFBG (MFBG), a positron-emitting analog of MIBG, is safe and feasible (PMID:28705916). In the follow-up phase II trial (NCT02348749) we compared MFBG-PET scans (MFBG) with MIBG.

**Methods:** Patients with neuroblastoma underwent whole-body PET-CT or PET-MR imaging one hour post-injection with 8mCi/1.7m<sup>2</sup> of MFBG. All patients had concurrent MIBG scans including SPECT-CT without intervening therapy. MFBG and MIBG images were independently analyzed for lesion targeting and number, site and uptake. Discordant lesions were further investigated with correlative imaging and/or clinical follow up. "MFBG score" was generated, similar to the modified Curie score.

**Results:** Twenty-five patients (median age 8 years) underwent MFBG scans at a median of 2(range 0-24) days after MIBG scans; in one MFBG was performed 1 day before MIBG. No MFBG-related adverse events were noted. 24 patients had both MIBG and MFBG positivity while in 1 both scans were negative. A total of 367 lesions were visualized on MFBG versus 217 on MIBG. There were no MIBG-positive lesions that were negative on MFBG. A median of 11 (0-57) lesions/patient were detected on MFBG. Uptake was noted in osteomedullary sites only (n=13), soft tissue only (n=1) and both soft tissue and skeleton (n=10). MFBG detected a median of 6 (range 1-24) additional lesions in 19 patients. In 16/19 patients where follow-up was available, discordance was related to true-positive disease, including in ≥116 sites. Respective median curie scores were 3(0-22) and 9(0-24) with MIBG and MFBG respectively.

**Conclusions:** MFBG detected disease in all patients with MIBG-positive disease. MFBG detected similar or more lesions than MIBG, with overall increased scores. Further analysis to evaluate impact on patient management is underway.

O165/#1114 | Free Paper Session (FPS)

FPS 12: SUPPORTIVE CARE

13-10-2023 14:10 - 15:40

## IMPACT OF EXPOSURE TO ACIDIC URINE DURING HIGH-DOSE METHOTREXATE ADMINISTRATION IN PEDIATRIC CANCER TREATMENT

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**Background and Aims:** High-dose methotrexate (HDMTX) has been a critical component of treatment protocols for a variety of cancer types in pediatric patients for decades, yet supportive care practices still vary widely. A registry of HDMTX was initiated in Europe to better understand supportive care practices and the incidence of complications. Site recruitment, onboarding, and data collection are ongoing. The Urine Acidity Index (UAI) was developed to quantify exposure to acidic urine during a course of HDMTX.

**Methods:** The UAI was calculated as the sum of a series of exponential functions  $10^{[7 - \text{observed urine pH}]}$  times [the number of hours until the next observed urine pH] for each urine pH observed during the first 48 hours of that course. For example, where the total acidic urine exposure was measured at 6 over 10 hours, the UAI equaled 100. Courses of HDMTX were grouped into "Low UAI" and "High UAI" when the UAI was less than or equal to 100 or greater than 100 respectively.

**Results:** Data collected included 145 pediatric patients (143 ALL and 2 NHL) who received 483 long infusion courses of HDMTX and included 87 males (290 courses) and 58 females (193 courses). A High UAI occurred in 41 courses (8.5%) and a Low UAI occurred in 442 courses (91.5%). Patients experienced acute kidney injury (AKI) in 46.3% of courses (N=19) with a High UAI and AKI occurred in 23.5% of courses with a Low UAI (N=104), (p=0.003).

**Conclusions:** A High UAI within 48 hours of the start of HDMTX administration was found to be associated with an increased risk of AKI. Further research is needed to explore the UAI as a predictor of AKI and other toxicities in heterogeneous populations. The association between a higher UAI and AKI highlights the importance of sufficient urine alkalization to amplify patient safety during HDMTX administration.

O166/#423 | Free Paper Session (FPS)

FPS 12: SUPPORTIVE CARE

13-10-2023 14:10 - 15:40

## ADMINISTRATION OF HIGH-DOSE METHOTREXATE WITHOUT MONITORING METHOTREXATE LEVELS BY USING EXTENDED HYDRATION AND ADDITIONAL LEUCOVORIN: A RETROSPECTIVE STUDY OF 1,713 CYCLES

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**Background and Aims:** Lack of access to methotrexate levels is common in low- and middle-income countries (LMIC), in which 80% of worldwide pediatric cancer patients reside. We evaluated whether high-dose methotrexate (HDMTX) can be administered safely using extended hydration, leucovorin rescue, and monitoring of serum creatinine in the absence of methotrexate levels.

**Methods:** Data were collected as part of Resonance's global retrospective registry of HDMTX from 2012-2021. Patients <21 years with acute lymphocytic leukemia (ALL) and non-Hodgkin lymphoma (NHL) were administered either 3 or 5 g/m<sup>2</sup> of methotrexate (24-hour infusion). Methotrexate levels were not obtained. Six doses of leucovorin (15 mg/m<sup>2</sup>/dose) were given beginning 42 hours from the start of HDMTX instead of the recommended three. Serum creatinine was measured at baseline, 24- and 48 hours. Hydration volume was increased (200 ml/m<sup>2</sup>/hr) if creatinine levels exceeded 1.25 times the baseline. Frequencies of toxicities (CTCAE v5 or Acute Kidney Injury Network) were determined.

**Results:** The analysis included 1,713 cycles of HDMTX in 446 patients: B-ALL, 1,093 cycles; T-ALL, 446; NHL, 174 cycles. The median age was 7 years (range 0.04-21). Patients were underweight in 463 (26.4%) cycles. Methotrexate doses were 3 and 5 g/m<sup>2</sup> in 68.1% and 31.2% cycles, respectively. Median duration of hospitalization was 5 days (IQR 4-5). Grade 3/4 mucositis was reported in 6.6% and febrile neutropenia in 4.5% cycles. Creatinine increased >1.25 times baseline in 16.6% cycles. Acute kidney injury was reported as stage 1, 2, and 3 in 9.0%, 4.9%, and 2.7% of cycles, respectively. There were no severe renal toxicities requiring dialysis. Five patients (1.1%) died from HDMTX-induced sepsis and febrile neutropenia.

**Conclusions:** It is safe to administer HDMTX (24-hour infusion) with extended hydration, additional leucovorin doses, lengthier hospitalization, and monitoring of serum creatinine when methotrexate levels are unavailable. Numerous centers in LMIC lacking access to methotrexate levels may consider this approach.

O167/#513 | Free Paper Session (FPS)

FPS 12: SUPPORTIVE CARE

13-10-2023 14:10 - 15:40

## CENTRAL VENOUS LINE (CVL) DYSFUNCTION AND INFECTIONS ARE INDEPENDENT RISK FACTORS FOR THROMBOEMBOLISM DURING PRIMARY CANCER THERAPY IN CHILDREN: A PROVINCIAL PROSPECTIVE COHORT STUDY

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**Background and Aims:** Dysfunction of CVLs is a common, yet understudied, complication. Prior retrospective studies showed association between CVL dysfunction (CVLD), infection and thromboembolism (TE). There are no prospective studies evaluating these CVL-related complications. We undertook a provincewide prospective cohort study to define the impact of infection and CVLD on the risk of TE in pediatric cancer patients.

**Methods:** Children (<18 years) with CVL, were recruited at the first cancer diagnosis from all provincial pediatric oncology centers. Patients with brain tumors, prior TE or anticoagulation therapy were excluded. Details of demography, cancer diagnosis, therapy, CVL insertion and removal were collected. Outcome measures included CVLD [defined as persistent or recurrent difficulty in infusion, blood draw or both], objectively confirmed TE and blood culture proven infection during primary cancer therapy. Patients were not screened for asymptomatic TE. Univariate and multivariable analyses evaluated the impact of CVLD, infection, other patient and CVL-related factors on the risk of TE.

**Results:** Of 486 evaluable patients (median age 6.27 yrs.; 212 (44%) females); 64 patients (13.2%; 95% confidence interval (CI) 10.2,16.2) developed 80 TE events. CVLD occurred in 173 (35.6%; 95%CI 31.3,39.9) patients and 135 (27.8%; 95%CI 23.8, 31.8) had blood culture-proven infection. Multivariable analyses adjusted for age, type of cancer and body mass index confirmed the independent impact of CVLD (Odds ratio (OR) 2.01; 95%CI 1.09,3.70 p= 0.026) and

infection (2.10; 95%CI 1.10,4.00;  $p=0.024$ ) on the risk of TE during cancer therapy. There was no interaction between CVLD and infection. **Conclusions:** CVLD and infection are independent risk factors for TE in children with cancer. Occurring in 35% patients, and the associated high-risk of TE, CVLD is a significant complication requiring prompt evaluation and management. Our data supports the need for an interventional trial of prophylactic anticoagulation to reduce CVLD, infection and the incidence of TE in children undergoing cancer therapy.

O168/#1182 | Free Paper Session (FPS)

## FPS 12: SUPPORTIVE CARE

13-10-2023 14:10 - 15:40

### TREATMENT-RELATED MORTALITY IN CHILDREN WITH CANCER IN LOW- AND MIDDLE-INCOME COUNTRIES: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background and Aims:** Of approximately 400,000 incident childhood cancer cases annually, 90% occur in low- and middle-income countries (LMICs), with estimated 5-year survival below 20%. Treatment-related mortality (TRM) in high-income countries is reported in three to five percent of cases, yet limited outcomes reported in LMICs vary significantly, with TRM as high as 45%. The primary objective of this study is to systematically explore the incidence and primary causes of TRM among children with cancer in LMICs.

**Methods:** A systematic search was conducted in PubMed, Trip, Web of Science, Embase, and World Health Organization Global Index databases to identify articles published between 2010-2021 describing TRM among cancer patients (0-21 years old) in LMICs. Two reviewers independently screened studies utilizing eligibility criteria,

extracted data, and evaluated data quality. Random and mixed effects models were used to estimate TRM burden and trends.

**Results:** This systematic review included 503 studies, capturing data from 68,684 pediatric oncology patients receiving treatment between 1989-2021 across 66 countries. The TRM estimate was 6.84% (95% CI, 6.02-7.67), accounting for 30.1% of overall mortality. Leading causes of death included sepsis/infection (71.7%), hemorrhage (10.5%), and tumor lysis syndrome (4.82%). TRM was significantly higher among hematologic malignancies (10.31%) compared to non-CNS solid tumors (2.91%) and CNS tumors (1.96%,  $p<0.0001$ ). TRM was inversely related to country income group ( $p<0.0001$ ). Low-income countries experienced higher incidence of TRM (14.2%) compared to lower middle-income (9.3%) and upper middle-income (4.5%) countries. In upper middle-income countries, the incidence of TRM decreased over time ( $p<0.005$ ); outcomes remained unchanged in low- ( $p=0.21$ ) and lower middle-income countries ( $p=0.16$ ).

**Conclusions:** Approximately one in fifteen children receiving cancer treatment in LMICs dies from treatment-related complications, with infection/sepsis identified as the leading cause of death. Wide disparities in childhood cancer outcomes demonstrate an ongoing need to inform targeted supportive care interventions to improve childhood cancer survival in resource-limited settings.

O169/#65 | Free Paper Session (FPS)

## FPS 12: SUPPORTIVE CARE

13-10-2023 14:10 - 15:40

### CLINICAL PRACTICE GUIDELINE AND EXPERT CONSENSUS RECOMMENDATIONS FOR REHABILITATION AMONG CHILDREN WITH CANCER: A SYSTEMATIC REVIEW

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**Background and Aims:** Increased attention to the rehabilitation needs of children with cancer is vital to enhance health, quality of life, and productivity outcomes. Among adults with cancer, rehabilitation recommendations are frequently incorporated into guidelines, but the extent to which recommendations exist for children is unknown. The purpose of this study was to synthesize available clinical practice guideline and expert consensus recommendations relevant to the rehabilitation of children with cancer.

**Methods:** Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) methodology was followed. Reports included in this systematic review are guideline or expert consensus reports containing recommendations related to rehabilitation referral, evaluation, and/or intervention for individuals diagnosed with cancer during childhood (<18 years). Rehabilitation includes physical therapy, occupational therapy, speech language pathology, psychology/neuropsychology, or physiatry. Eligible reports were published in English between January 2000 to August 2022.

**Results:** Through database searches, 42,982 records were identified; 62 records were identified through citation and website searching. Twenty-eight reports were included in the review: 18 guidelines and 10 expert consensus reports. Guidelines/consensus reports were identified for individuals on and off cancer treatment and those in long-term survivorship. Rehabilitation recommendations were identified in disease-specific (e.g., acute lymphoblastic leukemia), impairment-specific (e.g., fatigue, neurocognition, pain), adolescent and young adult, and long-term follow-up/survivorship reports. While rehabilitation recommendations are included for a range of topics, recommendations were sometimes too vague to inform care (e.g., recommendation for evidence-based rehabilitation training). Additionally, few intervention recommendations were included in guideline and consensus reports.

**Conclusions:** Guideline-concordant care and further development of pediatric oncology rehabilitation guidelines is critical to enhancing the care and outcomes of children with cancer. Adhering to guidelines would increase the number of children referred to rehabilitation and can support equity in how rehabilitation services are provided. Including pediatric oncology rehabilitation providers in guideline and consensus development initiatives across oncology and rehabilitation groups is critical.

O170/#355 | Free Paper Session (FPS)

## FPS 12: SUPPORTIVE CARE

13-10-2023 14:10 - 15:40

### IMPLEMENTING A BEREAVEMENT CARE PROGRAM IN A RESOURCE-CONSTRAINED LATIN AMERICAN COUNTRY: A SOURCE OF LIGHT AND COMPASSION (LOVE) IN THE MIDST OF CLOUDY TIMES

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**Background and Aims:** The death of a child is one of the most devastating events a family can face resulting in significant physical and psychosocial morbidity. Bereavement support programs have been developed and published in high-income contexts. However, little is known about implementing bereavement programs in low-and middle-income countries (LMICs). Here, we describe the implementation of a bereavement program for parents who lost their children due to cancer and other catastrophic illnesses.

**Methods:** The bereavement program was developed in a nonprofit, teaching hospital and referral center for southwestern Colombia. The program was implemented between 2017 and 2021. This program was developed in several stages including an assessment of family needs, development of program guidelines, staff training in bereavement care, piloting of the program, refinement, and finally standardization.

**Results:** Several tools were developed as key components of the bereavement program: A virtual bereavement course, guidance for End of Life (EoL) and bereavement communication and care, memory making, follow-up calls, a condolence letter template, and group support workshops. A total of 956 healthcare professionals (HCPs) were trained, 258 follow-up calls to bereaved parents were made, 150 individual psychological follow-ups to parents with complicated grief occurred, 79 condolence letters were sent, and 10 group support workshops were carried out. Many challenges were identified and overcome, such as limited resources and staff, and cultural perceptions of death. In 2021, this program received an award by the hospital as the Best Strategy to Humanize Healthcare.

**Conclusions:** A bereavement program for families can be implemented, despite the significant barriers that exist in the context of LMICs. Raising awareness of bereavement needs, education for HCPs at all levels of care, mentorship, and collaboration with bereaved parents were key strategies for success. Future plans include creating an implementation package of measures that help other hospitals from LMICs to improve bereavement care.

O171/#693 | Free Paper Session (FPS)

## FPS 13: SURVIVORSHIP

13-10-2023 14:10 - 15:40

### EXCESS HEALTHCARE EXPENDITURE IN ADULTS TREATED FOR SOLID CANCER IN CHILDHOOD: A COHORT STUDY IN FRANCE

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**Background and Aims:** Due to late effects, childhood cancer survivors (CCS) are more likely to have multiple chronic conditions than the general population. However, little is known about the economic burden of care of CCS in the long term. We aim to estimate excess healthcare expenditure for long-term CCS in France compared to the general population and to investigate the associated factors.

**Methods:** We included 5353 5-year solid CCS diagnosed before the age of 21 years before 2000 from the French Childhood Cancer Survivors Study and obtained a random reference sample from the general population for each CCS, matched on age, gender and region of residence. We used the French national health data system to estimate annual healthcare expenditure between 2011 and 2018 for CCS and the reference sample and computed the excess as the net difference between CCS expenditure and the median expenditure of the reference sample. We used repeated-measures generalized linear models to estimate associations between excess healthcare expenditure and CCS characteristics.

**Results:** Annual mean (95% CI) excess healthcare expenditure was €3,920 (3539; 4301), mainly for hospitalization (39.6%) and pharmacy expenses (17%). Higher excess was significantly associated with having been treated before the 1990s and having survived a central nervous system tumor, whereas lower excess was associated with CCS who had not received treatment with radiotherapy.

**Conclusions:** Of the variables that influence excess healthcare expenditure, a lever for action is the type of treatment administered. Future research should focus on addressing the long-term cost-effectiveness of new approaches, especially those related to radiotherapy.

O172/#334 | Free Paper Session (FPS)

FPS 13: SURVIVORSHIP

13-10-2023 14:10 - 15:40

#### HEALTH CARE UTILIZATION AMONG SURVIVORS OF CHILDHOOD, ADOLESCENT AND YOUNG ADULT CANCER (AYA): A POPULATION BASED STUDY

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**Background and Aims:** Survivors of childhood and AYA cancers are at increased risk for late effects. Few studies have investigated if this translates into increased health care utilization during survivorship. We aim to compare rates of healthcare utilization between childhood and AYA cancer survivors and their matched controls without a prior history of cancer.

**Methods:** This was a retrospective population-based matched cohort study using administrative databases in Ontario, Canada. The survivor cohort included individuals diagnosed with cancer  $\leq 21$  years old between July 1986 to December 2013, and who had survived  $\geq 5$  years from their primary cancer or relapse/recurrence. Cancer-free controls were matched in a five-to-one ratio based on birthdate, sex, and geographic location. The index date was the later of age 18 or the 5-year survivorship mark. Follow-up was terminated at a cancer-related event, death, or December 2019, whichever occurred first. Andersen-Gill recurrent event models were used to evaluate the association between survivorship and the rates of hospitalization, surgeries, diagnostic imaging, visits to primary care physician (PCP), and sub-specialists, adjusting for income quintile, comorbidity, and accounting for the matched design.

**Results:** We identified 8,090 survivors and 40,450 matched controls; median follow-up time from index was 9 years (interquartile range: 5-15). Compared to their controls, survivors had higher rates of hospitalizations (adjusted relative rate (aRR): 1.82, 95% Confidence Interval [CI] 1.68-1.96), surgeries (aRR 1.26, 95%CI: 1.20-1.32), diagnostic imaging (RR 1.49, 95%CI 1.44-1.53), and sub-specialist visits (aRR 1.55, 95%1.50-1.61). Rates of PCP visits did not differ (aRR: 1.01, 95%CI: 0.99-1.03). Across all healthcare services, individuals with more comorbidities had higher rates of utilization.

**Conclusions:** We demonstrated higher rates of healthcare use among survivors in a publicly funded healthcare system. Our findings suggest survivors do not seek additional care from their PCPs. Further research is needed to quantify the economic impact of survivorship care.

O173/#276 | Free Paper Session (FPS)

FPS 13: SURVIVORSHIP

13-10-2023 14:10 - 15:40

#### PREVALENCE AND DETERMINANTS OF DYSLIPIDEMIA IN A NATIONAL COHORT OF 2,338 DUTCH CHILDHOOD CANCER SURVIVORS: A DCCSS-LATER STUDY

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Höfer<sup>7</sup>, Geert Janssens<sup>2,8</sup>, Leontien Kremer<sup>2,9</sup>, Jacqueline Loonen<sup>10</sup>, Marloes Louwerens<sup>11</sup>, Heleen Van Der Pal<sup>2</sup>, Saskia Pluijm<sup>2</sup>, Cecile Ronckers<sup>2,12</sup>, Wim Tissing<sup>2,13</sup>, Birgitta Versluijs<sup>2,14</sup>, Andrica De Vries<sup>2,15</sup>, Aart-Jan Van Der Lelij<sup>1</sup>, Marry Van Den Heuvel-Eibrink<sup>2,14</sup>, Sebastian Neggers<sup>1,2</sup>

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**Background and Aims:** Endocrine and metabolic disorders, including dyslipidemia, are within the most common late effects in childhood cancer survivors (CCS). Dyslipidemia is associated with accelerated atherosclerosis and increases the risk for subsequently cardiovascular disease. We aimed to assess the prevalence, also using different international classifications to identify their impact, and to identify determinants of dyslipidemia in CCS.

**Methods:** The prevalence of dyslipidemia was assessed in our cohort of 2,338 long-term adult CCS (treated in 1963-2002), with the Lifelines (control) cohort (n=132,226) as a reference, using various international classifications (National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP-III), World Health Organization, European Group for the Study of Insulin Resistance, and the Modified version of the NCI Common Terminology Criteria for Adverse Events). Multivariable logistic regression analysis with separate models (demographic, treatment- and comorbidity related) were used to identify associated determinants.

**Results:** Our cohort had a median age of 34.0 (interquartile range (IQR) 27.8-40.1) years and had a median follow-up time of 26.0 (IQR 20.6-32.8) years. The prevalence of dyslipidemia (defined by NCEP-ATP-III) was 41.7% in our survivor cohort compared to 25.6% in the control cohort (median age 39.0 (IQR 31.0-45.0) years) (OR 2.08, 95%CI 1.90-2.27). The prevalence varied between 25.0-41.7% among CCS and 13.4-37.2% among controls according to different

classifications. We identified female sex, older age, higher BMI, a history of abdominal/pelvic- and/or cranial radiotherapy, total body irradiation, alkylating agents, hematopoietic stem-cell transplantation, growth hormone deficiency and diabetes as associated determinants for dyslipidemia in CCS.

**Conclusions:** CCS show a two-fold increased odds of dyslipidemia compared to controls. Our findings underscore the importance of an universally accepted definition and validated thresholds for its components, as substantial differences in prevalence of dyslipidemia were observed across the usage of different classifications.

O174/#281 | Free Paper Session (FPS)

### FPS 13: SURVIVORSHIP

13-10-2023 14:10 - 15:40

### OUTCOMES OF CHILDHOOD, ADOLESCENT, AND YOUNG ADULT CANCER SURVIVORS (CAYACS) WITH SOLID ORGAN TRANSPLANTS (SOT): A POPULATION-BASED STUDY

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**Background and Aims:** Organ toxicity requiring SOT is a rare but serious effect of cancer treatment. CAYACS requiring SOT are assessed against potential recipients with non-malignant indications; decisions are limited by scant long-term data. We compared long-term outcomes for CAYACS requiring SOT with other SOT recipients.

**Methods:** All Ontario children <18 years diagnosed with cancer 1986-2021 and AYA aged 15-21 diagnosed at adult centres for leukemia, lymphoma, sarcoma, or testicular cancer 1992-2012 were identified, excluding those with SOT prior to cancer. Linkage to healthcare databases identified SOT; patients were matched 1:2 to non-malignant SOT recipients by sex, SOT year and type, and birth year. Post-SOT outcomes [overall survival (OS), post-SOT cancers] were compared between CAYACS and controls.

**Results:** Among 16,533 CAYA with cancer, 85 received SOT (46 liver, 18 kidney, 11 lung, 10 heart). Among liver recipients, 33 (71.7%) were for primary cancer treatment (e.g. hepatoblastoma) vs. 13 (28.3%) for organ toxicity. Median age at original cancer diagnosis was 4 years [interquartile range (IQR) 1-13] and at SOT was 13 (IQR 3-20). CAYACS with SOT for long-term toxicity (liver subset plus all renal, lung, heart, N=52) had median time from cancer diagnosis to SOT of 9 years (IQR 4-16) and experienced lower 10-year OS from time of SOT

[67.7%, 95<sup>th</sup> confidence interval (95CI) 50.8-79.9] vs. SOT controls [86.0% (74.8-92.5); hazard ratio (HR) 3.9; 95CI 1.6-9.7;  $p=0.003$ ]. Similar trends were seen by SOT type but were only statistically significant among lung SOT recipients. Among CAYACS requiring SOT following organ toxicity, 10-year cumulative incidence of second cancers was  $8.6\% \pm 4.2\%$ , similar to incidence of first cancer among SOT controls ( $6.4\% \pm 2.6\%$ ; HR 1.6, 95CI 0.6-4.0;  $p=0.34$ ).

**Conclusions:** Though CAYACS with SOT have inferior survival compared to other SOT patients, the majority achieve long-term cancer-free survival. These data inform discussions on the suitability of CAYACS for SOT.

O175/#846 | CCI

CCI: PROVIDING PSYCHOSOCIAL SUPPORT 02

13-10-2023 14:10 - 15:40

#### PROVIDING PSYCHOSOCIAL SUPPORT TO CHILDREN DIAGNOSED WITH CANCER IN MALAWI USING A SLEEP AWAY CAMP/FAMILY WEEKEND MODEL

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**Background and Aims:** Children diagnosed with cancer (CDWC) and their families face emotional and social challenges leading to anxiety and depression. They are isolated from friends, and family, and restricted from their normal daily activities. Stigma around cancer diagnosis in Low-and-Middle Income Countries (LMIC) further compounds these realities. We partnered with Serious Fun Children's Network to host annual family weekend oncology camps to provide psychosocial support to CDWC. While oncology camps are well described in high income countries, this is a first report from Sub-Saharan Africa (SSA).

**Methods:** Campers aged 5-15 years were selected from a list of patients currently receiving or recently completed treatment for cancer at Kamuzu Central Hospital, Malawi. They were selected using stringent criteria that included physical assessments. Pre- and post-evaluations were administered to patients and guardians to measure selected outcomes. All camp staff underwent a 5-day intentional programming and child-focused training, and these activities were done using the Therapeutic Recreation Model (TRM).

**Results:** Forty-eight children have participated in the oncology camp from 2021-2022. The median age of campers was 10.5 years (Interquartile range 9-13) and 65% ( $n=26$ ) were adolescents. The most common diagnoses were leukemias (54%) solid tumors (38%) and lymphomas (8%). Two campers were accompanied by a sibling and 27% of the participants had completed therapy. Post-camp evaluation demonstrated 31% increase in children's/peer interaction and 50% reduction in stress among guardians. All guardians (100%) indicated that camp had a positive psychosocial impact on their children, and it was a fun experience for their children.

**Conclusions:** The camp TRM model has proved to have a positive impact on the psychosocial health of children diagnosed with cancer at our center in Malawi. Other LMIC countries can benefit from integrating this model into their clinical care.

O176/#1104 | CCI

CCI: PROVIDING PSYCHOSOCIAL SUPPORT 02

13-10-2023 14:10 - 15:40

#### THE IMPACT OF PSYCHOSOCIAL SUPPORT GROUPS FOR CHILDREN WITH CANCER, THEIR FAMILIES, AND CAREGIVERS IN NIGERIA

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**Background and Aims:** Background Cancer is a bully. When a child is diagnosed with cancer, the parents, siblings, and others who surround and love them share their anguish. A cancer diagnosis has an impact on the entire family. Aim

This study assesses the effectiveness of psychosocial support groups using quantitative and qualitative measures in assisting families and caregivers of children with cancer.

**Methods:** The impact of support group meetings for families and caregivers was assessed using a longitudinal approach.

There were 11 meetings, with 40 participants representing direct families of children with cancer and 20 caregivers. A cognitive-behavioral assessment was used to collect quantitative data, and semi-structured interviews were used to collect qualitative data.

**Results:** The study highlights the impact of a psychosocial intervention on helping families and caregivers cope with the emotional and psychological distress caused by cancer. The group experience provided effective, relational, and informative support that allowed 46.5% of participants to create a coping network, and 40% of participants feel reassured that they are not alone, and their feelings, reactions, fear, hopes, and enthusiasm are well noted, while 13.5% of participants are indicative due to outcome fear.

**Conclusions:** The findings point to the significance of psychological support groups for patients, families, and caregivers. This kind of intervention has significance not only at an individual level but also for the entire system. Psychosocial support groups are vital for patients, families, and caregivers to lessen the strain and guarantee the greatest outcomes for children with cancer.

O177/#1690 | Free Paper Session (FPS)

FPS 14: ALL DIAGNOSIS AND TREATMENT

13-10-2023 14:10 - 15:40

#### REINDUCTION WITH BLINATUMOMAB ALONE OR WITH NIVOLUMAB FOR FIRST RELAPSE OF B-ACUTE LYMPHOBLASTIC LEUKEMIA: RESULTS FROM GROUP 1 OF THE CHILDREN'S ONCOLOGY GROUP TRIAL AALL1821

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**Background and Aims:** Reinduction chemotherapy for first relapse of B-ALL is often ineffective and toxic. Immunotherapy agents, including blinatumomab, are promising alternatives. The COG trial AALL1821 (NCT04546399) examined whether blinatumomab with or without the addition of nivolumab would be effective to induce remission without intensive chemotherapy for Group 1 patients.

**Methods:** AALL1821 is an open-label, risk-stratified Phase 2 study. Patients with first marrow relapse were eligible for Group 1 if they were either <18 years old (y.o.) with relapse <24 months from diagnosis, or ≥18 y.o. with relapse of any duration. Patients were randomized 1:1 to reinduction with either 28 days blinatumomab (Arm A) or blinatumomab with nivolumab on days 11 and 25 (Arm B). Patients with extramedullary disease or a white blood cell count >30,000/ $\mu$ l at relapse received mandatory low intensity pre-immunotherapy treatment (PIT). The primary objective was to compare rates of minimal residual disease (MRD) negative second remission after up to two cycles of reinduction.

**Results:** Fifty-nine patients (57 evaluable) were randomized as of 12/31/2022. Overall, 19% (5/26) Arm A patients achieved MRD negative remission compared to 32% (10/31) in Arm B ( $p=0.13$ ). Response was associated with a lower marrow blast percentage at 1<sup>st</sup> relapse ( $p=0.02$ ). Thirteen received PIT, with 2/8 (A) and 5/5 (B) patients achieving MRD negative remission. Of those ≥18 y.o. with relapse ≥24 months from initial diagnosis, 2/8 (A) and 6/11 (B) achieved MRD negative remission. Immunotherapy as reinduction was safe and well tolerated, with no dose limiting toxicities.

**Conclusions:** Blinatumomab combined with nivolumab was safe and well-tolerated in patients with first marrow relapse of B-ALL. The use of immunotherapy as reinduction is promising, although is limited when there are high levels of disease burden at relapse. Future directions will use low intensity chemotherapy to debulk patients with high disease burden at relapse prior to initiation of immunotherapy.

O178/#1402 | Free Paper Session (FPS)

## FPS 14: ALL DIAGNOSIS AND TREATMENT

13-10-2023 14:10 - 15:40

## INDIVIDUALIZING PEG-ASPARAGINASE TREATMENT IN ACUTE LYMPHOBLASTIC LEUKEMIA -A NOPHO ALL2008 STUDY

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**Background and Aims:** PEG-asparaginase is an indispensable part of the multiagent treatment of acute lymphoblastic leukemia (ALL). However, PEG-asparaginase treatment comes with substantial toxicity which often leads to discontinuation of therapy and thus an increased risk of relapse. Hypersensitivity is the most common toxicity. A recent (unpublished) ALLTogether Pilot study evaluated Asparaginase enzyme activities (AEA) from intravenous administered PEG-asparaginase in a newly developed Pharmacokinetic (PK) model and illustrated a possibility to detect induced clearance before inactivation occurred. The model has not yet been validated on external data. We aimed to validate the PK model to clarify the possibility to predict hypersensitivity in patients treated with IM PEG-asparaginase.

**Methods:** Patients with ALL aged 1-45 years treated according to the NOPHO ALL2008 Protocol from March 1<sup>st</sup> 2016 to December 31<sup>st</sup> 2022 in the Nordic and Baltic countries were eligible. A total of 7,424 AEA samples from 864 patients were included. Sampling included AEA 14 days after every dose and additional AEA between 1<sup>st</sup> and 2<sup>nd</sup> dose of PEG-asparaginase.

**Results:** AEA from 864 patients entered analyses and hypersensitivity was seen in 13.2% of the patients. In preliminary external validation the PK model was able to predict allergy with a sensitivity on 72.1% and a specificity on 86.5% when evaluating AEA from IM administered PEG-asparaginase.

**Conclusions:** PK analysis of AEA enables early identification of increased clearance, which opens new possibilities to predict hypersensitivity during PEG-asparaginase treatment and provides ability to intervene before inactivation of PEG-asparaginase occurs. Thus, a PK model would allow clinicians to use the estimated probability for a hypersensitivity response given the TDM measurements but also to guide in dose reduction if predicted AEA show unnecessary high trough levels of AEA.

O179/#542 | Free Paper Session (FPS)

## FPS 14: ALL DIAGNOSIS AND TREATMENT

13-10-2023 14:10 - 15:40

## AUGMENTED SALVAGE CHEMOTHERAPY FOR CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA WITH HIGH MINIMAL RESIDUAL DISEASE LOAD: RESULTS OF CCLSG ALL 2004 STUDY

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**Background and Aims:** Childhood acute lymphoblastic leukemia (ALL) with high minimal residual disease (MRD) load has a poor prognosis. We previously analyzed MRD status in 911-protocol of Children's Cancer and Leukemia Study Group of Japan (CCLSG) for childhood ALL patients at 3 months after the initiation of chemotherapy (Time Point 2; TP2). The relapse rate of the TP2 MRD-positive group (TP2+) was 100%. In CCLSG ALL 2000 protocol, we employed a risk-upregulation strategy for TP2+ patients. In CCLSG ALL 2004 study, we conducted augmented chemotherapy protocols specifically designed to salvage TP2+ patients.

**Methods:** From June 2004 to September 2009, we prospectively enrolled 333 consecutive children with ALL. Eligible patients were allocated to treatment protocols on the stratification based on NCI risk criteria and WBC counts (SR, HR, and HHR). Patients were stratified again at TP2; patients with T-cell receptor/immunoglobulin PCR-MRD levels equal or over  $10^{-3}$  were assigned to salvage arm and treated with augmented therapy arms.

**Results:** Among 333 patients, 326 were eligible. The overall 3y-EFS rate of the TP2 MRD-negative group (TP2-, n=297) was 0.90 (95% CI, 0.86-0.93) and TP2+ (n=29) was 0.75 (95% CI, 0.55-0.89) ( $p=0.0029$ ). In the SR group, 3y-EFS of TP2- (n=191) was 0.87 (95% CI, 0.88-0.91), and that of TP2+ (n=15) was 0.87 (95% CI, 0.56-0.97) ( $p=0.8$ ). In the HR group, 3y-EFS of TP2- (n=79) was 0.92 (95% CI, 0.82-0.96) and that of TP2+ (n=7) was 0.57 (95% CI, 0.17-0.84) ( $p=0.0248$ ). In the HHR group, 3y-EFS of TP2- (n=26) was 0.84 (95% CI, 0.62-0.96) and that of TP2+ (n=7) was 0.51 (95% CI, 0.12-0.81) ( $p=0.0838$ ). Nine patients of TP2+ relapsed, and all the patients died of the primary disease. None of the live patients developed life-threatening late complications.

**Conclusions:** Augmented chemotherapy contributes to the salvage of TP2+ patients without obvious life-threatening late complications in CCLSG ALL 2004 study.

O180/#1451 | Free Paper Session (FPS)

#### FPS 14: ALL DIAGNOSIS AND TREATMENT

13-10-2023 14:10 - 15:40

#### L-ASPARAGINASE HYPERSENSITIVITY REACTIONS ARE ASSOCIATED WITH CYP1B1 AND IMMUNE REGULATORY PATHWAYS

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**Background and Aims:** L-asparaginase is a critical component of a multi-modal treatment for acute lymphoblastic leukemia, the most common cancer in children. Hypersensitivity reactions occur in up to 70% of treated patients and can be severe, resulting in emergency care, hospitalization, or death. The goal of this study is to quantify the timing of L-asparaginase induced hypersensitivity reactions and identify genes strongly associated with the pathogenesis of hypersensitivity.

**Methods:** 927 children who received L-asparaginase were assessed for the occurrence of hypersensitivity through the Canadian Pharmacogenomics Network for Drug Safety. Severity of hypersensitivity was graded based on the Common Terminology Criteria for Adverse Events v5. Cases were defined as patients who experienced  $\geq$  grade 2 hypersensitivity and controls were those who did not experience hypersensitivity despite equivalent exposure to L-asparaginase. A genome-wide association study (GWAS) was conducted utilizing the Illumina Global Screening Array v2.

**Results:** 86% of patients with documented hypersensitivity experienced anaphylaxis or required hospitalization due to their reactions ( $\geq$  grade 3, n=194). The median number of doses to hypersensitivity was 10 (interquartile range = 5-12) for patients receiving *E. coli* L-asparaginase and 2 doses (IQR = 2-3) for pegylated L-asparaginase. Median time-to-toxicity was 89 days (IQR = 50-114 days) for *E. coli* L-asparaginase and 73 days (IQR = 51-91 days) for pegylated L-asparaginase. Results from the GWAS showed significant associations for variants in *CYP1B1* ( $p = 1.7 \times 10^{-8}$ ; OR = 6.1 [3.0-12.5]) and *ANKLE2* ( $p = 2.2 \times 10^{-8}$ ; OR = 5.6 [2.9-11.0]) genes.

**Conclusions:** L-asparaginase-induced hypersensitivity reactions are most likely to be severe and require hospitalization for management. Results from the GWAS suggest genes that are involved in the regulation and development of immune cells, and in key lipid metabolism pathways that regulate immune response are associated with L-asparaginase-induced hypersensitivity.

O181/#1426 | Free Paper Session (FPS)

#### FPS 14: ALL DIAGNOSIS AND TREATMENT

13-10-2023 14:10 - 15:40

#### EVALUATING MULTIDISCIPLINARY PROVIDER PERCEPTIONS OF BLINATUMOMAB IMPLEMENTATION BARRIERS AND EARLY IMPLEMENTATION OUTCOMES IN LOW-AND MIDDLE-INCOME COUNTRIES

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**Background and Aims:** Blinatumomab is a targeted immunotherapy for B-ALL, FDA-approved in 2014. In addition to high cost, contextual barriers including access, supportive care, and institutional capacity have limited utilization in low and middle-income countries (LMIC). In partnership with a drug-donation program, we used implementation science to facilitate the translation of blinatumomab, a therapeutic evidence-based intervention (EBI), into 5 hospitals in India and Pakistan.

**Methods:** Informed by the Consolidated Framework for Implementation Research (CFIR), we evaluated pediatric provider perceptions of barriers to blinatumomab administration and "leading indicator" implementation outcomes. A 2-part electronic survey was developed comprising 54 close-ended questions from previously validated surveys assessing feasibility, acceptability, appropriateness, implementation climate, organizational readiness, drug complexity, and 8 open-ended questions assessing provider demographics, worries, and health system adaptations. Institutional leads identified multidisciplinary champions for blinatumomab implementation (4-7 individuals/site). Close-ended responses were scored using a 5-point Likert-type scale (5=completely agree, 1=completely disagree). Miles & Huberman's matrix approach was used for the thematic analysis of qualitative data collected from open-ended responses.

**Results:** Prior to the survey, all sites had completed an on-line training program and 3 were administering blinatumomab. Across 5 institutions, 13 respondents (13/25, 52%) completed the survey (9 physicians, 2 nurses, 2 pharmacists). Females comprised 62% of the respondents. Respondents reported high feasibility, acceptability, and appropriateness (4.31, 4.65, and 4.77 respectively). Aggregate mean scores for implementation climate indicated an organizational focus on EBI (4.51), but a relative lack of incentive and compensation for providers using EBIs (2.33). Thematic analysis revealed concerns about adverse events, medical supply availability, patient costs, and prolonged hospitaliza-

tion; perceived benefits included improved survival and quality of life.

**Conclusions:** Implementation outcomes including feasibility, acceptability, and appropriateness are critical predecessors to establishing real-world effectiveness. This implementation evaluation was critical to build contextual understanding and inform future in-depth qualitative assessments and adaptation of resource-adapted management guidelines in LMICs.

O182/#176 | Free Paper Session (FPS)

FPS 14: ALL DIAGNOSIS AND TREATMENT

13-10-2023 14:10 - 15:40

#### IMPROVED OUTCOME FOR CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA BY PROLONGING THERAPY FOR IKZF1 DELETION AND DECREASING THERAPY FOR ETV6::RUNX1, DOWN SYNDROME OR PREDNISONE POOR RESPONSE

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**Background and Aims:** The ALL10 protocol improved outcome for children with ALL by stratifying and adapting therapy in minimal residual disease (MRD) defined standard risk (SR), medium risk (MR) and high risk (HR). IKZF1 deleted (IKZFdel) ALL in the largest MR group still showed poor outcome, in line with protocols worldwide, accounting for a high number of overall relapses. ALL10 showed high toxicity in Down syndrome (DS) and excellent outcome in ETV6::RUNX1 ALL. Poor prednisone responders (PPR) were treated as HR in ALL10. In ALL11, we prolonged therapy for IKZFdel from 2 to 3 years to improve outcome. We aimed to reduce therapy for DS by omitting anthracyclines completely and omitting anthracyclines for ETV6::RUNX1 in intensification and for PPR by treatment as MR instead of HR without abrogating their outcome.

**Methods:** 819 ALL patients (aged 1-18 year) were enrolled on ALL11 and stratified as in ALL10. Results were compared to ALL10.

**Results:** Five years overall survival (OS), event-free survival (EFS), cumulative risk of relapse (CIR) and death in complete remission (CID) on ALL11 were 94.2% (SE 0.9%), 89.0% (1.2), 8.2% (1.1), 2.3% (0.6) respectively. Prolonged maintenance for IKZF1del MR improved the

5-year CIR by 2.2-fold (10.8% vs 23.4%;  $p=0.035$ ) and EFS (87.1% vs 72.3%;  $p=0.019$ ). Landmark analysis at 2 years from diagnosis showed a 2.9-fold reduction of CIR (25.6% to 8.8%;  $p=0.008$ ) and EFS improvement (74.4% to 91.2%;  $p=0.007$ ). Reduced therapy did not abrogate the 5-years outcome for ETV6::RUNX1 (EFS 98.3%; OS 99.4%), DS (EFS 87.0%; OS 87.0%) and PPR (EFS 81.1%; OS 94.9%).

**Conclusions:** Children with IKZF1del ALL benefit from prolonged maintenance therapy. Chemotherapy was successfully reduced for ETV6::RUNX1, DS and PPR ALL patients. **Trial registration number:** EudraCT 2012-000067-25; NL3227 (clinicaltrialregister.nl)

O183/#212 | Nursing

#### NURSING: EDUCATION ABSTRACT PRESENTATIONS

13-10-2023 16:40 - 17:40

#### NURSING EMPOWERMENT OF RADIONUCLIDE THERAPY IN PAEDIATRIC ONCOLOGY

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**Background and Aims:** Radionuclide therapy is the use of therapeutic radiopharmaceuticals to introduce ionizing radiation to the cancer cell for disease management or pain palliation such as iodine-131. It is highly radioactive and accordingly, occupational radiation protection is worth noting. Majority nurses reported anxiety whilst providing nursing care although training was received beforehand. Aims of this intensive education program were equipping oncology nurses with knowledge on various kinds of radionuclide therapy and relevant radiation protection principles; empowering nurses to deliver safe and effective nursing care to paediatric patients receiving radionuclide therapy.

**Methods:** Three advanced practice nurses and thirteen registered nurses ( $n=16$ ), who were working in paediatric oncology-solid tumor teams being recruited in July 2022. A pre-training knowledge assessment which was validated by a local oncology expert panel was completed first. Meanwhile, a questionnaire was distributed to collect their demographic data and anxiety level. In September 2022, a face-to-face training workshop was conducted with the use of PowerPoint and videos on skills demonstration. Post-training knowledge assessment, anxiety questionnaire and program evaluation form were completed afterwards.

**Results:** From the pre-training questionnaire, eight participants reflected on considering job-quitting due to health concerns, and eight participants addressed experiencing mild-to-moderate anxiety. The primary cause of anxiety was related to their competency in handling radionuclide therapy. A significant knowledge enhancement on radiation principle and precaution after the program (mean score

from 6.4/12 to 9.6/12). Further, they all expressed appreciation and agreed that the program was rewarding, and their worries alleviated with only two participants reporting mild-to-moderate anxiety. They had confidence in providing nursing care independently subsequently. **Conclusions:** This empowerment program can successfully equip nurse's knowledge and skills on radiation safety and care. Their competence is enhanced, and safe radiation care ensured. Additionally, it empowered nurses to provide health education to patients, parents and supporting staff. Finally, most nurses remain in the unit.

O184/#721 | Nursing

#### NURSING: EDUCATION ABSTRACT PRESENTATIONS

13-10-2023 16:40 - 17:40

#### INCREASING CAPACITY FOR QUALITATIVE RESEARCH IN PEDIATRIC ONCOLOGICAL CARE IN THE EASTERN MEDITERRANEAN REGION

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**Background and Aims:** Qualitative research provides an avenue for the collection of valuable non-numerical data exploring local contexts and experiences of patients, families, healthcare professionals, and community members. Despite its potential to improve quality of pediatric cancer care delivery, gaps exist in training and available protected time for conducting qualitative research globally. St. Jude's Global Culture and Communication team hosted four research workshops in the Eastern Mediterranean region to introduce the fundamentals of qualitative research. This abstract explores the process and effectiveness of those workshops.

**Methods:** Each workshop was conducted by an interdisciplinary team, including experts in public health, health communication, anthropology, pediatric oncology, and palliative care. Workshops consisted of a didactic segment supplemented with visual slides and interactive activities that engaged participants in study design, data collection, interviewing, and thematic content analysis. Upon workshop conclusion, participants were invited to evaluate their prior exposure to qualitative research training, workshop effectiveness, and interest in

conducting future qualitative research. All workshops were conducted in March 2023.

**Results:** The workshops were hosted at three hospital sites and one regional pediatric cancer conference. In total, 260 participants attended the workshop in-person ( $n=165$ ) or virtually ( $n=95$ ), including researchers, healthcare professionals, and foundation representatives. Approximately 23.8% of participants ( $n=62$ ) completed the post-workshop evaluation. Fifty-eight percent of respondents had no prior qualitative research education or training. After participation in the workshop, 93.5% of respondents reported increased general knowledge of qualitative research methodology, 88.7% reported feeling more prepared to conduct qualitative research, and 90.3% reported increased interest in incorporating qualitative methods into current/future research.

**Conclusions:** Further qualitative research education and training in the Eastern Mediterranean and globally has the potential to enhance knowledge of qualitative research methodologies, increase interest in pediatric cancer-focused qualitative research, and build greater capacity and institutional support for qualitative research in the global pediatric cancer context.

O185/#1813 | Nursing

#### NURSING: EDUCATION ABSTRACT PRESENTATIONS

13-10-2023 16:40 - 17:40

#### NURSING TEAM LEADING THE SITE-SPECIFIC NURSE INITIATED TIME OUT (NATO) IMPLEMENTATION IN PANAMA

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**Background and Aims:** The NATO project emphasizes the nurses' role in reviewing antimicrobial therapy in pediatric oncology patients at hour 72 after initiation for febrile neutropenia. The successful implementation of this initiative relies on the nursing team's knowledge, leadership, and empowerment. We report the nurses' experience and leadership in implementing the NATO initiative in a pediatric unit in Panama.

**Methods:** Through quality improvement approach, the NATO processes were adapted to the hospital. The pediatric oncology nurses received training on the new processes and started implementation in October 2022. A review of the first five months of NATO implementation was conducted. Data collected included: number of trained nurses, knowledge assessment, nurses' satisfaction rates with the training program, physician's perception of nurses', and compliance rates with NATO processes. We analyzed data through descriptive statistics and used findings to identify opportunities for improvement.

**Results:** The NATO adaptation focused on introducing a communication script that unit nurses activate at 72 hours after antimicrobial

therapy. A total of 22 nurses were trained with a 90% satisfaction rate. Likewise, 90% of the trained nurses successfully completed the knowledge assessment. During the first round of review, 25 patients met the inclusion criteria for NATO. The compliance rate with NATO initiation was 96% ( $n=24$ ). NATO documentation was complete as per the NATO policy in 92% ( $n=23$ ) of the cases. Six physicians responded to NATO physicians' perspective survey ( $n=6$ ), rating nurses' NATO communication with them as objective in 100% of the responses and as effective in 83% of the cases. A challenge in implementing the training was the continuous rotation of nurses between unit.

**Conclusions:** The initial implementation of NATO in Panama emphasized the nurses' contributions and leadership in appropriate antimicrobial use in pediatric oncology. Continued monitoring and implementation reviews will help improve NATO processes to optimize antimicrobial use while relying on the nursing team.

O186/#451 | Nursing

#### NURSING: EDUCATION ABSTRACT PRESENTATIONS

13-10-2023 16:40 - 17:40

#### NAUSEA AND NAUSEA-RELATED SYMPTOMS IN CHILDREN WITH CANCER: PRESENCE, SEVERITY, RISK FACTORS AND IMPACT ON QUALITY OF LIFE DURING THE FIRST YEAR OF TREATMENT

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**Background and Aims:** This study aimed to identify 1) the presence and severity of nausea and nausea-related symptoms during the first year of treatment, 2) associations between patient-related factors and nausea, 3) the relationship between nausea-related symptoms and health-related quality of life (HRQoL) in children with cancer.

**Methods:** A large historical cohort study of 781 children and adolescents with cancer (2-21 years) was conducted. Presence and severity of nausea were assessed at 3, 6, 9, and 12 months after diagnosis using the nausea scale of the PedsQL3.0 Cancer Module, comprising 5 symptoms, using proxy-report (2-7 years) or self-report (8-21 years). Multivariable multilevel analyses were performed to evaluate the association between patient-related factors and nausea. Overall HRQoL



(generic PedsQL total scores) was compared between children with presence (sometimes-often-almost always) and absence (never-almost never) of nausea related-symptoms.

**Results:** Nausea during medical treatment was present in 41.8% and 42.9% of the children at 3 and 6 months respectively, and decreased to 24.8% at 12 months after diagnosis. Highest symptom presence was seen on the item "food not tasting good" (range 51.6%-62.8%).

Pain, treatment anxiety and worry were significantly associated with nausea in all children. Additionally, in patients aged 8-21 years, male gender, a solid tumor diagnosis and BMI were significantly associated with nausea. Patients with a solid tumor were at higher risk of nausea compared to patients with a hematological malignancy or brain/CNS tumor. Patients with a high BMI reported less nausea compared to patients with a normal BMI.

For all nausea-related symptoms, average HRQoL scores were 11.6-14.4 (2-7 years) and 9.9-13.3 (8-21 years) points lower for patients with symptoms compared to patients without symptoms.

**Conclusions:** Nausea is still a major problem in children with cancer. In addition to adequate implementation of antiemetic treatment, psychosocial support regarding anxiety, worry and pain management could diminish nausea-related symptoms and improve HRQoL.

O187/#603 | Award Session

#### SCHWEISGUTH PRIZE LECTURE

13-10-2023 17:05 - 17:35

#### SELECTIVE PRESSURES OF PLATINUM COMPOUNDS SHAPE THE EVOLUTION OF THERAPY-RELATED MYELOID NEOPLASMS

Eline Bertrums<sup>1,2,3</sup>, Jurrian De Kanter<sup>1,2</sup>, Mark Verheul<sup>1,2</sup>, Markus Van Roosmalen<sup>1,2</sup>, Henrik Hasle<sup>4</sup>, Evangelia Antoniou<sup>5,6</sup>, Dirk Reinhardt<sup>5,6</sup>, Marry Van Den Heuvel-Eibrink<sup>1</sup>, C. Michel Zwaan<sup>1,3</sup>, Bianca Goemans<sup>1</sup>, Ruben Van Boxtel<sup>1,2</sup>

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**Background and Aims:** Treatment regimens of childhood cancer mainly consist of chemotherapy. The DNA-damaging effect of chemotherapy can affect both cancerous and normal cells. However, their precise role in the evolution of pediatric therapy-related myeloid neoplasms (t-MN) remains ambiguous. Here, we study how the selective pressures of platinum shape the evolution of pediatric t-MN.

**Methods:** We studied mutation accumulation and clonal evolution of t-MN in 43 pediatric patients, included via an international collaboration. We performed whole genome sequencing (WGS) of bulk and single t-MN blasts and single hematopoietic stem and progenitor cells (HSPCs).

**Results:** The assessed patients were previously treated for a variety of solid and hematological cancers. Both t-MN blasts and HSPCs showed an increased mutation burden compared to a previously established baseline of mutation accumulation in healthy HSPCs. In some patients, this increase was caused by distinct treatment-associated signatures. We identified platinum- and thiopurine-associated mutation patterns in exposed patients. However, in other patients the increase in mutations was caused by processes also active in healthy individuals, pointing towards indirect mutagenicity. We used phylogenetic inference, based on shared somatic mutations between cells of the same patient, to study the clonal evolution of t-MN in platinum-exposed patients. Generally, the DNA-crosslinking effect of platinum prohibits t-MN expansion during exposure. This was shown by a lack of platinum-linked mutations in the unique mutations of the t-MN blasts, pointing towards expansion after cessation of platinum treatment. Contrarily, in two germline *TP53*-mutated patients, the unique mutations in single cell t-MN blasts did show platinum-linked mutations, indicating the t-MN clone expanded during exposure.

**Conclusions:** Our results demonstrate that germline aberrations can interact with treatment exposures. In children with aberrant *TP53*, t-MN already expands during treatment and is therefore subjected to a different selection process compared to *TP53*-wildtype cells. These results are important in the development of patient-specific treatment regimens and follow-up.

O188/#2265 | Late Breaker Session

#### LATE BREAKER SESSION

13-10-2023 17:45 - 18:30

#### TREATMENT AND OUTCOMES OF CLEAR CELL SARCOMA OF THE KIDNEY: A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP STUDIES AREN0321 AND AREN03B2

Daniel Benedetti<sup>1</sup>, Lindsay Renfro<sup>2</sup>, Ian Tfirm<sup>3</sup>, Najat C Daw<sup>4</sup>, John Kalapurakal<sup>5</sup>, Peter Ehrlich<sup>6</sup>, Geetika Khanna<sup>7</sup>, Elizabeth Perلمان<sup>8</sup>, Anne Warwick<sup>9</sup>, Kenneth Gow<sup>10</sup>, Arnold Paulino<sup>11</sup>, Nita Seibel<sup>12</sup>, Paul Grundy<sup>13</sup>, Conrad Fernandez<sup>14</sup>, Jim Geller<sup>15</sup>, Elizabeth Mullen<sup>16</sup>, Jeffrey Dome<sup>17</sup>

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Ann Arbor, United States of America,<sup>7</sup> Emory University, Radiology & Imaging Sciences, Atlanta, United States of America,<sup>8</sup> Northwestern University Feinberg School of Medicine, Pathology And Laboratory Medicine, Chicago, United States of America,<sup>9</sup> Uniformed Services University of the Health Sciences, Pediatrics, Bethesda, United States of America,<sup>10</sup> Seattle Children's Hospital, Pediatric General And Thoracic Surgery, Seattle, United States of America,<sup>11</sup> MD Anderson Cancer Center, Radiation Oncology, Houston, United States of America,<sup>12</sup> National Cancer Institute, Division Of Cancer Treatment And Diagnosis, Bethesda, United States of America,<sup>13</sup> University of Alberta, Immunology, Hematology, Oncology, Palliative Care And Environmental Interactions, Edmonton, Canada,<sup>14</sup> Dalhousie University, Department Of Pediatric Hematology/oncology, Halifax, Canada,<sup>15</sup> Cincinnati Childrens Hospital, Oncology, Cincinnati, United States of America,<sup>16</sup> Dana-Farber Cancer Institute, Pediatric Hematology/oncology, Boston, United States of America,<sup>17</sup> George Washington University School of Medicine, Pediatrics, Washington DC, United States of America

**Background and Aims:** On NWTS-5, treatment for clear cell sarcoma of the kidney (CCSK) included Regimen I (alternating cycles of cyclophosphamide/etoposide with vincristine/doxorubicin/cyclophosphamide) and radiation therapy (RT), yielding 5-year EFS estimates of 100%, 88% (95% CI: 77-99%), 73% (95% CI: 59-87%), and 29% (95% CI: 0-76%) for stage I, II, III, and IV, respectively. COG study AREN0321 adapted therapy based on recurrence risk: RT was omitted for stage I disease provided that lymph nodes were sampled, and carboplatin was added for stage IV disease (Regimen UH-1). Patients with stage II/III received the same agents as in NWTS-5.

**Methods:** Four-year EFS was analyzed overall and by disease stage. To increase knowledge of this rare cancer, we also analyzed outcomes of patients enrolled on the AREN03B2 Renal Tumor Biology Study who received AREN0321 stage-appropriate chemotherapy regimens.

**Results:** Eighty-two patients with CCSK enrolled on AREN0321 and 51 on AREN03B2-only. For all stages combined, 4-year EFS was 82.7% (95% CI: 74.8-91.4%) for AREN0321 and 89.8% (95% CI: 81.7-98.7%) for AREN03B2-only ( $p=0.28$ ). Combining studies, 4-year EFS estimates for stage I ( $n=10$ ), II ( $n=48$ ), III ( $n=65$ ), and IV ( $n=10$ ) were 90% (95% CI: 73.2-100%), 93.5% (95% CI: 86.7-100%), 82.8% (95% CI: 74.1-92.6%), and 58.3% (95% CI: 34-100%), respectively. No local recurrences occurred among seven stage I patients who did not receive RT. The sole recurrence for stage I occurred in the brain, which was the most common relapse site overall. Among patients with local stage III tumors, neither initial procedure type, margin status, nor lymph node involvement were prognostic.

**Conclusions:** Patients with stage I CCSK had excellent outcomes without local recurrence when treated with Regimen I without RT. Patients with stage IV disease appeared to benefit from a carboplatin-containing regimen, though their outcomes remain unsatisfactory. Further research is needed to improve outcomes for patients with advanced stage disease.

O189/#2227 | Late Breaker Session

## LATE BREAKER SESSION

13-10-2023 17:45 - 18:30

### SUSTAINED-RELEASE TOPOTECAN EPISCLERAL CHEMOPLAQUE FOR RETINOBLASTOMA

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**Background and Aims:** Salvage of eyes with intraocular retinoblastoma remains challenging despite current therapies, including focal, intravitreal, systemic and intra-arterial chemotherapy, brachytherapy, and external beam radiotherapy. We report initial experience using episcleral chemoplaques that deliver intraocular topotecan chemotherapy.

**Methods:** Two parallel phase I studies were conducted to evaluate the toxicity of topotecan chemoplaques in children with intraocular retinoblastoma. Eligible patients were 8 weeks - 20 years with active residual retinoblastoma after first-line therapy or advanced intraocular disease at diagnosis. Patients with extraocular disease or receiving concomitant anti-cancer therapy were excluded. Five dose levels of topotecan (0.6 mg-1.8 mg) were evaluated using a rolling-six design. Chemoplaques were in situ for 6 weeks with dose limiting toxicity (DLT) evaluated during initial 9-week period.

**Results:** Forty-one participants were treated at doses 0.6 mg ( $n=8$ ), 0.9 mg ( $n=12$ ), 1.2 mg ( $n=10$ ), 1.5 mg ( $n=6$ ) and 1.8 mg ( $n=5$ ). Three for primary therapy; 38 had recurrence after failing other therapies. Excepting one patient at DL1 with grade 4 neutropenia coincident with benign ethnic neutropenia, all DLTs were ocular and related to inflammation at the site of chemoplaque: vitritis/scleritis (1 each at DL1 and 2), scleral necrosis (2 at DL4, 2 at DL5), and choroidal detachment/vitreous hemorrhage (1 at DL5). These were managed with steroid therapy and protocol amendment to add prophylactic subconjunctival steroid. Systemic topotecan concentrations were at/below limit of detection at all dose levels/timepoints. Sustained complete response was seen in 26/38 evaluable eyes (68%). Median follow-up 1.8 yr (range 0.4-3 yr).

**Conclusions:** These studies confirm minimal systemic toxicity of topotecan chemoplaque but dose-limiting ocular inflammation.

Current recommended phase 2 doses are 1.2 mg (2x0.6 mg chemo-plaques) and 0.9 mg chemoplaque for patients aged <6 months. Impressive overall response rate indicates that this new therapeutic approach has the potential to transform the therapeutic approach to intraocular retinoblastoma.

O190/#2267 | Late Breaker Session

#### LATE BREAKER SESSION

13-10-2023 17:45 - 18:30

#### EXPANSION OF VD1+ GAMMA DELTA T CELLS IN HUMAN NEUROBLASTOMA TUMORS REVEALS NOVEL POSSIBILITIES FOR IMMUNOTHERAPY

Bronte Manouk Verhoeven<sup>1</sup>, Kewei Ye<sup>2</sup>, Jakob Stenman<sup>1</sup>, Per Kogner<sup>3</sup>, John Inge Johnsen<sup>1</sup>, Ninib Baryawno<sup>1</sup>, Taras Kreslavskiy<sup>2</sup>  
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**Background and Aims:** Gamma delta ( $\gamma\delta$ ) T cells are considered the bridge between innate and adaptive immunity. The activation of  $\gamma\delta$  T cells is independent of MHC class I molecules. Neuroblastoma tumors express particularly low levels of MHC class I and therefore  $\gamma\delta$  T cells are an attractive cell type for immunotherapy. In addition,  $\gamma\delta$  T cells are being tested in several clinical trials focused on different cancer types, yet without clear clinical benefit. This may be due to main usage of V $\delta$ 2 cells whereas V $\delta$ 1 may be more cytotoxic and the general lack of knowledge on  $\gamma\delta$  T cell clonal expansion and ligand recognition. Here, we aimed to elucidate  $\alpha\beta$  and  $\gamma\delta$  T cell clonality,  $\gamma\delta$  T cell ligand recognition and possible therapeutic potential for  $\gamma\delta$  T cells in human neuroblastoma.

**Methods:** We ran flow cytometry identifying  $\gamma\delta$  T cell subtypes in six human neuroblastoma patient samples. In addition, we performed single-cell RNA/VDJ-sequencing on three matched tumor and peripheral blood samples to characterize clonal composition and functional states of  $\alpha\beta$  and  $\gamma\delta$  T cells infiltrating human neuroblastomas.

**Results:** Flow cytometric analysis revealed the  $\gamma\delta$  T cell compartment consists of the same subtypes and varies in proportion between individual patients. Thirty to fifty percent of the detected infiltrating  $\gamma\delta$  T cells were V $\delta$ 1+ cells. Single-cell RNA/VDJ-seq revealed prominent clonal expansion of both  $\alpha\beta$  and  $\gamma\delta$  T cells neuroblastoma tumors. Interestingly, we detected V $\delta$ 1/ V $\delta$ 3 expanded clones with both a clear cytotoxic signature and with a possible wound healing phenotype. Clonal expansion was particularly prominent in one patient for  $\gamma\delta$  T cells where nearly half of the cells represented one of the two top expanded clones with private V $\delta$ 1 and V $\delta$ 3 TCRs.

**Conclusions:** Drastic clonal expansion of  $\gamma\delta$  T cells suggests that they may recognize antigens present in the tumor environment. This provides exciting new possibilities for immunotherapy.

O191/#1789 | Nursing

#### NURSING: RESEARCH ABSTRACT PRESENTATIONS 02

14-10-2023 08:00 - 09:30

#### DEVELOPMENT OF AN E-HEALTH INTERVENTION TO SUPPORT HOME INFUSION THERAPY: IDENTIFYING FAMILIES' AND HEALTH CARE PROFESSIONALS' NEEDS AND PREFERENCES

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**Background and Aims:** At the University Hospital of Copenhagen children with cancer can receive home infusion therapy by a portable pump with no assistance from a nurse at home. eHealth technologies can bridge the transition between hospital and home, supporting home care to ensure safety, continuity and quality of care. There is a lack of eHealth interventions to support parents' management of home infusion therapy and the present study is the first part of developing an eHealth intervention. The aim was to identify: 1) the needs among families in home infusion therapy and healthcare professionals working with it, and 2) families' and healthcare professionals' preferences for technology elements needed for an eHealth intervention.

**Methods:** A qualitative study including 16 interviews with 14 families and five focus groups interviews with clinical staff (n=15). Data was collected in February–July 2020 and analysed with qualitative content analysis in November 2022–April 2023.

**Results:** The preliminary analysis shows three main themes and eight sub-themes, which described the needs and preferences of the families and healthcare professionals. Main themes are: 1) Extended responsibility, 2) Need for ensuring quality of care, and 3) Common preferences for digital elements. We identified key elements that an eHealth intervention should have such as guidelines and training via instruction videos and video consultations, to meet the needs of children, their parents, and healthcare professionals during home infusion therapy.

**Conclusions:** The parents were well prepared for providing home infusion therapy but would feel safer with an eHealth intervention as support. Both the families and the health care professionals emphasized that the digital solution had to benefit and be user-friendly for all users. They had the same proposals for solutions that could enable

reassurance, self-management, solve problems as well as ensuring quality and safety and improving access to home infusion therapy.

O192/#1805 | Nursing

## NURSING: RESEARCH ABSTRACT PRESENTATIONS 02

14-10-2023 08:00 - 09:30

### IMPROVING CHILDREN'S ONCO-HEMATOLOGY NURSING (ICON), BRAZIL: A COLLABORATIVE PILOT STUDY TO CREATE A COUNTRY-SPECIFIC STRATEGY FOR NURSING

Monnie Abraham<sup>1</sup>, Fernanda Bazaglia<sup>2</sup>, Rima Saad<sup>1</sup>, Lorena Segovia-Weber<sup>3</sup>, Maria Aurelia De Silveira Assoni<sup>4</sup>, Talita Bueno<sup>5</sup>, Laila Yamamoto<sup>5</sup>, Eliane Francelino<sup>5</sup>, Carolina Alvarenga<sup>2</sup>, Yichen Chen<sup>1</sup>, Meenakshi Devidas<sup>6</sup>, Patricia Logetto<sup>4</sup>, Paola Friedrich<sup>7</sup>, Carlos Rodriguez-Galindo<sup>8</sup>, Luiz Fernando Lopes<sup>9</sup>

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**Background and Aims:** Childhood cancer is the leading cause of death in children aged 1-19 years and is a public health priority in Brazil. To attain the World Health Organization's goal of reaching at least a 60% survival rate for children with cancer, a national strategy for improving nursing care is essential. We report creating a collaborative country-specific strategic plan based on the current pediatric oncology-hematology nursing situation.

**Methods:** We utilized a mixed-methods design to collect data from official normative documents review, literature review on pediatric onco-hematology nursing in Brazil, situational analysis survey, and institutional policies review. We conducted the survey and the institutional policy review in hospitals providing pediatric onco-hematology services using a survey founded on six SIOP nursing standards and a checklist. For the analysis, we triangulated the data, used thematic analysis and descriptive statistics, and co-developed a 5-year strategy.

**Results:** Twenty-six public and private hospitals from 5 regions of Brazil participated in the study. We reviewed 50 regulatory documents and 52 research articles. The nursing regulation outlined the scope of practice for nursing roles and recommended using a patient classifi-

cation system. The articles called for improving nursing practices in pain management and end-of-life care. The survey showed that nurses rotate between units in 38% of hospitals, and the in-patient nurse-to-patient ratio exceeds 1:5 in 73%. Among the 26 hospitals, 46.2% had a policy on end-of-life care, 53.8% had a pain management policy, and 38.3% had a patient and family education policy. Overall, the study identified 25 areas for improvement for the next five years, eight of which were prioritized for 2023.

**Conclusions:** The study findings form a baseline to understand the current situation of pediatric onco-hematology nursing in Brazil. The identified gaps inform local and collaborative initiatives to improve nursing care for children with cancer for next 5 years

O193/#330 | Nursing

## NURSING: RESEARCH ABSTRACT PRESENTATIONS 02

14-10-2023 08:00 - 09:30

### TOP 10 RESEARCH PRIORITIES FOR CHILDREN'S CANCER IN THE UNITED KINGDOM: PARTNERSHIP BETWEEN CHILDREN, SURVIVORS, CARERS AND PROFESSIONALS

Faith Gibson<sup>1,2</sup>, Rachel Hollis<sup>3</sup>, Bob Phillips<sup>3,4</sup>, Susie Aldiss<sup>2</sup>

<sup>1</sup>Great Ormond Street Hospital for Children NHS Foundation Trust, Centre For Outcomes And Experience Research In Children's Health, Illness And Disability (orchid), London, United Kingdom, <sup>2</sup>University of Surrey, School Of Health Sciences, Guildford, United Kingdom, <sup>3</sup>Leeds Teaching Hospitals NHS Trust, Department Of Paediatric Haematology And Oncology, Leeds, United Kingdom, <sup>4</sup>University of York, Hull-york Medical School And Centre For Reviews And Dissemination, York, United Kingdom

**Background and Aims:** Historically the research agenda has been set by professionals and researchers. Children with cancer have unique physical, psychological, and social responses to their diagnoses, with distinct outcomes. We aimed to engage children, childhood cancer survivors, their carers, and professionals in a systematic method to identify and prioritise research questions about childhood cancer.

**Methods:** We followed the well-established James Lind Alliance process. We brought together a multidisciplinary steering group, this included patient/parent representatives. Potential research questions were gathered via an online survey from survivors, carers, and professionals. Questions were checked to ensure they were unanswered. Shortlisting was via a second survey to identify the highest priority questions. A parallel process to collect and prioritise questions from children was undertaken. A final consensus workshop was held to determine the Top 10 priorities.

**Results:** Four hundred and eighty-eight people submitted 1299 potential questions. These were refined into 108 unique questions; four were already answered and three were under active study, therefore

removed. Three hundred and twenty-seven respondents completed the shortlisting survey. Seventy-one children submitted questions in the children's surveys, and eight children attended a workshop to prioritise these questions. The Top 5 questions from children were taken to the final workshop where 23 questions in total were discussed by 25 participants (young adults, carers and professionals). The top priority was, 'Can we find effective and kinder (less burdensome, more tolerable, with fewer short- and long-term effects) treatments for children with cancer, including relapsed cancer?' The Top 10 questions reflect the breadth of the childhood cancer experience including diagnosis, relapse, experience in hospital, support during and after treatment and the long-term impact of cancer.

**Conclusions:** The Top 10 research priorities have been identified using a rigorous and person-centred approach involving stakeholders not usually involved in setting the research agenda. These should inform funding of future research.

O194/#576 | Nursing

#### NURSING: RESEARCH ABSTRACT PRESENTATIONS 02

14-10-2023 08:00 - 09:30

#### FACTORS INFLUENCING NUTRITION CARE PRACTICES FOR PEDIATRIC ONCOLOGY PATIENTS IN MALAWI

Memory Sabantini, Jessy Simkhonde, Chikondi Chodzadza  
Baylor College of Medicine, Nursing, Lilongwe, Malawi

**Background and Aims:** Malnutrition, particularly undernutrition, is a poor prognostic factor in children with cancer. Over 50% of children admitted to pediatric oncology units in Malawi are malnourished and just like many low- and middle-income (LMIC) countries, the cancer survival rate is low. Studies conducted across the globe demonstrate that proper nutritional interventions promote survival in childhood cancer. In Malawi no specific guidelines for the assessment and management of malnutrition in cancer children exist and current nutritional care practices remain unclear. There is limited information on the barriers within LMIC settings that prevent optimal nutrition care practices. The aim of this study was to explore health care workers' (HCWs) nutrition care practices in two pediatric hospitals in Malawi where children with cancer are treated.

**Methods:** This qualitative study used in-depth interviews to evaluate nutrition care practices among HCWs that included nurses, doctors, and nutrition personnel working at two pediatric oncology units. Purposive sampling was used to select 30 most experienced HCWs on the units. Data was analyzed using thematic analysis and guided by the Donabedian model of health care quality, with an emphasis on structure and processes related to nutrition care practices.

**Results:** An overarching theme from the qualitative surveys revealed less than optimal nutrition care practices among HCWs. Inadequacies

included inconsistent nutritional screening and assessment, inadequate and inconsistent nutritional supplement provision, and lack of proper follow up. Nutrition care practices were greatly influenced by hospital resources for nutrition supplements, existing nutrition unit, use of cancer treatment protocols, and use of nutrition care guidelines to manage care.

**Conclusions:** Lack of clear nutritional guidelines for cancer children remains a major setback in nutritional care for children with cancer. Significant barriers exist in LMIC countries and must be addressed to ultimately improve cure outcomes for children with cancer.

O195/#1563 | Nursing

#### NURSING: RESEARCH ABSTRACT PRESENTATIONS 02

14-10-2023 08:00 - 09:30

#### HOW DO HEALTHCARE PROFESSIONALS HANDLE THEIR MAIN CONCERN WHEN GUIDING ETHICS CASE REFLECTION ROUNDS IN NORDIC PAEDIATRIC ONCOLOGY? - A QUALITATIVE STUDY

Cecilia Bartholdson<sup>1</sup>, Bert Molewijk<sup>2</sup>, Pernilla Pergert<sup>1</sup>

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**Background and Aims:** In paediatric oncology, moral dilemmas often arise and includes different perspectives about what is right/best for the child. With help from clinical ethics support services, such as ethics case reflection (ECR) rounds, moral dilemmas can be handled. A Nordic working group on ethics has organized a training program for health-care professionals to become facilitators to learn how to guide ECR rounds at clinics. **Objectives/Aim:** To explore facilitators' main concern and how they handle their main concern when guiding ECR rounds in paediatric oncology.

**Methods:** Data were collected by inviting all (n=24) trained facilitators in focus groups and individual interviews. Totally, 22 facilitators participated in the 3 focus group interviews and in 27 individual interviews. Data analysis followed classic grounded theory methodology.

**Results:** When facilitators were guiding ECR rounds in paediatric oncology their main concern was to deliver a meaningful experience of ethics support. They handled their main concern by *carrying the facilitator responsibility*. Facilitators felt responsible for defining the latent meaning of what was being expressed and the outcome, including to identify the moral dilemma followed by relevant actions, as they believed it would influence the care of the child. To be able to carry the facilitator responsibility the facilitators used different strategies including *allying*, *defining their role*, and *safe practicing*.

**Conclusions:** Facilitators take their role very seriously and they experience that they carry a great responsibility when guiding ECR rounds in paediatric oncology. This experience should be addressed during facilitator training and in facilitator networks to strive for decreasing the burden of responsibility, which could constitute a barrier for performing ECR rounds. However, when facilitators are carrying responsibility, they endeavour to improve paediatric oncology by making an effort to handle moral dilemmas. A possible study limitation is interviews performed via phone and not face to face.

O196/#1386 | Nursing

#### NURSING: RESEARCH ABSTRACT PRESENTATIONS 02

14-10-2023 08:00 - 09:30

##### FLASH CARDS FOR CHEMOTHERAPY: LEARNING MADE EASY THROUGH REFLECTION PRACTICE FOR ON-BOARDING NURSES IN A RESOURCE LIMITED SETTING

Mohita Kuhar<sup>1</sup>, Preeti Dabas<sup>2</sup>, Payal Malhotra<sup>1</sup>, Sandeep Jain<sup>1</sup>, Gauri Kapoor<sup>1</sup>

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**Background and Aims:** Paediatric oncology nurse skills are a very specific set of competencies with one of the most challenging being administering of chemotherapy and managing its toxicities. This study was undertaken as an active intervention to enhance new nurse's knowledge on safe administration of chemotherapy by aid of Professional Competencies Toolkit(ProComp ToolKit) like flash cards.

**Methods:** This was an observational study carried out in department of paediatric haematology oncology at our institute from June 2021 to December 2022. A preceptor was appointed to explain flash cards (specific to tumor, eliciting drugs and doses & infusion-hours, adverse effects and its management) and assured its compliance during 8-weeks supervision period for on-boarding nurses. A pre and post intervention formal assessment (written/bedside) was carried (score out of 10) and re-enforcement training was carried out for those with score < 7. A feedback was also collected for usefulness of flash cards on a score of 10.

**Results:** 22 New nurses were appointed in the department and underwent training for flash cards. Nearly 33%(13/22) had competent level of nursing core competencies through nurse's reflection(flashcards) pre-intervention compared to 78%(17/22)post-intervention. 60%(3/5) nurses who cleared chemotherapy competency and flash card assessment after first exposure, had previous oncology experience prior to joining our unit. Only 18%(4/22) nurses required a third re-enforcement, and all(100%) had no previous clinical experience in nursing. 32%( 7/22) and 68%( 15/22) nurses found the flash cards use-

ful (score 7-8) and extremely useful(score 9-10) respectively. Median score of nurse's feedback for flash card was 8.5(7-10).

**Conclusions:** Our experience using the Pro Comp Tool-Kit shows that teaching reflective practice is feasible and extremely useful for new on-boarding nurses and may have value for other oncology centres treating childhood cancer. It is part of our on-going effort to rigorously initiate and enhance safe chemotherapy administration practices in a resource limited setting.

O197/#1099 | Free Paper Session (FPS)

#### FPS 15: EPIDEMIOLOGY II

14-10-2023 08:00 - 09:30

##### CANCER PREDISPOSITION GENE PANEL SEQUENCING AMONG ALL CHILDREN WITH CANCER: "YES, WE CAN, BUT SHOULD WE?"

Jette Bakhuizen<sup>1,2</sup>, Freerk Van Dijk<sup>1</sup>, Marco Koudijs<sup>1,2</sup>, Melissa Tachdjian<sup>3</sup>, Reno Bladergroen<sup>1</sup>, Sebastian Bon<sup>1</sup>, Saskia Hopman<sup>2</sup>, Lennart Kester<sup>1</sup>, Mariëtte Kranendonk<sup>1</sup>, Jan Loeffen<sup>1</sup>, Stephanie Smetsers<sup>1</sup>, Edwin Sonneveld<sup>1</sup>, Catherine Goudie<sup>3,4</sup>, Hans Merks<sup>1,5</sup>, Roland Kuiper<sup>1,2</sup>, Marjolijn Jongmans<sup>1,2</sup>

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**Background and Aims:** Paired tumor-germline sequencing is rapidly being adopted in pediatric oncology and eases germline testing. To guide genetic counseling, we need insight into the diagnostic value, risks, and benefits of extensive sequencing among all children with cancer compared with genetic testing based on clinical selection.

**Methods:** All newly diagnosed children (age 0-19 years) with neoplasms in the Princess Máxima Center between June 2020 and August 2022 were offered two different approaches to identify Cancer Predisposition Syndromes (CPSs). In a phenotype-driven approach, pediatric oncologists used a CPS-screening eHealth tool (MIPOGG) to select children for referral to a clinical geneticist, and eventually (targeted) genetic testing. In a genotype-driven approach, germline CPS-gene panel sequencing (142 genes)<sup>1</sup> was offered to all patients. Patients with a known CPS before cancer diagnosis (n=39) were excluded.

**Results:** A total of 896 patients were included for analysis of the phenotype-driven approach of which 612 (68%) also consented for CPS-gene sequencing. In 50 patients, a CPS was identified, of which 12 were solely diagnosed by the phenotype-driven approach, 20 solely

by CPS-gene sequencing, and 18 by both approaches. In 27/50 (54%) patients, the identified CPS was considered causative for the child's cancer. MIPOGG correctly recognized 26/27 patients (96%) as requiring referral for genetic evaluation. In 23/50 patients, a CPS with uncertain causality was identified, including a high number of adult-onset CPSs (n=12). The CPSs with uncertain causality were mainly detected by CPS-gene panel sequencing (19/23).

**Conclusions:** The two diagnostic approaches, phenotype-driven genetic testing and CPS-gene panel sequencing are supplementary to each other. The phenotype-driven approach, supported by MIPOGG, identified most causative CPSs. CPS-gene panel sequencing identified additional CPSs, many of those with uncertain causality, but some with clinical utility. Therefore, we advise extensive germline genetic testing in children with cancer only to be conducted after thorough pretest counseling. <sup>1</sup> <https://research.prinsesmaximacentrum.nl/en/childhood-cancer-predisposition-genes>

O198/#1599 | Free Paper Session (FPS)

## FPS 15: EPIDEMIOLOGY II

14-10-2023 08:00 - 09:30

### A NOVEL FUNCTIONAL CLASSIFICATION OF TP53 GERMLINE VARIANTS: CAN THIS INFORM CANCER SCREENING PRACTICES IN YOUNG CHILDREN?

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**Background and Aims:** Li-Fraumeni syndrome (LFS), a cancer predisposition syndrome caused by germline pathogenic variants in *TP53*, is associated with an elevated risk of developing early-onset cancers. Individuals with LFS typically embark on a cancer screening program, involving radiological, clinical and biochemical evaluations. Disease presentation and penetrance are heterogeneous, leading to efforts to characterise subgroups within patients with LFS. A new analysis of genotype-phenotype correlations based on fine resolution clustering of *TP53* variants into five functional classes was developed by Hainaut et al (data unpublished). We aim to evaluate if this novel *TP53* classification can inform cancer screening strategies in young children. Specifically, we focus on sarcoma and brain tumor screening as this involves magnetic resonance imaging (MRI), a challenging test to perform in children.

**Methods:** A systematic review using PubMed (1990-2022) provided clinical (type/age at cancer diagnosis, therapy and follow-up details) and *TP53* variant information on individuals with LFS. Patients were then classified in five classes (A, B, C, D, Null) according to their germline variant. We evaluated the frequency of brain tumors and sarcomas according to three age groups and functional classes.

**Results:** Of 253 patients with LFS, 184 could be classified into classes (A:68%, B:16%, C:10%, D:3%, Null:3%). We focussed our analysis on patients who developed cancer in class A, of which a third of cancers occurred prior to age 3 years. Among 68 individuals with brain tumors and sarcomas, 48%, 15%, 37% were aged <3, 3-6, and >6 years respectively.

**Conclusions:** These preliminary results show the importance of early initiation of surveillance for brain tumors and sarcomas in individuals within class A. This data will contribute to a larger analysis evaluating genotype-phenotype correlations based on all functional classes, and will inform practical utility of this classification on cancer screening modalities and subsequent cancer risks.

O199/#382 | Free Paper Session (FPS)

## FPS 15: EPIDEMIOLOGY II

14-10-2023 08:00 - 09:30

### SURVIVAL DISPARITIES BETWEEN CHILDREN AND ADOLESCENTS & YOUNG ADULTS FOR THE MAJOR SUBTYPES OF NON-HODGKIN LYMPHOMA: A LARGE DUTCH POPULATION-BASED STUDY

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**Background and Aims:** Adolescents & young adults (AYAs) with non-Hodgkin lymphoma (NHL) have an inferior prognosis than children. Data on subtype-specific survival disparities are, however, scarce. We aimed to compare the survival of children (0-17 years) and AYAs (18-39 years) diagnosed with NHL in the Netherlands between 1990-2015 for the major histological subtypes: T-lymphoblastic lymphoma (T-LBL), Burkitt lymphoma (BL), diffuse large B-cell lymphoma (DLBCL), and anaplastic large cell lymphoma (ALCL).

**Methods:** Data on 5,639 children and AYAs with NHL (T-LBL: 361, BL: 569, DLBCL: 2,061, ALCL: 319, and other: 2,329) were obtained from the population-based Netherlands Cancer Registry. Subtype-specific 5-year relative survival was determined for children and AYAs. Multivariable-adjusted associations between age and excess mortality from NHL subtypes were evaluated using Poisson regression models.

**Results:** Children with T-LBL consistently had an approximately 20 percent-point higher 5-year relative survival than AYAs (1990-2015: 78% vs. 55%). For BL, the survival advantage of children in the 1990s (+35 percent-points) decreased over time due to the marked increase in survival among AYAs (48% to 79%). In 2010-2015, less favorable outcome was restricted to the oldest AYAs. Survival of DLBCL improved over time and reached 88% in both children and AYAs. Although 5-year relative survival did not significantly differ between children and AYAs with ALCL (79% vs. 72%), excess mortality was increased among AYAs after multivariable adjustment.

**Conclusions:** By comparing the survival of children treated by pediatric oncologists with that of AYAs treated by hematologists, this study identified areas of interest for optimizing pediatric and (young) adult therapy regimens. Children with DLBCL had similar survival as AYAs despite more dose-intensive treatment, suggesting that there could be possibilities to reduce treatment intensity for (some) pediatric DLBCL patients. AYAs with T-LBL continued to experience inferior survival compared with children, notwithstanding the introduction of pediatric-inspired therapy.

O200/#1194 | Free Paper Session (FPS)

## FPS 15: EPIDEMIOLOGY II

14-10-2023 08:00 - 09:30

### SUCCESSFUL DEVELOPMENT OF A CENTRALIZED TRIAGE CENTER FOR CHILDREN DIAGNOSED WITH CANCER AND BLOOD DISORDERS IN RESPONSE TO WAR IN UKRAINE

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**Background and Aims:** The Supporting Action for Emergency Response (SAFER) Ukraine collaborative was formed to respond to the Russian invasion of Ukraine in February 2022, including facilitation of safe evacuation of Ukrainian children diagnosed with cancer and blood disorders to re-establish medical care abroad. Here, we describe the establishment of a Polish triage center to support patient evacuation and international referral.

**Methods:** When war erupted, many affected families left Ukraine to access medical care, saturating health systems of neighboring countries. To mitigate and re-distribute patient volume, a pathway for evacuation was established. Families were directed to an evacuation hub in Lviv and through humanitarian convoys, stable patients were transported to a Polish triage center staffed by international medical teams, organizations, and foundations. Unstable patients were transported directly to a hospital. This infrastructure also assisted with triage center operations, a patient registry, translating and distributing medical records, stakeholder communication, and psychosocial support.

**Results:** In the first six months of war, the triage center supported 509 patients and their families, including 468 (92%) children with cancer, 28 (6%) with blood disorders, and 11 (2%) with other chronic illnesses. Of the pediatric cancer patients, 63 (13%) were newly diagnosed, 380 (81%) were receiving treatment, and 19 (4%) had completed therapy. Ten patients (2%) transported to the triage center required transfer to a local pediatric hematology-oncology (PHO) department for urgent medical assessment. Two patients died during the evacuation process. To enhance triage efficiency, standardized approaches for hand-off, international referral pathways, and a formal onboarding program for rotating staff were implemented.



**Conclusions:** This triage center has successfully facilitated the safe referral of Ukrainian PHO patients and their families to centers across Europe and North America. As the war continues, SAFER Ukraine remains dedicated to supporting patient evacuations, with ongoing planning to accommodate potential future mass evacuations should the need arise.

O201/#408 | Free Paper Session (FPS)

FPS 15: EPIDEMIOLOGY II

14-10-2023 08:00 - 09:30

#### MODE OF DELIVERY AND CHILDHOOD LEUKEMIA RISK—A SWEDISH POPULATION-BASED COHORT STUDY

Christina Evmorfia Kampitsi, Hanna Mogensen, Maria Feychting, Giorgio Tettamanti  
Karolinska Institutet, Institute Of Environmental Medicine, Stockholm, Sweden

**Background and Aims:** Worldwide cesarean section (CS) rates continue to rise beyond medically warranted thresholds, despite potential long-term adverse outcomes. Previous research on delivery via CS and childhood leukemia is conflicting but points towards an increased acute lymphoid leukemia (ALL) risk; studies distinguishing between planned and unplanned CS found increased risks only for the former. As maternal and pregnancy conditions predisposing to birthing difficulties might confound such an association, we aimed to elucidate the relationship between mode of delivery and leukemia in Swedish children.

**Methods:** We identified all children born in Sweden between 1982–1989 and 1999–2014, when comprehensive information on mode of delivery was available ( $n=2,429,432$ ). Pregnancy conditions, delivery mode, and childhood leukemia diagnoses (<20 years at diagnosis) were retrieved from nationwide registers. The association between mode of delivery and childhood leukemia and subtypes was evaluated using Cox proportional hazards regression, adjusting for offspring sex, birth decade, birth weight by gestational age, region of residence at birth, any birth defect, and maternal age, education, preeclampsia, diabetes, and infections during pregnancy.

**Results:** We observed an increased risk of leukemia among children delivered via planned CS (HR=1.14, 95% CI 0.92–1.41), driven by ALL (HR=1.21, 95% CI 0.96–1.54) and specifically b-cell precursor ALL (HR=1.29, 95% CI 1.01–1.67). The associations persisted after adjustment for maternal and pregnancy conditions, as well as offspring perinatal factors. Delivery via unplanned CS was not associated with increased risk of childhood leukemia.

**Conclusions:** In this nationwide, register-based cohort study, children delivered via planned CS had an increased b-cell precursor ALL risk, irrespective of maternal and pregnancy conditions. Mechanisms that may underlie the relationship between mode of delivery and childhood

ALL, including a lack of exposure to maternal vaginal microbiota or decreased levels of stress hormones at birth, should be explored further. Regardless, the results of this study offer support to reconsidering non-medically warranted CS.

O202/#193 | Free Paper Session (FPS)

FPS 16: SOFT TISSUE SARCOMAS

14-10-2023 08:00 - 09:30

#### COMPARISON OF CLINICAL OUTCOME OF PATIENTS WITH INFANTILE FIBROSARCOMA (IFS) TREATED WITH LAROTRECTINIB IN THE SCOUT STUDY VERSUS HISTORICAL COHORT: THE EPI-VITRAKVI STUDY

Daniel Orbach<sup>1</sup>, Lauriane Lemelle<sup>1</sup>, Matthieu Carton<sup>2</sup>, Soumeya Khadidja Khadir<sup>3</sup>, Marion Feully<sup>4</sup>, Milena Kurtinecz<sup>5</sup>, Christian Vokuhl<sup>6</sup>, Ewa Koscielniak<sup>7</sup>, Gaelle Pierron<sup>8</sup>, Monika Sparber-Sauer<sup>7</sup>  
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**Background and Aims:** For patients with infantile IFS, clinical trials have shown pronounced and durable responses to larotrectinib, a TRK kinase inhibitor. Conventional chemotherapy has also shown an important efficacy. Until now, no comparative data exist. The aim of this study is to assess the effectiveness of larotrectinib over standard of care (SOC) with chemotherapy, by comparing the time to medical treatment failure (next systemic therapy, mutilating surgery, radiation therapy or death due to any cause) in both groups.

**Methods:** Retrospective comparative observational externally-controlled phase IV study (NCT-05236257) of patients with locally advanced or metastatic IFS, treated in the phase I/II 'SCOUT' trial with larotrectinib and historical control cohorts (data from Institut Curie and Cooperative Weichteilsarkom Studiengruppe CWS database) receiving conventional chemotherapy-based regimen.

**Results:** Mean (SD) age of 93 included patients ( $n=51$  [larotrectinib] and  $n=42$  [control]) was 1.4 (2.9) years at inclusion: larotrectinib 2.0 (3.5); control 0.7 (1.8). Locally advanced IFS represent 80.4% (larotrectinib) and 92.9% (control). Median follow-up durations were 30.9 (larotrectinib) and 72.9 months (control). Four larotrectinib patients (7.8%) reported a medical treatment failure event (new systemic treatment [ $n=2$ ], mutilating surgery [2]) versus 15 (35.7%) in control group

(new systemic treatment [6], mutilating surgery [5], radiation therapy [2] and death [2]). Time to medical treatment failure was significantly longer in the larotrectinib group (weighted log-rank test:  $p=0.0161$ ). Weighted Hazard Ratio, stratified by IRS groups, was 0.20 (95%CI: 0.06-0.63;  $p=0.0060$ ), which corresponds to an 80% lower likelihood of experiencing a medical treatment failure in the larotrectinib group. These results were confirmed by sensitivity analyses, including exact matching and subgroup analysis for number of lines of treatment.

**Conclusions:** This original study, providing comparative data, indicates that larotrectinib prolonged the time to medical treatment failure, reduced the morbidity and the need of aggressive local therapies compared to SOC in children with IFS. Supported by Bayer-Healthcare and *Enfants-Cancers-Santé/SFCE*.

O203/#265 | Free Paper Session (FPS)

#### FPS 16: SOFT TISSUE SARCOMAS

14-10-2023 08:00 - 09:30

#### SHOULD WE CONSIDER ALVEOLAR SOFT PART SARCOMAS IN CHILDREN AND YOUNG ADULTS IN THE SAME WAY? THE FRENCH NATIONAL NETSARC+ NETWORK EXPERIENCE

Anne-Laure Genevois<sup>1</sup>, Matthieu Carton<sup>2</sup>, Myriam Jean-Denis<sup>3</sup>, Joanna Cyrta<sup>4</sup>, Nadege Corradini<sup>5</sup>, Pablo Berlanga<sup>6</sup>, Claire Chemin-Airiau<sup>3</sup>, Marie Karanian<sup>7</sup>, Stéphanie Pannier<sup>8</sup>, Sophie El Zein<sup>4</sup>, Anne-Sophie Defachelles<sup>9</sup>, Emmanuelle Bompas<sup>10</sup>, Justine Gantzer<sup>11</sup>, Charles Honoré<sup>12</sup>, Sabine Noal<sup>13</sup>, Sébastien Héritier<sup>14</sup>, Cécile Guillemet<sup>15</sup>, Philippe Anract<sup>16</sup>, Jill Serre<sup>17</sup>, François Le Loarer<sup>18</sup>, Mehdi Brahmi<sup>19</sup>, Gaëlle Pierron<sup>20</sup>, Anne Gomez-Mascard<sup>21</sup>, Carmen Llacer<sup>22</sup>, Françoise Ducimetière<sup>3</sup>, Maud Toulmonde<sup>23</sup>, Jean-Yves Blay<sup>19</sup>, Daniel Orbach<sup>24</sup>

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Tours, France, <sup>18</sup>Institut Bergonié, Department Of Biopathology, Bordeaux, France, <sup>19</sup>Centre Léon Bérard, Department Of Oncology, Lyon, France, <sup>20</sup>Institut Curie, Siredo Oncology Center (care, Innovation And Research For Children, Adolescents And Young Adults With Cancer), Institut Curie, Paris Saclay University, Paris, France. Electronic Address: Anne-laure.genevois@hotmail.fr., Paris, France, <sup>21</sup>IUCT, Department Of Biopathology, Toulouse, France, <sup>22</sup>Institut du Cancer de Montpellier, Department Of Radiotherapy, Montpellier, France, <sup>23</sup>Institut Bergonié, Department Of Oncology, Bordeaux, France, <sup>24</sup>Institut Curie, Pediatric Siredo Oncology Center, Paris, France

**Background and Aims:** Alveolar soft part sarcoma (ASPS) is a chemoresistant sarcoma occurring preferentially in young adults, and ultrarare in children. The aim of this study was to describe and compare its clinical presentation and behavior in children and young adults and to determine if the same therapeutic strategy can be considered for both populations.

**Methods:** National retrospective comparative multicenter study of children (0-18 years) vs. young adults (19-30 years) with ASPS included in the "ConticaBase" Sarcoma database, treated between 2010 and 2019 with bio-pathology reviewed via the NETSARC+ network.

**Results:** Overall, 45 patients were identified: 19 children (42%) and 26 young adults (58%), with a female predominance (sex ratio: 2/3). Histopathological diagnosis was confirmed by the detection of TFE3 rearrangement (43/45). All clinical characteristics were similar in both populations. Overall time to diagnosis were long (12.9 vs. 23.8 months) with large tumors (>5cm; 10/19 vs. 15/26) and a preferential location in limbs (12/19 vs. 19/26). Metastases at diagnosis were frequent: 8/19 vs. 10/26. Treatment was based on surgery (17/19 vs. 21/26), radiotherapy (8/19 vs. 12/26),  $\pm$  systemic treatment (4/19 vs. 4/26 chemotherapy and 4/19 vs 5/26 targeted therapies). Among localized ASPS, metastatic relapse occurred only in adults (8/16). Among metastatic ASPS, metastatic progression occurred in both groups (5/8 vs. 8/10). After a median follow-up of 5.2 years (range, 0.2-12.2), 5-year EFS was 74% [95%CI, 56-96] in children vs. 47% [30-74] in adults ( $p=0.07$ ), 5-year MFS is 100% [100-100] vs. 60% [39-91] respectively ( $p=0.005$ ), while 5-year OS was 95% [85-100] vs. 85% [70-100] ( $p=0.84$ ).

**Conclusions:** In this national cohort, ASPS seem to have the same initial clinical characteristics, but a more aggressive behaviour in young adults than in children. However, despite frequent metastases at diagnosis, long-term survivals is high in both groups. Overall, the same therapeutic strategies could be considered for both populations with ASPS.

O204/#381 | Free Paper Session (FPS)

#### FPS 16: SOFT TISSUE SARCOMAS

14-10-2023 08:00 - 09:30

## EARLY RESULTS OF PROTON BEAM THERAPY IN PATIENTS WITH RHABDOMYOSARCOMA OF THE PELVIS; RESULTS FROM THE PROSPECTIVE REGISTRY STUDIES KIPROREG AND PROREG

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**Background and Aims:** Radiotherapy (RT) plays an important role in local treatment of pelvic sarcomas. Proton beam therapy (PT) is increasingly used to reduce adverse events. Therefore, we analysed the outcome of patients with rhabdomyosarcoma (RMS) receiving PT at our institution.

**Methods:** Patients receiving PT for pelvic RMS between May 2013 and October 2022 and consenting to study inclusion in KiProReg or ProReg were included. Data on patient and tumour characteristics, applied therapies and adverse events (according to CTCAEv4/5) was collected and evaluated. Follow up (FU) was calculated from first diagnosis to last FU or event.

**Results:** Sixty-seven patients met inclusion criteria (40 m, 27 f; median age 4.9 yrs, range 0.9-33.7). Forty-two patients were treated under sedation. All patients received chemotherapy before and 71.6% concurrent to PT. Treatment concepts were definite (n=43), adjuvant (n=22) or neoadjuvant (n=2) PT. Gross total resection was achieved in 26.9%. In 60 patients, PT was delivered only to primary tumour or local recurrence, 7 patients received PT for metastases. Three patients had already received RT within the PT-area. Median total PT dose was 50.4 Gy (range 21.6-70). During PT, 41 patients developed  $\geq$ grade 3 bone marrow toxicities. Other toxicities were related to skin (n=17), GI (n=2) or GU (n=1). Median FU was 20.8 months (range 4.5-161.0). Tumour control was achieved in 76.1%. Sixteen patient experienced tumour failure (8 local, 6 distant, 2 both). New maximal late toxicities ( $\geq$ grade 2) within the PT-area were mucositis (n=1), GI pain (n=1), proctitis (n=1), bladder spasm (n=1), urinary retention (n=1), urinary tract pain (n=1), faecal incontinence (n=2), cystitis (n=2), urinary frequency (n=3) and urinary incontinence (n=5).

**Conclusions:** PT for patients with pelvic RMS was both feasible and effective. However, findings have to be confirmed with larger FU in order to better define the role of RT and PT.

O205/#1133 | Free Paper Session (FPS)

FPS 16: SOFT TISSUE SARCOMAS

14-10-2023 08:00 - 09:30

## THERAPY AND OUTCOME OF PATIENTS WITH RELAPSE OF NONMETASTATIC RHABDOMYOSARCOMA: A REPORT FROM THE FRENCH SOCIETY OF PEDIATRIC ONCOLOGY (SFCE) MALIGNANT MESENCHYMAL TUMOR (MMT) COMMITTEE

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**Background and Aims:** Around 30% of patients with localized rhabdomyosarcoma experience recurrence. Survival after relapse is poor, with limited evidence on optimal second-line therapy. Our aim was to describe the management and outcome of a national series of patients after relapsed rhabdomyosarcoma.

**Methods:** We retrospectively reviewed all patients enrolled in France in RMS2005 study with nonmetastatic rhabdomyosarcoma who had relapse from January 2007 to December 2019. Data on initial diagnosis and relapse was extracted from the RMS2005 database and patient's medical records.

**Results:** Overall, 95 patients experienced relapse at a median age of 6.0 years (range:1.0-27.0). Median interval from diagnosis to first relapse was 17.5 months (range:7.4-82.0). Relapses were mainly local/locoregional (71.6%) and non-alveolar (65.3%). Wide somatic

molecular profiling was performed in 16 patients. Treatment at first relapse included chemotherapy in all but 2 patients, radiotherapy in 50, and surgery in 46. Different chemotherapy regimens were used as second-line, with an objective response of 58.5% after  $3 \pm 1$  cycles. Ten of the 43 patients with prior radiotherapy were reirradiated in a field at least partially similar with curative intent. Second complete remission was achieved in 55 patients (57.9%). Thirty-one of them received maintenance therapy. With a median follow-up of 7.2 years (0.3-11.3) from first relapse, 5-year progression-free survival (PFS) and overall survival were 26% (95%CI:18-36) and 35% (95%CI:25-45), respectively. Six-month PFS of patients with local/locoregional relapse was 60% (95%CI:48-71). A significant association between the nomogram-based prognostic score developed by the Malignant Mesenchymal Tumor committee of the International Society of Pediatric Oncology (SIOP-MMT) and the risk of death (HR=0.03,95%CI:0.01-0.11, $p < 0.001$ ) was confirmed.

**Conclusions:** This study confirmed the poor prognosis of relapsed rhabdomyosarcoma, the lack of consistency in therapy, but also the importance of early local treatment. We recommend systematic molecular profiling and enrollment in phase I/II clinical trials to improve outcomes in these patients in high-risk situations.

O206/#852 | Free Paper Session (FPS)

FPS 16: SOFT TISSUE SARCOMAS

14-10-2023 08:00 - 09:30

#### GENOMIC PROFILING AND CLINICAL OUTCOME OF SPINDLE CELL/SCLEROSING RHABDOMYOSARCOMA: A REPORT FROM CHINESE PPOG TRIAL

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**Background and Aims:** Spindle cell/sclerosing rhabdomyosarcomas (SSRMS) is a rare variant of rhabdomyosarcoma, designated in the latest WHO classification as a stand-alone pathologic entity. However, little is known about the molecular profile and outcome of patients with SSRMS. The Pediatric Precision Oncology Group (PPOG) is a multicenter project aimed at defining tumor molecular profiles in pediatric oncology patients across China.

**Methods:** From June 2021 to July 2022, 56 patients with SSRMS were enrolled in the PPOG (NCT05076071), 31 patients were eligible for analysis. Panel sequencing (830 DNA and 395 RNA) was performed on 17 tumors from 17 patients. The Kaplan-Meier method was used to estimate overall survival (OS) and event-free survival (EFS).

**Results:** Two-year EFS and OS for patients with low risk ( $n = 7$ ), intermediate risk ( $n = 13$ ), high risk ( $n = 11$ ) were 85.7%, 69.2%, 21.2% ( $P = 0.036$ ), and 100%, 92.3%, 47.7% ( $P = 0.006$ ), respectively. The most common recurrently aberrated genes were MYOD1 mutation (41%), MDM2 amplification (18%), NRAS mutation (12%), and PIK3CA mutation (12%). All 7 cases with MYOD1 mutation showed a p.Leu122Arg (c. 365 T > G) mutation, which was consistent with previous reports. Six of seven patients with MYOD1 mutation had relapsed. One case with NRAS mutation showed a p.Gly12Ser (c.34G > A) mutation and another case with PIK3CA mutation showed a p.Glu545Lys (c.1633G > A) mutation, which have never been reported. PI3K (29%), P53(24%), and RAS-RAF (29%) pathways were mainly altered in SSRMS tumors. Almost half of the patients (47%) had therapeutic targets. Germline cancer predisposition mutations (TP53 and BRCA1) were identified in 18% (3/17) of patients. Four fusion genes have been detected, including two forms of BRAF rearrangement.

**Conclusions:** Together with the development of new molecularly-derived clinical data that we reported, a large sample is warranted to improve risk stratification and outcome for patients with SSRMS.

O207/#251 | Free Paper Session (FPS)

FPS 16: SOFT TISSUE SARCOMAS

14-10-2023 08:00 - 09:30

#### SEQUENTIAL GENOMIC ANALYSIS USING A MULTISAMPLE/MULTIPLATFORM APPROACH TO BETTER DEFINE RHABDOMYOSARCOMA PROGRESSION AND RELAPSE

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**Background and Aims:** Although the genomic landscape of rhabdomyosarcoma (RMS) has been well characterized, the progression of the tumors' molecular spectrum from primary to metastatic disease or clonal evolution during relapse is not fully understood. However, metastatic and relapsing disease remain the most prominent factors of poor prognosis for patients.

**Methods:** In this study we investigate 35 patients with relapsed RMS from two contributing institutions (Institut Curie, Paris and MSKCC, NY), 18 fusion-positive (FP-RMS) and 17 fusion-negative RMS (FN-RMS). Targeted DNA or whole exome sequencing (WES) was used to detect alterations in paired primary/relapsed samples. In 10 cases, circulating tumor DNA (ctDNA) from multiple timepoints through clinical care and progression was analyzed for feasibility of liquid biopsy in monitoring treatment response/relapse. ctDNA alterations were evaluated using a targeted custom RMS panel at high coverage for single

nucleotide variation and fusion detection, and a shallow whole genome sequencing for copy number variation.

**Results:** FP-RMS had a stable genome with relapse, with the most common secondary alterations: *CDKN2A/B*, *MYCN* and *CDK4* alterations, being present at baseline diagnosis and impacting on survival. FP-RMS lacking these major secondary events at baseline most frequently acquired *MYCN* and *AKT1* alterations. FN-RMS acquired a higher number of new alterations, most commonly, novel *SMARCA2* missense mutations. ctDNA analyses detected pathognomonic variants in all RMS patients at diagnosis, regardless of FP/FN or type of alterations, while at relapse selected alterations were confirmed in 86% of FP-RMS and 100% FN-RMS. Moreover, a higher number of fusion reads was detected with increased disease burden and at relapse in patients following a fatal outcome.

**Conclusions:** These results underscore patterns of tumor progression within a relatively stable genomic landscape and provides rational to use liquid biopsy in treatment response monitoring. This study also demonstrates the feasibility and added value of trans-Atlantic collaborations, especially beneficial in pediatric soft tissue oncology.

O208/#621 | Free Paper Session (FPS)

#### FPS 17: NOVEL THERAPEUTIC APPROACHES

14-10-2023 08:00 - 09:30

#### COMBINATORIAL IMMUNOTHERAPEUTIC AND TARGETED KINASE INHIBITION APPROACH IN *KMT2A*-REARRANGED ACUTE LYMPHOBLASTIC LEUKEMIA

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**Background and Aims:** Infants with *KMT2A*-rearranged B-cell acute lymphoblastic leukemia (*KMT2A*-R ALL) have poor clinical outcomes with conventional chemotherapy. CD19-targeting chimeric antigen receptor immunotherapy (CD19CART) has proven highly effective in remission induction and long-term cure of some infants and older children with relapsed/refractory ALL. However, 50% of CD19CART-treated patients relapse again, and antigen-loss and lineage-switch relapse are particularly problematic in those with *KMT2A*-R ALL. Alternative therapies, potentially targeting the unique biology of *KMT2A*-R ALL with FLT3 protein overexpression and high frequency of RAS mutations, are needed.

**Methods:** We previously developed FLT3-directed CAR T cells (FLT3CART) and demonstrated robust preclinical activity in *KMT2A*-R ALL patient-derived xenograft models (Niswander *Haematologica*

2023). In this study, we hypothesized that multi-modal therapy with FLT3CART and RAS/MAPK pathway inhibition would have superior activity against *KMT2A*-R ALL. We specifically defined the effects of the MEK inhibitor trametinib upon FLT3CART and tested the anti-leukemia efficacy of FLT3CART+trametinib in *KMT2A*-R ALL models.

**Results:** Combined treatment with FLT3CART+trametinib in *KMT2A*-R ALL xenografts in vivo resulted in enhanced and sustained leukemia clearance above either monotherapy. Potent combinatorial effects were detected in RAS-mutant ALL, but surprisingly also in RAS wild-type models insensitive to single-agent trametinib. We observed a robust increase in FLT3CART expansion and efficacy when combined with trametinib, suggesting direct MEK inhibitor augmentation of FLT3CART. Targeted gene expression analysis (Nanostring) of FLT3CART flow-sorted from trametinib-treated mice revealed increased expression of stem/memory-associated genes and decreased expression of effector-associated genes, indicating a stem/memory T cell phenotype, which clinically has been associated with CD19CART persistence and efficacy.

**Conclusions:** Co-administration of FLT3CART+trametinib evokes potent preclinical activity against *KMT2A*-R ALL with enhanced FLT3CART expansion and induction of a stem/memory T cell program. Pediatric phase 1 clinical trials of FLT3CART are in development, and results from these studies may further strengthen FLT3-targeting immunotherapeutic strategies for patients with high-risk leukemias.

O209/#1123 | Free Paper Session (FPS)

#### FPS 17: NOVEL THERAPEUTIC APPROACHES

14-10-2023 08:00 - 09:30

#### POE14-01: A PHASE I STUDY OF CARFILZOMIB IN COMBINATION WITH CYCLOPHOSPHAMIDE AND ETOPOSIDE FOR CHILDREN, ADOLESCENTS AND YOUNG ADULTS WITH RELAPSED/REFRACTORY LEUKEMIAS OR SOLID TUMORS

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**Background and Aims:** Novel combination therapies are needed for children and AYAs with relapsed/refractory leukemias or solid tumors. Carfilzomib, a proteasome inhibitor, demonstrated significant in vitro activity alone and in combination against several pediatric tumors. Therefore, a multicenter, dose-escalation, phase I study of carfilzomib given in combination with cyclophosphamide and etoposide was undertaken in pediatric and AYA patients with relapsed/refractory non-CNS malignancies.

**Methods:** Patients 6 months to < 30 years were eligible if they had: 1) relapsed/refractory leukemia with  $\geq 2$  relapses (Stratum A); 2) relapsed/refractory non-CNS solid tumor (Stratum B); 3) Karnofsky/Lansky score  $\geq 50\%$ ; and 4) adequate organ function. Patients were excluded if previously treated with carfilzomib. A 5-day dosing schedule of cyclophosphamide 440 mg/m<sup>2</sup>/day IV, etoposide 100 mg/m<sup>2</sup>/day IV and carfilzomib IV were administered every 28 days with growth factor support. The carfilzomib starting dose was 11 mg/m<sup>2</sup>/day. Dose escalation proceeded independently for each stratum using a rolling-six design. Dose limiting toxicity (DLT) was assessed during the first cycle, and response after 1 cycle (Stratum A) and 2 cycles (Stratum B).

**Results:** A total of 38 patients were treated (Stratum A: 14 and Stratum B: 24). For Stratum A, the MTD was 11 mg/m<sup>2</sup>/day. Three DLTs were observed: grade 4 thrombocytopenia, grade 4 pericarditis and grade 4 Posterior Reversible Encephalopathy Syndrome (PRES). The majority of patients received only 1 cycle. For Stratum B, the MTD was 20 mg/m<sup>2</sup>/days 1-2 and 36 mg/m<sup>2</sup>/days 3-5. There was one DLT, grade 3 PRES. Myelosuppression with febrile neutropenia were the main adverse events. Twenty patients received  $\geq 2$  cycles (range: 2 to 14). Clinical benefits were observed primarily in patients with sarcomas.

**Conclusions:** The 5-day dosing schedule of carfilzomib/cyclophosphamide/etoposide was well tolerated with an acceptable toxicity profile in solid tumor patients. Patients with sarcomas benefitted the most from this combination, warranting further evaluation.

O210/#1268 | Free Paper Session (FPS)

FPS 17: NOVEL THERAPEUTIC APPROACHES

14-10-2023 08:00 - 09:30

## DRUG SENSITIVITY PROFILING ON PATIENT DERIVED MATERIAL: GLOBAL COLLABORATION TO DRIVE IMPLEMENTATION INTO PAEDIATRIC PRECISION MEDICINE

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**Background and Aims:** Paediatric precision medicine programs including iTHER (The Netherlands), INFORM (international), and ZERO (Australia), report potentially actionable molecular drug targets in the majority of children with cancer. This paradigm-changing approach has led to clinical benefit in selected subgroups. However, clinical uptake of treatment recommendations has been low, and clinical impact for individual patients remains hard to predict. This stresses the need to integrate functional approaches into therapeutic decision making. Here, we report high-throughput drug screening (HTS) integrated with molecular profiles from the global collaboration between iTHER, INFORM and ZERO.

**Methods:** HTS and molecular profiling was performed on patient-derived material of high-risk, relapsed or refractory solid and CNS tumours after short-term or long-term culture, and/or in vivo expansion. All data were combined, and clustering analysis was used to identify drug sensitivity patterns across tumour types.

**Results:** HTS was performed for 235 (iTHER=37; INFORM=119; ZERO=79) solid and 93 (iTHER=7; INFORM=45; ZERO=41) CNS tumours. Results are available through the R2 platform (<http://r2platform.com/>), in which visualization and analysis options were implemented. As a result, a powerful reference set is available, reflecting distinct known pharmacologic vulnerabilities, e.g., sensitivity of NTRK-fusion positive samples to NTRK inhibition. HTS also identified additional therapeutic vulnerabilities, e.g., mesenchymal signature and venetoclax sensitivity. In addition, in vitro insensitivity is confirmed, potentially avoiding ineffective treatments. We explored clinical follow-up in a subset of patients, confirming correlation with in vitro drug sensitivity.

**Conclusions:** Our data support complementary HTS to omics-guided precision medicine by strengthening genomic and transcriptomic results; identifying novel treatment options; and by avoiding ineffective treatments. Global collaboration and data sharing through dynamic platforms such as R2 is essential since childhood cancer remains a rare disease, and innovative approaches are urgently needed to improving outcomes for all patients in the future.

O211/#772 | Free Paper Session (FPS)

### FPS 17: NOVEL THERAPEUTIC APPROACHES

14-10-2023 08:00 - 09:30

#### LENVATINIB IN CHILDREN, ADOLESCENTS, AND YOUNG ADULTS WITH RELAPSED OR REFRACTORY (R/R) SOLID TUMORS: RESULTS FROM THE SINGLE-ARM, PHASE 2 HOPSKIP STUDY

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**Background and Aims:** Lenvatinib, a multitargeted TKI, has shown activity of interest in pediatric patients with R/R osteosarcoma. HOPSKIP, a single-arm, phase 2 basket study (NCT04447755), assessed efficacy and safety of lenvatinib in other pediatric R/R solid tumors.

**Methods:** Patients aged 2-21 years with R/R high-grade glioma (HGG), rhabdomyosarcoma, Ewing sarcoma (EWS), or other solid tumors, excluding osteosarcoma, measurable disease per RECIST v1.1 or RANO for HGG, and a Lansky play score (age  $\leq 16$  years) or Karnofsky performance scale (age  $> 16$  years)  $\geq 50$  received lenvatinib 14 mg/m<sup>2</sup> orally once daily. Primary outcome was ORR at week 16 per RECIST v1.1 or RANO by investigator assessment. Secondary outcomes included DOR and safety. Futility was assessed using sequential probability ratio testing.

**Results:** 127 patients were treated (9 EWS, 17 rhabdomyosarcoma, 8 HGG, 9 diffuse midline glioma [DMG], 9 medulloblastoma, 9 ependymoma, 66 other solid tumors). Median follow-up was 17.1 months (range, 3.6-24.7). Median age was 14 years (range, 2-21); 51 patients (40.2%) had 2-3 prior lines of therapy. In 124 evaluable patients, ORR (95% CI) was 22.2% (2.8-60.0; 2 PR) for EWS, 11.8% (1.5-36.4; 2 PR) for rhabdomyosarcoma, and 7.7% (2.5-17.0; 5 PR) for other solid tumors; no objective responses occurred in HGG, DMG, medulloblastoma, or ependymoma. Median (range) DOR was not reached (5.7-17.7+ months) for EWS, 4.6 months (3.7-5.5) for rhabdomyosarcoma, and 4.6 months (3.7-8.5) for other solid tumors. Grade 3-5 treatment-related adverse events (AEs) occurred in 48.0% of all 127 patients, most frequently ( $\geq 10\%$ ) proteinuria (12.6%) and hypertension (11.8%). One patient died because of a treatment-related AE (intracranial pressure increased).

**Conclusions:** Although objective responses occurred in some patients, protocol criteria for antitumor activity were not met for any cohort. No new lenvatinib safety signals were identified, and AEs were effectively managed.

O212/#128 | Free Paper Session (FPS)

### FPS 17: NOVEL THERAPEUTIC APPROACHES

14-10-2023 08:00 - 09:30

#### GENERATION OF EVIDENCE-BASED DOSING GUIDELINES FOR NEONATES AND INFANTS RECEIVING CARBOPLATIN AND VINCRIStINE

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**Background and Aims:** The administration of chemotherapy to neonates and infants represents a significant dilemma. Commonly used dosing adjustments are supported by limited scientific rationale, with inconsistencies in dose reductions applied to many

anticancer drugs. We have utilised data generated from a national Therapeutic Drug Monitoring (TDM) programme of work, to determine evidence-based dosing guidelines for this challenging patient population.

**Methods:** Pharmacokinetic data from a total of 108 neonates and infants receiving carboplatin or vincristine were generated from a clinical trial investigating the use of TDM in challenging childhood cancer patients across 16 national centres (ISRCTN10139334). Collation of dosing information, alongside quantification of individual patient drug concentrations, allowed the determination of drug clearance values and drug exposures in the first weeks and months of life.

**Results:** Marked differences in dosing regimens recommended for neonates and infants were observed between tumour types and treatment protocols for both carboplatin and vincristine. Neonates and infants being treated with carboplatin commonly targeted an AUC of 5.2 mg/mL.min, but commonly required marked dose changes to achieve this target exposure. Patients <5kg receiving doses of 4.4mg/kg/day achieved significantly lower carboplatin exposures than patients 5-10kg, dosed at 6.6mg/kg/day ( $p = <0.0001$ ). Pharmacological evidence would recommend a carboplatin dose of 6mg/kg/day for all infant and neonate patients. For vincristine, the use of doses <0.05mg/kg in neonates and infants was shown to result in significantly lower AUC values than observed with doses  $\geq 0.05$ mg/kg ( $p = <0.0001$ ) and older children receiving doses of 1.5mg/m<sup>2</sup>.

**Conclusions:** Pharmacokinetic data generated in neonate and infant patients facilitate the calculation of evidence-based dosing regimens for carboplatin and vincristine. Currently used dosing regimens can lead to potentially sub-therapeutic drug exposures in this challenging patient population, particularly for neonates <5kg (Barnett et al, *Eur J Cancer* 2022 164:127-136; Nijstad et al, *Eur J Cancer* 2022 164:137-154).

O213/#1293 | Free Paper Session (FPS)

FPS 17: NOVEL THERAPEUTIC APPROACHES

14-10-2023 08:00 - 09:30

#### ASSESSMENT OF A NOVEL READY-TO-USE TEMOZOLOMIDE ORAL SUSPENSION IN CHILDREN WITH SOLID TUMORS: RESULTS OF TEMOKIDS, A POPULATION PHARMACOKINETIC, ACCEPTABILITY AND SAFETY PHASE-1 STUDY

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**Background and Aims:** Children with cancer should have access to age-appropriate pediatric medicines to improve drug administration and treatment compliance. To address a major unmet medical need, a ready-to-use oral suspension of temozolomide specifically formulated for children (Ped-TMZ/KIMOZO) has been developed. This novel formulation is bioequivalent to temozolomide capsules and guarantees ease-of use and stability of temozolomide over its shelf life. TEMOKids (NCT04610736) is a clinical study conducted in 12 centers and assessing pharmacokinetics, acceptability and safety of Ped-TMZ and collecting treatment response data in children with solid tumors.

**Methods:** Pediatric patients in need of temozolomide were included in the open-label, non-randomized, single-arm phase 1 study. They received Ped-TMZ (75 to 200 mg/m<sup>2</sup>/day on days 1-5) alone or in combination with other anti-cancer drugs for at least one cycle of treatment (21 or 28 days). Pharmacokinetic data was generated on day 1 of the first cycle.

**Results:** Among 49 screened patients, 43 patients aged 1.2 to 14.8 years (median, 5.4 years) were eligible. The therapeutic indications were neuroblastoma (n=20), rhabdomyosarcoma (n=6), medulloblastoma (n=6), glioblastoma/glioma (n=4), Ewing sarcoma (n=2) and other CNS embryonic tumors (n=5). Patients received 1 to 12 cycles (median, 3 cycles) of Ped-TMZ. Regarding the safety profile, two episodes of febrile neutropenia were reported as serious among 168 adverse events related to temozolomide. No suspected unexpected serious adverse reaction was reported.

**Conclusions:** Ped-TMZ demonstrated a positive benefit-risk profile in children and was readily usable in routine common care practice. The pharmacokinetic parameters are used to derive key estimates of exposure of Ped-TMZ in children and acceptability conclusion are provided. Given the unmet needs, an expanded access program has been launched in Europe. The first targeted indication of Ped-TMZ is relapsed or refractory neuroblastoma, which affects



young children and for which temozolomide is a standard backbone chemotherapy.

O214/#504 | Nursing

#### NURSING: INTERACTIVE POSTER SESSION

14-10-2023 09:40 - 10:10

#### CO-CREATION OF A DIGITAL PLATFORM FOR PEER SUPPORT BETWEEN ADOLESCENT AND YOUNG ADULT CANCER PATIENTS

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**Background and Aims:** AYAs diagnosed with cancer report psychological challenges and social isolation due to their situation. Peer support has been shown to be a valuable resource for coping with these experiences. The aim of this study is to map the needs for emotional peer support among AYA cancer patients in Sweden; and building on these results to develop and test a prototype of a digital tool for peer support between AYA cancer patients.

**Methods:** The study was conducted in close collaboration in a research team consisting of AYA cancer survivors, researchers, and a health tech company in Sweden. Through interviews the needs for emotional support among was investigated. Based on this information, a prototype of a digital platform was co-created by the research team. The platform was tested by AYAs and evaluated through an online survey and follow-up interviews as part of the iterative development process.

**Results:** The AYAs described feeling lonely and having a need for processing their cancer experiences with peers. A combination of support through interaction with peers in both digital and physical meetings was preferred. A prerequisite for being a valuable resource, the digital platform had to have a high degree of security. Piloting the prototype, 87% reported feeling secure, all participants found it valuable to interact with peers on the platform. In the follow-up interviews the AYAs reported the log-in procedure to be difficult and the need to make this easier, while still maintaining high security.

**Conclusions:** A secure digital platform for peer support can be a valuable and easily accessible complement to other forms of support. The presence of moderators was found to enhance security and perceived usefulness of the platform. Co-creating tools for support with AYAs ensures relevance and usability. **Acknowledgement** We thank all AYA cancer patients for participating in this study

O215/#1049 | Nursing

#### NURSING: INTERACTIVE POSTER SESSION

14-10-2023 09:40 - 10:10

#### IMPLEMENTATION OF A QUALITY IMPROVEMENT PROGRAM IN THE TIMELY ADMINISTRATION OF ANTIBIOTICS IN HOSPITALIZED PEDIATRIC HEMATO-ONCOLOGY PATIENTS WHO DEVELOP FEVER

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**Background and Aims:** The timely administration of antibiotics in pediatric hemato-oncology patients with fever (PHOPf) within 60 minutes or less ("Golden Hour") after arrival at emergency has been shown to reduce the incidence of sepsis, septic shock and mortality. In our hospital, "Golden Hour" (GH) was effectively implemented in the emergency department, but there are still important gaps to ensure timely antibiotic administration in hospitalized PHOPf. Aims We evaluated the implementation and impact of GH in hospitalized PHOPf at the Hospital Infantil Teletón de Oncología over a 12-month period against a historical cohort.

**Methods:** A before - after comparison was used between a historical cohort of the years 2017-2019 and 2021 versus the year 2022. The Innovative Series Model developed by the Institute for Healthcare Improvement (IHI) and a certified quality improvement competency program were applied. A theory of change was developed with multimodal strategies of interventions focused on increasing the reliability of clinical processes, ensuring adherence to clinical practice algorithms, identifying fever in a timely manner, promoting communication and teamwork.

**Results:** 166 events were analyzed in PHOPf, 53 of them during GH implementation. During 2022, 10 change ideas were tested using 20 Plan-Do-Study-Act cycles. GH adherence increased from 71.6% to 86.5%,  $p=0.035$ ; with a median of 46 minutes. The presence of sepsis decreased from 13.2% to 11.3%,  $p=0.731$ ; septic shock events from 16.8% to 3.8%; and all-cause mortality from 8.9% to 4.1% after GH implementation.

**Conclusions:** The implementation of the "Golden Hour" was improved through the application of the IHI Innovative Series model, with a favorable impact on the development of septic shock and mortality in hospitalized pediatric hemato-oncology patients who developed fever.

O216/#472 | Nursing

## NURSING: INTERACTIVE POSTER SESSION

14-10-2023 09:40 - 10:10

## SYMPTOM CLUSTERS IN CHILDREN RECEIVING CELLULAR THERAPIES: A MULTICENTER LONGITUDINAL COHORT STUDY

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**Background and Aims:** Cellular therapies, hematopoietic stem cell transplantation (HSCT) and chimeric antigen receptor T-cell (CAR-T) therapy, are potentially curative for pediatric cancers but associated with a constellation of physical and psychological symptoms. Limited research has characterized symptom clusters (one or more co-occurring symptoms) in this patient population. The aim of this presentation is to describe symptom clusters among children undergoing HSCT or CAR-T therapy.

**Methods:** A secondary analysis of data collected from a longitudinal multicenter study was conducted. Primary data obtained from children aged 2-18 years who underwent autologous or allogeneic HSCT or CAR-T therapy for any indication were included. The Memorial Symptom Assessment Scale was used to measure symptoms using self-report for children aged 8-18 and parent-proxy for children aged 2-7. Descriptive statistics were used to characterize symptom prevalence and corresponding frequency, severity, and distress scores. Hierarchical cluster analysis was performed to cluster symptom data at each timepoint (pre-cell infusion, days 30, 60, and 90).

**Results:** Data were generated from a sample of 140 children who had a mean age of 8.4 years. Most children had a malignant diagnosis (72.9%) and either received an allogeneic HSCT (57.9%), autologous HSCT (25.7%), or CAR-T therapy (16.4%). Symptoms with <15% prevalence were removed prior to analysis. Co-occurring symptoms with greater than 15% at each time point decreased over time (n = 24 pre-cell infusion, then n = 20, n = 16, n=13 at days 30, 60 and 90, respectively). Five symptom clusters emerged and reflected gastrointestinal, mood, cognitive, pulmonary, and skin symptom categories. Gastrointestinal symptoms were prevalent in all clusters, at all time points.

**Conclusions:** Distinct symptom clusters were identified in children receiving cellular therapies. Gastrointestinal symptoms were present

within all clusters, suggesting an opportunity for enhanced supportive care intervention.

O217/#554 | CCI

## CCI: MOBILIZING SUPPORT AND COLLABORATION

14-10-2023 09:40 - 10:10

## BLOOD DONATION, A CRUCIAL LIFE SAVER. A CAREGIVER'S EXPERIENCE AT THE UGANDA CANCER INSTITUTE

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**Background and Aims:** Blood and blood products are essential in the management of cancer. The Uganda cancer institute (UCI) registers more than 500 new cases of paediatric cancer annually. The majority of these children will at some point during the course of treatment require blood transfusions. The devastating news of our daughter's cancer diagnosis was broken to us on the first day of the COVID-19 lockdown in Uganda. During this time, Uganda faced crisis level blood shortages.

**Methods:** We aim at describing the role that care givers can play in mobilising blood donations. As our daughter's treatment progressed, there was need for frequent blood transfusions not only for her but also for other hospitalised children at UCI. We therefore held unstructured individual as well as focus group discussions with 15 care givers with the aim of coming together to donate blood. This effort was futile as none donated. The majority expressed fear that blood donation was linked to the mandatory covid vaccination. Others expressed their fear of blood and needles. Undeterred by the negative response, we then purposed to mobilise our immediate family and friends to donate blood. We coined this campaign, "Friends of Dr. Lalala's blood donation drive" as she came to be known during her treatment. This was successful, we collected 330 units of blood.

**Results:** We partnered with the Uganda Blood Transfusion Services and reached out to individuals and schools who overwhelmingly responded. We have so far collected over 750 units of blood.

**Conclusions:** Owing to the great success that we have so far achieved and the life saving transfusions we have witnessed, we realised we can do more when we partner with other like minded care givers. We have since started AHAVAH CHILD CANCER CARE UGANDA to address the many challenges that children and care givers face during the course of treatment.

O218/#827 | CCI

## CCI: MOBILIZING SUPPORT AND COLLABORATION

14-10-2023 09:40 - 10:10

## ESTABLISHING THE FIRST THALASSEMIA AND BLOOD DISEASES ICU IN PAKISTAN: A COMMUNITY-DRIVEN APPROACH TO PROVIDING DEDICATED CARE

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**Background and Aims:** Thalassemia and related blood disorders pose a significant health burden in Pakistan, where dedicated care is crucial for managing these conditions. However, the lack of intensive care unit (ICU) facilities for patients with blood disorders remains a major challenge, leading to higher mortality rates. To address this issue, **Afzaal Memorial Thalassemia Foundation (AMTF) - Helping Blood Disorders** established the first Thalassemia and Blood Diseases ICU in Pakistan, with the concept of “**Community Helps Community (CHC)**.” **Aims & Objective:** To reduce mortality rates among patients with blood disorders, sensitize practitioners to pediatric management in ICU, train allied health workers, and engage local donors to sustain the project.

**Methods:** **Methods:** The project was established through one-time international funding, with sustainability ensured through community support, including sharing progress data. The ICU provides free-of-cost services to pediatric and adolescent patients with various blood disorders, including thalassemia.

**Results:** **Results:** The project has been operational for ten years, with approximately 9,000 patients availing its services. The ICU has extended its services to the provincial levels and established a high dependency unit (HDU) to manage the flow of patients. The project has also trained numerous skilled personnel, serving the community and contributing to building a pool of human resources.

**Conclusions:** The establishment of the first Thalassemia and Blood Diseases ICU in Pakistan is a community-driven approach to providing dedicated care for patients with blood disorders, which has significantly reduced mortality rates. Completion of 10yrs of Pakistan first cashless ICU is a successful model with constraints of resources with multiple stakeholders each with assigned strategies. The project's success demonstrates the value of community engagement in healthcare and serves as a model for developing countries to establish similar facilities. The project's training programs for practitioners and allied health workers have also con-

tributed to building a skilled workforce, improving healthcare in the country.

O219/#1392 | Free Paper Session (FPS)

## FPS 18: INTERESTING SOLID TUMORS

14-10-2023 10:40 - 12:10

## THE ORIGIN AND EVOLUTION OF PEDIATRIC SECONDARY NEOPLASMS

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**Background and Aims:** Pediatric cancer patients without known germline predisposing mutations that present with a second malignancy during their young age are rare. When this occurs it is often assumed that the second malignancy could be related to the treatment received for the first one. Other possible explanations for the second tumor include shared early driver mosaic mutations. In this study, we investigated the origin and evolution of second neoplasms from ten pediatric patients at Sant Joan de Déu Barcelona Children's Hospital.

**Methods:** We performed whole-genome sequencing of the tumors and normal tissue samples. We investigated the timing of clonal expansion of the secondary neoplasms through treatment-related mutational signatures.

**Results:** We have identified cases of secondary acute myeloid leukemia with clonal treatment-related mutations, pointing to an initiation of leukemogenesis posterior and likely related to the treatment. Solid secondary tumors showed no clonal treatment-related mutations, suggesting the possibility that the clonal expansion of the tumor occurred before the treatment. In a few cases we identified an early mosaic mutation shared by the two tumors that could explain the appearance of two tumors in a patient. Additionally, we conducted a lineage tracing study to an extremely rare case of two solid tumors without a shared driver event, to identify the relationship between the two tumors and its origin.

**Conclusions:** In conclusion, we show that mutational signatures can be used as barcodes to study the origin and evolution of secondary neoplasms. Lineage tracing and the study of driver mutations also sheds light onto this evolution.

O220/#515 | Free Paper Session (FPS)

## FPS 18: INTERESTING SOLID TUMORS

14-10-2023 10:40 - 12:10

## ASSESSMENT OF CELL-FREE DNA CONCENTRATION AND RB1 PATHOGENIC VARIANT DETECTION IN AQUEOUS HUMOUR – FINDINGS FROM AN EXTENDED RETINOBLASTOMA COHORT

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**Background and Aims:** The identification of somatic *RB1* variation is crucial for the diagnosis of non-heritable retinoblastoma. We previously demonstrated that, when tumour DNA is unavailable, the analysis of cell-free DNA (cfDNA) in aqueous humour (AH) can be used to identify somatic *RB1* pathogenic variants. However, sample numbers in our proof of principle publication and subsequent replication studies have been relatively small. We now report *RB1* pathogenic variant detection using AH-derived cfDNA in an extended cohort of 75 AH samples.

**Methods:** Aqueous humour from 68 retinoblastoma patients (71 eyes) was collected following eye enucleation (n=34) or during conservative treatment (n=41). AH-derived cfDNA was analysed by capture-based NGS of the *RB1* gene and selected regions across chr13. An in-house bioinformatics pipeline was used to detect SNVs, CNVs and loss of heterozygosity. CfDNA was quantified using high sensitivity Agilent TapeStation and Qubit.

**Results:** We were able to detect 94% of known *RB1* pathogenic variants in AH-derived cfDNA from primary enucleated eyes. In contrast, just 41% of expected *RB1* pathogenic variants could be identified in AH collected during intravitreal chemotherapy (IVIc). Quantification of cfDNA within all AH samples determined that AH from eyes which had undergone chemotherapy treatment had significantly less detectable cfDNA (>5pg/ $\mu$ l) than treatment naive eyes (34% vs 89%,  $P < 0.001$ ). We also established that a cfDNA input of  $\geq 250$ pg corresponded with the detection of 95% of *RB1* pathogenic variants. Below this threshold, detection was <30%. We therefore collected AH taps from 13 eyes that had undergone  $\leq 3$  chemotherapy cycles, compared to an average of 6 cycles performed prior to AH collection during IViC. CfDNA was detected in 12/13 samples and *RB1* pathogenic detection rate was 81%.

**Conclusions:** Our analysis shows that the time point of AH sampling is crucial to maximize cfDNA concentration and subsequent detec-

tion of somatic *RB1* pathogenic variants in retinoblastoma patients undergoing conservative treatment.

O221/#1032 | Free Paper Session (FPS)

## FPS 18: INTERESTING SOLID TUMORS

14-10-2023 10:40 - 12:10

## EFFECT OF CISPLATIN REDUCTION IN CHILDHOOD NASOPHARYNGEAL CARCINOMA (NPC) WITH INDUCTION CHEMOTHERAPY AND CONCURRENT CHEMORADIOTHERAPY

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**Background and Aims:** The ARAR0331 study evaluated the impact of induction chemotherapy (IC) and concurrent chemoradiotherapy (CCR). During the study, CCR was reduced to include 2 instead of 3 cycles of cisplatin in a feasibility amendment. In this project we investigated the effect of cisplatin reduction on efficacy and toxicity.

**Methods:** Patients with stages IIb to IV NPC were enrolled. We considered two approaches to evaluate the cisplatin reduction: (1) the *intention-to-treat* (ITT) analysis. All eligible patients starting consolidation therapy were evaluable. Patients were classified into two groups according to protocol allocated treatment regardless of the actual treatment. (2) The *per protocol* (PP) analysis evaluated only patients who completed all cycles of consolidation therapy assigned to them.

**Results:** Between 2006 and 2012, 111 patients were enrolled. Median age was 15 years, and 46.8% of the patients were Black. From ITT analysis, the 5-year EFS for the 3-cycle and 2-cycle groups were 90.8% (95% CI: 77.3%-96.4%) and 81% (95% CI: 68.2% - 89.0%), respectively. Differences were not significant ( $p = 0.26$ ). There were no differences in OS between the two groups ( $p = 0.58$ ). The incidence of Grade 3+ AEs in the 3-cycle group was significantly higher (84.1% vs 52.5%,  $p = 0.0016$ ). From the PP analysis, there was also trend toward a better

outcome for patients who were assigned to the 3-cycle group, but differences were not significant (5-year EFS, 86.4% vs 78.8%,  $p = 0.67$ ). There were no differences in OS between the two groups ( $p = 0.94$ ). The incidence of Grade 3+ AEs in the 3-cycle group was significantly higher (86.7% vs 47.7%,  $p = 0.0015$ ).

**Conclusions:** Both approaches led to the conclusion that patients in the 3-cycle group tended to have better outcomes, but the differences were not significant. However, a higher rate of toxicity was observed in this group.

O222/#194 | Free Paper Session (FPS)

#### FPS 18: INTERESTING SOLID TUMORS

14-10-2023 10:40 - 12:10

#### DOES SPONTANEOUS INFANTILE FIBROSARCOMA REGRESSION EXIST?

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**Background and Aims:** Infantile fibrosarcoma (IFS) is a rare soft tissue intermediate malignancy occurring in young infants: 172 cases were reported in the European pediatric Soft tissue Sarcoma Group (EpSSG) and Cooperative Weichteilsarkom Studiengruppe (CWS) studies (1979-2016). At diagnosis, primary tumors are considered unresectable in 48-62% of patients, and need a multimodal strategy with preoperative systemic treatment before conservative delayed resection. However, very few spontaneous tumor regressions have been reported. Aim is to analyze if this situation exists.

**Methods:** Retrospective survey of histologically confirmed patients with IFS in France, Italy, Ireland or Germany presenting spontaneous tumor control during follow-up without any systemic treatment, nor resection.

**Results:** From 2012 to 2022, only six patients meeting the eligible criteria were found. Median age at diagnosis was 1.5 months [range, 7 days-2.5 years]. Primary tumor was located in head-and-neck ( $n=3$ ), limbs ( $n=2$ ) and thorax ( $n=1$ ). Tumor size was  $< 5$  cm in four patients and T1/T2 status in 4/2. Somatic molecular analysis documented an *ETV6::NTRK3* ( $n=3$ ), *EMLA::NTRK3* ( $n=1$ ), *EGFR::KDD* ( $n=1$ ) fusion transcript. No molecular alteration was present despite a RNA sequencing in one patient. No therapy was delivered mainly due to initial difficult diagnosis and apparition of an early spontaneous tumor regression.

After a median follow-up of 15 months (range, 7-123), all patients are alive. Maximum tumor spontaneous decrease was very good ( $> 80%$ ,  $n=3$ ), partial (20-80%;  $n=2$ ), or complete ( $n=1$ ).

**Conclusions:** Spontaneous IFS regression seems exceptional. Therefore, short term observation with early clinical and radiological control for an IFS in a non-threatening situation could be considered before starting therapy in order to avoid treatment side effects in this very favorable subset of patients. Biology of these tumors should be compared to other IFS that frequently grow rapidly and need multimodal treatment including systemic treatment (chemotherapy or TRK inhibitors)  $\pm$  tumor resection.

O223/#1676 | Free Paper Session (FPS)

#### FPS 18: INTERESTING SOLID TUMORS

14-10-2023 10:40 - 12:10

#### EXPRESSION OF THE TUMOR-ASSOCIATED ANTIGENS TYROSINASE, MAGE-A3, NY-ESO-1 AND TPTE IN PEDIATRIC MELANOMA AND THEIR CORRELATION WITH PROGNOSIS

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**Background and Aims:** Targeting tumor-associated antigens (TAAs) in malignant non-acral melanoma could facilitate targeted therapies. BNT111, a therapeutic cancer vaccine targeting specific TAAs (tyrosinase, NY-ESO1, MAGE-A3, TPTE), is undergoing clinical testing in adults (BNT111-01, NCT04526899 and Lipo-MERIT, NCT02410733). It is unclear whether these TAAs are also expressed in pediatric melanoma and whether this treatment approach could be feasible in children suffering from malignant melanoma. We aimed to characterize

TAA expression in pediatric melanomas compared with melanoma in young adults, adult melanomas, and childhood melanocytic nevi, and analyze the correlation of pediatric melanoma TAA expression profiles with melanoma subtype as well as patient outcome.

**Methods:** Expression of tyrosinase, NY-ESO1, MAGE-A3, and TPTE was analyzed using immunohistochemical staining and digital pathology (QuPath) as well as reverse transcription-quantitative PCR. These markers were investigated in 25 pediatric melanomas, 31 melanomas of young adults, 29 adult melanomas, and 30 benign nevi in children.

**Results:** Pediatric melanomas showed an expression of tyrosinase (100 %), TPTE (44 %), MAGE-A3 (12 %), and NY-ESO-1 (8 %). Young adult melanomas expressed tyrosinase (97 %), NY-ESO-1 (19 %), MAGE-A3 (19 %), and TPTE (3 %). Adult melanoma showed expression of tyrosinase (86 %), NY-ESO-1 (48 %), MAGE-A3 (76 %), and TPTE (48 %). Childhood nevi only expressed tyrosinase (93 %). The TAA expression pattern did not differ in subtypes of pediatric melanoma, and no association with prognosis was found. MAGE-A3 and TPTE were associated with prognosis in adult melanomas. NY-ESO-1, MAGE-A3, and tyrosinase showed a trend towards age-dependent expression.

**Conclusions:** The TAAs studied were all expressed in pediatric melanoma, albeit to a lesser extent than in adult melanoma. No TAAs correlated with prognosis in pediatric melanoma. The data presented here support the exploration of BNT111 in the treatment of pediatric melanoma.

O224/#1605 | Free Paper Session (FPS)

#### FPS 18: INTERESTING SOLID TUMORS

14-10-2023 10:40 - 12:10

#### ORTHOTOPIC LIVER TRANSPLANT IN CHILDREN WITH HEPATOBLASTOMA: A SINGLE INSTITUTION EXPERIENCE

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**Background and Aims:** Patients that receive orthotopic liver transplant (OLT) are predicted to have inferior oncological outcomes. OLT is indicated in patients with unresectable primary tumors to achieve cure. We reviewed our experience of all OLTs performed for hepatoblastoma (HB) at Children's Hospital Los Angeles (CHLA).

**Methods:** Retrospective medical record review of all children undergoing OLT for HB from the first OLT performed in December 2002 to December 2018 after IRB approval. Demographic, clinical features including PRETEXT stage, presence of distant metastases, AFP levels, time from diagnosis/relapse to OLT and vital status were collected. Kaplan-Meier method was used to estimate survival outcomes.

**Results:** Forty children with HB underwent OLT; median age 1.6 (0.4-13.9) years, 31 (78%) male, 30 (75%) had HB confined to the liver at diagnosis, 7 (18%) were metastatic. Majority (83%) of primaries were unresectable at initial diagnosis and 7 (17%) with resectable primaries underwent OLT for multifocal disease/local relapse. Median AFP at diagnosis was 171050 ng/mL (144-2,630,000) and 948 (11-36,300) at the time of OLT. Thirty-four (85%) had OLT during primary treatment and 6 (15%) following relapse. Median time from initial diagnosis to OLT for the 34 patients was 3.9 months (0.4-7.9) and for 6 from relapse to OLT was 7.3 months (6.4-8.3). Four children (10%) relapsed following OLT including 1 that had OLT following relapse. Thirty-eight were alive at last follow up including five that had OLT following relapse. The median follow-up time for patients alive at last follow up was 7.42 (0.5-23.3) years. Five-year event-free and overall survival (95% confidence interval) were 91.3% (75.4%-97.1%) and 94.5% (79.7%-98.6%) respectively.

**Conclusions:** Survival following OLT for HB despite recipient's poor prognostic features are excellent. A comparison to HB patients with poor prognostic features that did not undergo OLT is ongoing using our established HB clinical dataset (JAMA Netw Open. 2022 Feb 1;5(2):e2148013) is ongoing.

O225/#975 | Free Paper Session (FPS)

#### FPS 19: SURVIVORSHIP - UNDERSTANDING DISEASE AND DEATH

14-10-2023 10:40 - 12:10

#### ASSOCIATION OF CUMULATIVE CARDIOVASCULAR BURDEN WITH MAJOR ADVERSE CARDIOVASCULAR EVENTS (MACE) IN SURVIVORS OF CHILDHOOD CANCER: AN ANALYSIS FROM THE ST. JUDE LIFETIME COHORT STUDY

Rawan Hammoud<sup>1</sup>, Qi Liu<sup>2</sup>, Aron Onerup<sup>1</sup>, Daniel Mulrooney<sup>3</sup>, I-Chan Huang<sup>1</sup>, John Jefferies<sup>4</sup>, Kevin Krull<sup>5</sup>, Kirsten Ness<sup>1</sup>, Matthew Ehrhardt<sup>1</sup>, Melissa Hudson<sup>3</sup>, Nickhill Bhakta<sup>6</sup>, Stephanie Dixon<sup>7</sup>, Yadav Sapkota<sup>1</sup>, Yutaka Yasui<sup>1</sup>, Gregory Armstrong<sup>1</sup>

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**Background and Aims:** Major adverse cardiovascular events (MACE) include non-fatal stroke, heart failure, myocardial infarction, and cardiovascular mortality. We aimed to assess the incidence of MACE and its association with the cumulative burden of non-MACE cardiovascular disease (CVD) in survivors of childhood cancer.

**Methods:** Cumulative incidence of MACE was estimated in the St. Jude Lifetime Cohort Study (SJLIFE; N=9,602), accounting for eligible non-participants using multiple imputation. Multivariable piecewise-exponential regression examined the association of time-dependent cumulative count of 22 types of non-MACE CVD (graded as per CTCAE v4.03) and incidence rate of MACE in 5,229 clinically assessed participants, adjusting for age, age at diagnosis, sex, race/ethnicity, treatment era, and doses of anthracycline and chest/cranial radiation.

**Results:** The cumulative incidence of MACE (at age of 50 years) was 16.9% (95% confidence interval (CI) 15.1-18.6%). Non-MACE CVDs with the highest contribution to the CVD burden were hypertension, hypercholesterolemia, heart valve disorders, hypertriglyceridemia, and conduction abnormalities (respectively 0.72, 0.55, 0.51, 0.50, and 0.29 events/survivor). Higher incidence rates of MACE were associated with exposure to  $\geq 250$  mg/m<sup>2</sup> of anthracyclines (Rate ratio (RR) 2.3, 95%CI 1.7-3.0),  $\geq 35$  Gy chest (RR 4.0, 95%CI 3.0-5.3) and  $\geq 50$  Gy cranial radiation (RR 2.7, 95%CI 1.9-3.9). Having a grade 1-4 non-MACE cardiovascular event increased the rate of MACE compared with none (RR 3.6, 95%CI 2.6-5.1) in a dose-response manner (4 or more non-MACE CVD RR 8.8, 95%CI 5.9-13.1) and remained elevated after stratifying non-MACE CVD burden by grade (1 grade 1-2 non-MACE CVD vs. none RR 2.8, 95%CI 2.0-3.9; 1 grade 3-4 non-MACE CVD vs. none RR 2.7, 95%CI 1.9-3.9).

**Conclusions:** Low-grade non-MACE CVDs were significantly associated with MACE among survivors with an effect size similar to high-risk treatment exposures. Risk prediction models to identify survivors with non-MACE CVD at high risk for MACE may inform prevention and intervention strategies.

O226/#182 | Free Paper Session (FPS)

FPS 19: SURVIVORSHIP - UNDERSTANDING DISEASE AND DEATH

14-10-2023 10:40 - 12:10

## CARDIOVASCULAR RISK FACTORS AND EARLY CARDIOVASCULAR DISEASE AMONG CHILDHOOD, ADOLESCENT, AND YOUNG ADULT CANCER SURVIVORS

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**Background and Aims:** Cardiovascular risk factors (CVRFs) later in life potentiate risk for late cardiovascular disease (CVD) from cardiotoxic treatment among childhood, adolescent, and young adult (CAYA) survivors. This study aimed to evaluate the association of CVRFs at, or shortly after, diagnosis and CVD in the early survivorship period.

**Methods:** The Oklahoma survivor cohort was comprised of patients ages 0-29 at initial diagnosis and reported in the institutional cancer registry between 2010 and 2017 (n=914). Patients with documented death within five years (n=168) and those with CVD prior to or during the first year of treatment (n=17) were excluded. CVD was defined based on ICD-9/10 codes for heart failure or cardiomyopathy, extracted from the electronic health record. CVRFs within one year of initial diagnosis, based on discrete clinical observations, ICD9/10 codes, and RxNorms coding for antihypertensive medication prescriptions, were classified by the Common Terminology Criteria for Adverse Events (version 5.0) for hypertension, diabetes, dyslipidemia, and obesity. Descriptive statistics were calculated. The Chi-square test with expected cell counts larger than 5 and Fisher's exact test with at least one expected cell count less than 5 was used to examine the association between each predictor and CVD.

**Results:** Among CAYA survivors (n=729), 24 incident cases (3.2%) of CVD were observed between one year and five years after the initial diagnosis. Survivors with Grade  $\geq 2$  hypertension during the first year of treatment were 3.6 times more likely to develop CVD compared to those without hypertension (95% Confidence Interval 1.62-8.02). Younger age at diagnosis was also associated with CVD (p=0.02). Diabetes, dyslipidemia, and obesity, primary diagnosis, sex, race/ethnicity, and late effects risk strata were not significantly associated with CVD.

**Conclusions:** Hypertension within the first year of diagnosis represents a potentially modifiable risk factor associated with CVD during the early survivorship period for CAYA survivors.

O227/#1664 | Free Paper Session (FPS)

FPS 19: SURVIVORSHIP - UNDERSTANDING DISEASE AND DEATH

14-10-2023 10:40 - 12:10

## PROTEOMIC PROFILING FOR ANTHRACYCLINE-ASSOCIATED CARDIOMYOPATHY AMONG CHILDHOOD CANCER SURVIVORS: A REPORT FROM THE ST. JUDE LIFETIME COHORT

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**Background and Aims:** **Background:** Anthracyclines, antineoplastic agents used to treat a variety of pediatric malignancies, are limited by their dose-dependent association with cardiomyopathy. Biomarkers of anthracycline-associated cardiomyopathy are needed for early detection and to guide interventions.

**Methods:** Untargeted proteomic profiling using tandem mass tags-mass spectrometry was performed on serum samples of anthracycline-exposed (no chest irradiation) White (self-reported) childhood cancer survivors with cardiomyopathy (n=87; CTCAE grade 2 [n=68] and grade 3 [n=19]) and 87 individually matched (on sex, primary cancer type, age at diagnosis, anthracycline dose and attained age) survivors without cardiomyopathy from the St. Jude Lifetime Cohort (SJLIFE; discovery sample). Linear mixed models assessed associations between levels of circulating proteins and cardiomyopathy. Significant results were evaluated in two SJLIFE validation samples, including 26 Black survivors (13 with cardiomyopathy) and 16 White survivors (8 with cardiomyopathy). Genome-wide association analyses were conducted in discovery sample to identify genetic determinants of cardiomyopathy-associated proteins.

**Results:** A total of 867 known canonical proteins were reliably detected in the discovery sample. Six proteins showed significant associations (FDR<5%) with cardiomyopathy and of these, associations were replicated for DCNL4 (fold-change [FC]<sub>discovery</sub>=1.38; FC<sub>replication</sub>=2.30; P<sub>replication</sub>=0.045) in Black survivors and AKAP4 (FC<sub>discovery</sub>=0.64; FC<sub>replication</sub>=0.33; P<sub>replication</sub>=0.010) in White survivors. Multiple common variants were identified at chr17q24.1 show-

ing genome-wide significant associations with DCNL4 (P<5×10<sup>-8</sup>). DCNL4 is essential for the neddylation (post-translational protein modification) of cullins. Dysregulation of neddylation can lead to the degradation of calcineurin and contribute to cardiomyopathy and/or heart failure. AKAP4 belongs to a class of scaffolding proteins that regulate the spatiotemporal signaling needed for cardiac function. Five additional proteins also showed P<0.05 in the discovery and validation samples (TFR1, APOB, CETP, KBTB4 and MYO5A).

**Conclusions:** Using an untargeted proteomics approach, we identified protein biomarkers associated with cardiomyopathy in childhood cancer survivors. These findings have potential implications for screening and earlier detection of anthracycline-associated cardiomyopathy.

O228/#263 | Free Paper Session (FPS)

FPS 19: SURVIVORSHIP - UNDERSTANDING DISEASE AND DEATH

14-10-2023 10:40 - 12:10

## FEMALE BREAST CANCER RISK AFTER ANTHRACYCLINES FOR CHILDHOOD CANCER: AN INTERNATIONAL POOLED ANALYSIS

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**Background and Aims:** Anthracycline-based chemotherapy is associated with increased subsequent breast cancer (SBC) risk in female childhood cancer survivors, but the current evidence was deemed insufficient to support early breast cancer screening recommendations for survivors treated with anthracyclines. We analyzed the dose-dependent effects of individual anthracycline agents on developing SBC and interactions with chest radiotherapy in an internationally pooled cohort.

**Methods:** We included female 5-year survivors from six cohort studies and one case-cohort study in Europe/North-America. We restricted our analyses to 17,903 women with complete radiotherapy and chemotherapy information. Cox regressions evaluated anthracycline-associated risks for SBC adjusted for chest and pelvic radiotherapy, diagnosis age, and alkylating agents.

**Results:** After a median follow-up of 24.9 years (IQR 19.1-33.2) after primary cancer diagnosis, 782 developed a first SBC. A dose-dependent increased SBC risk was seen for doxorubicin (HR per 100 mg/m<sup>2</sup>: 1.24, 95% CI: 1.18-1.31), and risk was more than two times higher for survivors treated with  $\geq 200$  mg/m<sup>2</sup> cumulative doxorubicin dose compared to the no doxorubicin treatment. For daunorubicin, a non-statistically significant increase was observed (HR per 100 mg/m<sup>2</sup>: 1.10, 95% CI: 0.95-1.29). Epirubicin was also associated with increased SBC risk (yes vs. no, HR: 3.25, 95% CI: 1.59-6.63). For patients treated with or without chest irradiation, HRs per 100 mg/m<sup>2</sup> of doxorubicin were 1.11 (95% CI: 1.02-1.21) and 1.26 (95% CI: 1.17-1.36), respectively. Joint effects of doxorubicin and chest radiation were less than multiplicative (HR<sub>multiplicative interaction</sub>: 0.86, 95% CI: 0.78-0.96,  $P_{multiplicative interaction}=0.006$ ) and compatible with additivity ( $P_{additive interaction}=0.99$ ).

**Conclusions:** Our findings support that early initiation of breast cancer surveillance is reasonable for childhood cancer survivors who received  $\geq 200$  mg/m<sup>2</sup> cumulative doxorubicin dose. The results of our study should be implemented in SBC surveillance guidelines for survivors and will inform future treatment protocols for newly diagnosed childhood cancer patients.

O229/#1443 | Free Paper Session (FPS)

## FPS 19: SURVIVORSHIP - UNDERSTANDING DISEASE AND DEATH

14-10-2023 10:40 - 12:10

### FEAR OF CANCER RECURRENCE IN ADULT SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY

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**Background and Aims:** Fear of cancer recurrence (FCR) is among the most distressing problems experienced by survivors of adult-onset cancer and is associated with anxiety and depression. However, little is known about the prevalence and associated risk factors of FCR among adult survivors of childhood cancer.

**Methods:** A representative sample of adult survivors of childhood cancer (N=229, median age=40 years, range=22-64, 50.6% female, median years since diagnosis=32.8) enrolled in the Childhood Cancer Survivorship Study completed the FCR Inventory Short Form, a validated and comprehensive measure of FCR over the past month as well as measures of anxiety (Generalized Anxiety Disorder 7-Item), depression (Patient Health Questionnaire 8-Item), chronic pain (assessing pain lasting  $\geq 3$  months), and perceived poor health status (1-item yes/no). Validated cut-off scores of  $\geq 22$ ,  $\geq 10$ , and  $\geq 10$  were used to define clinically significant levels of FCR, anxiety, and depression, respectively. Poisson regression models estimated prevalence ratios (PR) with 95% confidence intervals (CI) adjusted for age, sex, and race to examine the effects of demographic, disease, treatment factors, and psychosocial variables on FCR.

**Results:** 16.6% (95% CI: 11.6-21.6) of survivors reported clinically significant FCR. Increased risk of clinically significant FCR was associated with female sex (PR[CI]: 2.0[1.0-3.7]), unemployment (2.1[1.1-4.2]), living in a nonmetropolitan area (2.2[1.2-4.3]), neurological conditions (3.4[1.8-6.3]), pelvic radiation (3.0[1.5-6.1]), and amputation or limb sparing surgery (2.1[1.03-4.2]). Higher risk of clinically significant FCR was also associated with clinically significant anxiety (4.8[2.7-8.4]) and

depression (4.1[2.3-7.3]), chronic pain (2.8[1.4-5.6]), and poor health status (5.5[3.1-9.7]). No associations were observed between FCR and prior primary cancer recurrence or subsequent malignant neoplasms.

**Conclusions:** Decades following treatment, a notable proportion of childhood cancer survivors reported clinically significant FCR. Treatment exposures, chronic conditions, anxiety, and depression were associated with clinical levels of FCR. Future longitudinal research is needed to investigate the direction of the relationship between FCR and depression as well as anxiety.

O230/#413 | Free Paper Session (FPS)

### FPS 19: SURVIVORSHIP - UNDERSTANDING DISEASE AND DEATH

14-10-2023 10:40 - 12:10

#### INTER-INDIVIDUAL VARIATION IN GONADOTOXICITY IN FEMALE CHILDHOOD CANCER SURVIVORS - A GENOME-WIDE ASSOCIATION STUDY: RESULTS FROM THE PANCARELIFE STUDY

M.E. Madeleine Van Der Perk<sup>1</sup>, Linda Broer<sup>2</sup>, Yutaka Yasui<sup>3</sup>, Joop Laven<sup>4</sup>, Leslie Robison<sup>5</sup>, Wim Tissing<sup>6,7</sup>, Birgitta Versluijs<sup>1</sup>, Dorine Bresters<sup>8</sup>, Gertjan Kaspers<sup>9,10</sup>, Cornelis Lambalk<sup>11</sup>, Annelies Overbeek<sup>11</sup>, Jacqueline Loonen<sup>12</sup>, Catharina Beerendonk<sup>13</sup>, Julianne Byrne<sup>14</sup>, Claire Berger<sup>15,16</sup>, Eva Clemens<sup>1</sup>, Eline Van Dulmen-Den Broeder<sup>1,17</sup>, Uta Dirksen<sup>18,19</sup>, Heleen Van Der Pal<sup>8</sup>, Andrica De Vries<sup>8</sup>, Jeanette Winther<sup>20,21</sup>, Andeas Ranft<sup>18,19</sup>, Sophie Fossa<sup>22</sup>, Desiree Grabow<sup>23</sup>, Monica Muraca<sup>24</sup>, Melanie Kaiser<sup>23</sup>, Tomas Kepak<sup>25</sup>, Jarmila Kruseova<sup>26</sup>, Dalit Modan-Moses<sup>27</sup>, Claudia Spix<sup>23</sup>, Oliver Zolk<sup>28</sup>, Peter Kaatsch<sup>23</sup>, Leontien Kremer<sup>29</sup>, Russell Brooke<sup>3</sup>, Fan Wang<sup>3</sup>, Jessica Baedke<sup>3</sup>, André Uitterlinden<sup>2</sup>, Annelies Bos<sup>1,30</sup>, Flora Van Leeuwen<sup>31</sup>, Kristen Ness<sup>32</sup>, Melissa Hudson<sup>5,33</sup>, Anne-Lotte Van Der Koor<sup>1,4</sup>, Marry Van Den Heuvel-Eibrink<sup>8,34</sup>

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Netherlands, <sup>13</sup>Radboud University Medical Center, Department Of Obstetrics And Gynaecology, Nijmegen, Netherlands, <sup>14</sup>Boyne Research Institute, Research, Bettystown, Ireland, <sup>15</sup>Jean Monnet University, Department Of Paediatric Oncology, University Hospital, St-Etienne, France, <sup>16</sup>University Hospital, Department Of Paediatric Oncology, St-Etienne, France, <sup>17</sup>Cancer Center Amsterdam, Emma Children's Hospital, Amsterdam UMC, Vrije Universiteit Amsterdam, Amsterdam, Pediatric Oncology, Amsterdam, Netherlands, <sup>18</sup>University Hospital Essen, Pediatrics Iii, Essen, Germany, <sup>19</sup>German Cancer Research Centre, Dtk, Essen, Germany, <sup>20</sup>Danish Cancer Society Research Center, Childhood Cancer Research Group, Copenhagen, Denmark, <sup>21</sup>Aarhus University, Department Of Clinical Medicine, Faculty Of Health, Aarhus, Denmark, <sup>22</sup>Oslo University Hospital, Department Of Oncology, Oslo, Norway, <sup>23</sup>German Childhood Cancer Registry, Division Of Childhood Cancer Epidemiology, Mainz, Germany, <sup>24</sup>IRCCS Istituto Giannina Gaslini, Epidemiology, Biostatistics Unit And Dopo Clinic, Genova, Italy, <sup>25</sup>University Hospital Brno, International Clinical Research Center, Brno, Czech Republic, <sup>26</sup>Motol University Hospital, Pediatric Oncology, Prague, Czech Republic, <sup>27</sup>Chaim Sheba Medical Center, The Edmond And Lily Safra Children's Hospital, Chaim Sheba Medical Center, Tel Hashomer, Tel-Aviv, Israel, <sup>28</sup>Brandenburg Medical School Theodor Fontane, Institute Of Clinical Pharmacology, Neuruppin, Germany, <sup>29</sup>Princess Máxima Center for Pediatric Oncology, Research, Utrecht, Netherlands, <sup>30</sup>University Medical Center Utrecht, Department Of Reproductive Medicine, Utrecht, Netherlands, <sup>31</sup>Netherlands Cancer Institute, -, Amsterdam, Netherlands, <sup>32</sup>St. Jude Children's Research Hospital, Epidemiology And Cancer Control, Memphis, United States of America, <sup>33</sup>St. Jude Children's Research Hospital, Oncology, Memphis, United States of America, <sup>34</sup>Wilhelmina Children's Hospital/University Medical Center Utrecht, Pediatric Oncology And Hematology, Utrecht, Netherlands

**Background and Aims:** Female childhood cancer survivors (CCS) are at risk of therapy-related gonadal impairment. Alkylating agents (AA) are well-established risk factors, and the inter-individual variability in gonadotoxicity may be explained by genetic polymorphisms. We aimed to discover new variants associated with AA-induced gonadotoxicity among adult female CCS using a genome-wide association study approach.

**Methods:** Anti-Müllerian hormone (AMH) levels served as a proxy for ovarian function in a discovery cohort of adult female CCS, from the pan-European PanCareLIFE cohort (n=743; median age=25.8years), excluding bilateral ovarian irradiation, bilateral oophorectomy, CNS or total body irradiation, or stem cell transplantation. Replication was attempted in the USA-based St. Jude Lifetime Cohort (n=391; median age=31.3years) and findings were combined in a meta-analysis.

**Results:** Three genome-wide significant ( $<5.0 \times 10^{-8}$ ) and 16 genome-wide suggestive ( $<5.0 \times 10^{-6}$ ) loci were associated with log-transformed AMH levels, adjusted for cyclophosphamide equivalent dose of AA, age at diagnosis, and age at study in the PanCareLIFE cohort. Based on effect allele frequency (EAF) ( $>0.01$  or genome-wide significant), p-value ( $<5.0 \times 10^{-6}$ ), and biological relevance, 15 SNPs were selected for replication. Meta-analysis revealed that rs78861946 was associated

at borderline genome-wide statistical significance (Reference/effect allele=C/T; EAF=0.04, Beta(SE)=-0.484(0.091), p-value=9.39×10<sup>-8</sup>). This SNP is located in the *RGS5* (regulator of G protein signaling 5) gene, near *RGS4* and *NUF2*, genes involved in follicle-stimulating hormone receptor(FSHR) signaling, cell cycle regulation and apoptosis.

**Conclusions:** A new variant rs78861946 was associated with lower AMH levels in female CCS in the meta-analysis of two independent cohorts and may affect susceptibility to AA-induced gonadal damage and accelerated depletion of the follicle pool via regulation of the FSHR by RGS. While FSHR pathways influence age at natural menopause these genes have not previously been associated with premature ovarian insufficiency, menopause or infertility. Identification of risk-contributing variants may be used in future polygenic risk scores for individualized counselling regarding the treatment-related risk of gonadotoxicity and fertility preservation options for CCS.

O231/#1685 | CCI

#### CCI: PROVIDING EDUCATIONAL AND EMOTIONAL SUPPORT AND IMPROVING COMMUNICATION

14-10-2023 10:40 - 12:10

#### PEDIATRIC ONCOLOGY: CREATION OF A BOOK IN BRAILLE

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**Background and Aims:** The importance of clear communication with children and adolescents about their diseases is often devalued by society, which neglects the emotional impacts of lack of information. In addition, not much is said about materials suitable for children with visual disabilities in oncological treatment. Up to now there has been no material in braille with specialized information about cancer treatment. Beaba Guide is a book that addresses the meaning of 165 words which are part of the routine of children diagnosed with cancer. From this material, we created a braille version, in Portuguese, co-created with a teenager who had retinoblastoma in childhood and is blind. The goal is to improve communication with children and adolescents with visual deficiency undergoing oncological treatment.

**Methods:** Creation of a braille version of the material, with inputs from a blind adolescent, who underwent cancer treatment, and her pedagogical mother, who works with inclusion. The printed material was submitted to the blind adolescent for approval.

**Results:** The accessible material was co-created with the teenager and her mother. The relevance of the material was approved by the participant.

**Conclusions:** This is the first book in braille which gives direct access to communication with children and adolescents with visual deficiency in oncological treatment. This points to the negligence of communication with children and adolescents with visual deficiency. New studies are needed, with a larger range of participants, for validation, printing and distribution of the material on a large scale.

O232/#1562 | CCI

#### CCI: PROVIDING EDUCATIONAL AND EMOTIONAL SUPPORT AND IMPROVING COMMUNICATION

14-10-2023 10:40 - 12:10

#### THERE IS NOTHING TO DO; YOU ARE OCCUPYING THE BED FOR NOTHING. AN INTERPRETATIVE APPROACH OF CAREGIVER-PATIENT COMMUNICATION IN ONCOPAEDIATRIC

Léopold Molel Belika<sup>1,2</sup>, Claude Njiki Ngassam<sup>1,3</sup>, Ruth-Grâce Ngo Nyobe<sup>4</sup>, Pierre Sambo Sodea<sup>5</sup>

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**Background and Aims:** When a child is diagnosed with a serious illness, the seriousness of the situation is related to the child's status as a child first and to the place given to the child in his or her original cultural universe. Thus, communication is very important not only for the quality of care, but also for the acceptance of the disease and compliance with treatment. The aim of this paper is to identify the elements of communication and their functions and to analyze their impact on patient management.

**Methods:** We identified three of the five childhood cancer care centers in Cameroon, namely the Mother and Child Center of the Chantal Biya Foundation in Yaounde and the Protestant Hospital of Ngaoubela. We observed and described, between 2017 and 2022, 120 situations of communication between caregiver and patient at different levels of treatment: diagnostic announcement, treatment, palliative care, death.

**Results:** We identified the following functions: (1) establishing relationships, (2) transmitting a message or information, (3) making decisions, (4) providing emotional support. Of the observed situations, the following outcomes were described: compliance with treatment 70%, refusal of treatment 20%, conflictual relationship 50%, fear 95%, shock 99%, denial of the disease 70% and choice of another therapy 50%.

**Conclusions:** This research has highlighted four main functions of communication in Cameroonian oncology. It also revealed the

difficulties of communication, mainly due to the limitations of the actors in the practice of communication and the weakness of cross-cultural skills and their influence on the therapeutic relationship. Although this study was consciously limited to the caregiver-patient relationship, it would reveal additional results if it were to include caregiver-patient communication.

O233/#525 | CCI

#### CCI: PROVIDING EDUCATIONAL AND EMOTIONAL SUPPORT AND IMPROVING COMMUNICATION

14-10-2023 10:40 - 12:10

#### CREATING AWARENESS ABOUT SUPERHEROES FIGHTING CANCER

Alejandra Mendez

FUNDACION NUESTROS HIJOS, Board Member, Santiago, Chile

**Background and Aims:** **Background:** In the global community it is very common to use war language to refer to childhood cancer patients and the experience of living this disease. Although this terminology is widely used and accepted, few are aware of its negative impact on patients and their families. **Aims:** To create awareness about this important issue and induce a change in this common and hurtful practice

**Methods:** Research in different global media shows that war language is widely used in different countries and contexts. Through personal experience as a mother of a childhood cancer survivor (who relapsed 3 times) and my experience of over 10 years working with patients and family members, I have learned that the use of war language has a negative impact in this population. (Examples will be presented and exposed)

**Results:** When war language is used, most patients and caregivers feel a burden of having to behave as “superheroes” who “fight” the disease. Superheroes are never afraid; they are proud to defend a cause and will be happy to give their lives for it. They know what to do and won't hesitate to do it. This is totally different to what most parents and patients feel: we are usually scared, sad, angry, and overwhelmed. What happens if the patient doesn't “win the battle”? Is he/she a loser? The superhero image prevents the patient and family members from showing their vulnerability and real feelings.

**Conclusions:** When a patient dies of cancer is the science who lost a battle. The team of doctors, researchers and scientists who have not yet found a cure to the disease. It is not the patient who didn't fight enough. This change of perspective has eased the pain of so many bereaved parents and has loosen the stress of so many patients and their families.

O234/#539 | Free Paper Session (FPS)

#### FPS 20: BASIC AND TRANSLATIONAL STUDIES

14-10-2023 10:40 - 12:10

#### TRANS-SPECIES ANALYSIS OF REPLICATION-REPAIR DEFICIENT (RRD) MEDULLOBLASTOMA AND RESPONSE TO IMMUNE-CHECKPOINT INHIBITION: AN IRRDC REPORT

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**Background and Aims:** Replication-repair deficiency (RRD) stemming from mismatch repair and polymerase-proofreading gene defects (MMRD/PPD) lead to hypermutant childhood cancers, most frequently brain tumors. While medulloblastoma is reported, the clinical, genomic and immune landscape remains unknown.

**Methods:** We analysed the genome, methylome, transcriptome (bulk and single-nuclei) and immune-microenvironment of the largest cohort of RRD-medulloblastoma patients enrolled by our international consortium, and correlated these to clinical outcomes. RRD mice-models were used to preclinically assess response to immunotherapy.

**Results:** RRD-Medulloblastoma (n=40) were enriched for anaplasia (55%) and localised disease (85%). Methylation/nano-string-based subgrouping failed to classify 40% of tumors while the remaining clustered with the SHH-subgroup. Copy-number changes were notably infrequent (<20%). All harboured hypermutation and microsatellite instability in contrast to non-RRD controls (p<0.0001). Pathogenic variants were frequent in *POLE/POLD1* (80%), *TP53* (48%) and SHH-pathway genes (*PTCH1*, *SUFU*, *SMO*: 56%). Interestingly, some tumors additionally had glioma-driver alterations (*ATRX*, *NF1*: ~50%), similar to RRD cerebellar glioblastoma, but distinct from both non-RRD medulloblastoma (n=791) and hemispheric glioblastoma (n=733) controls. Moreover, although bulk-transcriptome matched non-RRD SHH-medulloblastoma, single-nuclei analyses suggested an earlier cell-of-origin potentially explaining the heterogenous phenotypes resulting from the driver mutations. Uniquely, immune analyses (gene expression and immunohistochemistry) demonstrated high intra-tumoral CD8 T-cell infiltration. Three-year progression-free survival was

60%. Outcome was worse for RRD-medulloblastoma harbouring *TP53* mutation ( $p=0.04$ ) and failing subgroup-classification ( $p=0.004$ ). Nestin/Cre *MSH2*<sup>-/-</sup> *POLE*;*p.S459F* mice developing medulloblastoma recapitulated human disease and demonstrated response to anti-PD1 monotherapy. Recurrent/progressive human tumors including those harbouring *TP53* mutations exhibited radiological responses to anti-PD1 monotherapy, which was associated with prolonged ongoing survival in comparison to those not treated with checkpoint-inhibitors ( $p=0.02$ ).

**Conclusions:** Hypermutant RRD-medulloblastoma reveal heterogeneous phenotypes due to unique spectrum of driver mutations and an early cell of origin. Their immune-hot microenvironment allows successful salvage treatment with checkpoint-inhibitors for those failing chemo-radiation, including the high risk *SHH/TP53* mutant and unclassified subgroups.

O235/#324 | Free Paper Session (FPS)

## FPS 20: BASIC AND TRANSLATIONAL STUDIES

14-10-2023 10:40 - 12:10

### PEDIATRIC DIFFUSE MIDLINE GLIOMA PATIENTS HAVE A HIGH PREVALENCE OF TARGETABLE GERMLINE VARIANTS IN HOMOLOGOUS RECOMBINATION AND MISMATCH REPAIR GENES

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**Background and Aims:** Pediatric Diffuse Midline Gliomas (DMG) with somatic *H3K27M* mutations have a dismal prognosis and novel therapeutic targets are urgently needed. The prevalence of actionable pathogenic/likely pathogenic (P/LP) germline variants in DMG, including diffuse intrinsic pontine glioma (DIPG), is currently unknown. **Methods:** Here, we examined a retrospective cohort of 252 patients with *H3K27*-altered DMG, including 153 with DIPG comprised of Australian, European, and North American patients. We assessed the prevalence of germline P/LP findings in established pediatric- and adult-type cancer predisposition genes (CPG) using American College of Medical Genetics and Genomics guidelines.

**Results:** We identified rare P/LP germline variants in CPG genes in 7.5% (19/252) of all patients. The prevalence was not significantly different according to age, location of DMG nor *H3K27M* mutational status. Nineteen patients harboured 21 P/LP germline variants, with two patients each having two separate germline P/LP variants. The majority of P/LP variants occurred in genes that are involved in homologous recombination repair ( $n=9$ ; *BRCA1*, *BRCA2*, *PALB2*) and the Fanconi anaemia pathway ( $n=4$ ). Pathogenic germline variants in the mismatch repair genes (*MSH2*, *PMS2*) were found in two patients. Reflecting the potential therapeutic relevance of these findings, we describe one *H3K27M*-mutant DMG patient with a pathogenic germline *BRCA2* and *FANCE* variant and multiple recurrences, who was treated with a PARP inhibitor (olaparib) and immune checkpoint inhibitor, leading to a near complete radiological response after 4 months.

**Conclusions:** This is the largest reported international series to date evaluating germline P/LP variants in DMG and DIPG patients, which shows a high prevalence of germline variants in CPG genes involved in the homologous recombination and mismatch repair pathways genes with potential therapeutic importance. It is predicted that these germline findings will also have impact on subsequent cascade testing of relatives. Our data suggest a role for germline analysis in DMG and DIPG patients at diagnosis.

O236/#798 | Free Paper Session (FPS)

FPS 20: BASIC AND TRANSLATIONAL STUDIES

14-10-2023 10:40 - 12:10

### THE CLINICAL AND BIOLOGICAL LANDSCAPE OF CONSTITUTIONAL MISMATCH REPAIR DEFICIENCY: AN IRRDC STUDY

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**Background and Aims:** Constitutional mismatch repair deficiency (CMMRD) is a cancer predisposition syndrome caused by biallelic mutations in mismatch repair. We investigated patient and tumor characteristics and uncovered novel genotype-phenotype associations.

**Methods:** Genetic, clinical, and outcome data were collected for confirmed cases of CMMRD in the Int. Replication-Repair Deficiency Consortium (IRRDC). Tumor genomic and molecular data were analyzed and correlated with clinical and genetic features.

**Results:** A total of 201 patients (median age: 8.8-years) fulfilled the diagnostic criteria. Although majority (69%) of patients were from low-consanguinity countries, enrichment was observed for immigrant/indigenous populations. Café-au-lait macules (CALM) were detected in 89% and NF1-criteria were fulfilled by 28% but none had germline NF1 mutations. Tumor spectrum (n=339) uncovered additional cancer types including embryonal (nephroblastoma, neuroblastoma) in early childhood and sarcoma in adolescence. Adult-type neoplasms (breast, bladder, prostate) were observed in survivors at young ages. Brain tumors had the worst OS (10-years 39%) followed by hematopoietic malignancies (67%) while improved survival was observed in other solid tumors (96%; p<0.0001). Muta-

tions in *POLE/POLD1*, *TP53*, and *RAS/MAPK* were common in brain and, gastrointestinal but rare in hematological and other malignancies. Observed tissue-specific mutational burden and MS-indel accumulation reflects cell divisions and polymerase mutagenesis which affect outcome. Unique genotype-phenotype associations were uncovered. Germline *MLH1* (6%) and *MSH2* (3%) were rare. Enrichment for homozygosity (p=0.001) and missense mutations (p=0.01) coupled with earlier cancer diagnosis (p<0.02) in *MSH2/MLH1* carriers supports a more aggressive phenotype. Moreover, missense mutations in all genes had retained expression (p=0.04), lower MS-indels (p=0.03), and later age of cancer-onset (p=0.004) than frameshift/stop-codon alterations. Patient OS at 15-years was 63% for *PMS2*, 49% for *MSH6*, 23% for *MLH1*, and 0% for *MSH2* (p<0.0001). The impact of genotype was mostly abrogated for those on surveillance and checkpoint-inhibitors.

**Conclusions:** We utilize the largest dataset of patients with CMMRD to define novel relationships between genotype, cancer spectrum, and outcome following surveillance and immunotherapy, which are important for future diagnosis and management of the syndrome.

O237/#1096 | Free Paper Session (FPS)

FPS 20: BASIC AND TRANSLATIONAL STUDIES

14-10-2023 10:40 - 12:10

### SPATIAL SINGLE-CELL ANALYSIS OF PEDIATRIC GLIOMA REVEALS A 'P53/PD-1/PD-L1 ECOSYSTEM'

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**Background and Aims:** Pediatric glioma are heterogeneous tumors, with heterogeneity in both the tumor cells and the tumor micro-environment (TME). These differences can affect the efficacy of treatment and can play a role in tumor recurrence, but are still incompletely understood.

**Methods:** High-dimensional multiplex immunohistochemistry was used to study the single-cell organization of 65 pediatric glioma samples covering 8 histologic diagnoses. This allows for the analysis of the spatial distribution of the tumoral and immune cells present and possible interactions between these cells.

**Results:** We observe a higher density of T-cells in close proximity of the blood vessels, implying a poor penetration into the tumor. We also

identified phenotypic changes of tumor cells, with a gradient ranging from neural-progenitor-like to oligodendrocyte-progenitor-like to astrocyte/mesenchymal-like; relative to the distance of the tumor cell from blood vessels. Cytotoxic T-cells expressed higher levels of activation markers when located closer to T-helper cells or macrophages, but the total activation was lower in high grade glioma compared to low grade glioma. The level of activation of cytotoxic T-cells was related to the level of PD-L1 expression in the macrophages. Furthermore, we observed that the presence of p53+ tumor cells has effects on the cells in the TME, where p53+ tumor cells influence the preservation of PD-L1 expression in macrophages and the PD-1 expression in cytotoxic T-cells.

**Conclusions:** Using multiplex immunohistochemistry, we identified a possible 'p53/PD-1/PD-L1 ecosystem' in pediatric glioma, which might play a role in the efficacy of (immuno)therapy.

O238/#274 | Free Paper Session (FPS)

## FPS 20: BASIC AND TRANSLATIONAL STUDIES

14-10-2023 10:40 - 12:10

### NOVEL PRECLINICAL MOUSE MODEL FOR EMBRYONAL TUMOUR WITH MULTILAYERED ROSETTES (ETMR)

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**Background and Aims:** The transcription factor MYCN is essential for neurogenesis. Overexpression of this gene is common in several childhood brain tumours, including the highly aggressive and heterogeneous embryonal tumour with multilayered rosettes (ETMR). This tumour type predominantly arises in infants under the age of 3 and remains refractory to treatment, with dismal 5-year survival rates. While the involvement of MYCN in ETMR was recently discovered, its oncogenic mechanisms remain poorly understood. In this study, we investigated whether overexpression of MYCN in human-hindbrain neuroepithelial stem (hbNES) cells is sufficient to form brain tumours resembling ETMR. Given their embryonal and neural characteristics, hbNES cells represent an excellent source of physiologically relevant cells for ETMR.

**Methods:** First, we generated hbNES cells overexpressing MYCN (via T58A mutation) in a Tet-On system. The transduced cells were

intracranially injected and monitored with MRI for tumour formation. The tumours produced in the animals were analysed through bulk RNA-sequencing, EPIC methylation, and standard immunostaining techniques.

**Results:** Animals formed aggressive tumours with heterogeneous tumour locations, spanning the supratentorial and infratentorial regions within 6 weeks post-injection, and with 100% penetrance. These hbNES-derived tumours resembled ETMR by histology, global gene expression, and DNA methylation.

**Conclusions:** In conclusion, we found that increased MYCN expression in hbNES cells is sufficient to transform these human neural progenitors into this rare group of paediatric brain tumours. We will utilise this inducible system to dissect the role of MYCN in ETMR origin and progression in a timely manner. Using xenografts and tumour spheroids, we can analyse this system comprehensively to map novel and insightful mechanisms in ETMR. Our goal is to fully characterize this tumour model for future pre-clinical studies. Given the current lack of robust models, we hope that this work will provide a better understanding of the tumour biology and generate more efficacious routes for the treatment of ETMR patients.

O239/#210 | Poster Discussion Session

### POSTER DISCUSSION 01: BEST OF GLOBAL PAEDIATRIC ONCOLOGY

14-10-2023 13:10 - 14:10

### TREATMENT OUTCOMES OF PEDIATRIC ACUTE MYELOID LEUKEMIA IN WESTERN KENYA BEFORE AND AFTER THE IMPLEMENTATION OF THE SIOP PODC TREATMENT GUIDELINE

Noa Wijnen<sup>1</sup>, Romy Van Weelden<sup>1</sup>, Festus Njuguna<sup>2</sup>, Kim Klein<sup>3</sup>, Terry Vik<sup>4</sup>, Gilbert Olbara<sup>5</sup>, Gertjan Kaspers<sup>6</sup>

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**Background and Aims:** The Pediatric Oncology in Developing Countries (PODC) committee (now: Global Health Network) of the International Society of Pediatric Oncology (SIOP) published a pediatric acute myeloid leukemia (AML)-specific adapted treatment guideline for low- and middle-income countries. We evaluated the outcomes of children with AML at a large Kenyan academic hospital before (period 1; 2010 - July 2019) and after (period 2; August 2019 - December 2021) implementing this guideline.

**Methods:** Records of children ( $\leq 17$  years) newly diagnosed with AML between 2010 and 2021 were retrospectively studied. In period 1, induction therapy comprised two courses with doxorubicin and cytarabine, and consolidation comprised two courses with etoposide and cytarabine. In period 2, a prephase with intravenous low-dose etoposide ( $50 \text{ mg/m}^2$ , days 1-7) was administered prior to induction therapy, induction course I was intensified ( $100 \text{ mg/m}^2$ , every 12h, days 1-7, instead of once daily), and consolidation was adapted to two high-dose cytarabine courses ( $3 \text{ g/m}^2$ , every 12h, days 1-3).

**Results:** One-hundred twenty-two children with AML were included, of whom 83 in period 1 and 39 in period 2. Overall, 95 patients received chemotherapy. The abandonment rate was 19% in period 1 and 3% in period 2. The early death, treatment-related mortality, complete remission, and relapse rates in periods 1 and 2 were 46% vs 44%, 36% vs 47%, 33% vs 38%, and 57% vs 17%, respectively. The two-year probabilities of event-free survival and overall survival in periods 1 and 2 were 5% vs 15% (Log-rank  $P=0.527$ ), and 8% vs 16% (Log-rank  $P=0.932$ ), respectively.

**Conclusions:** The implementation of the SIOP PODC guideline did not result in a statistically significant improvement in survival of Kenyan children with AML. Survival of these children remains dismal, which is mainly caused by a high early death rate. Improved supportive care seems crucial to improve their outcome.

O240/#970 | Poster Discussion Session

#### POSTER DISCUSSION 01: BEST OF GLOBAL PAEDIATRIC ONCOLOGY

14-10-2023 13:10 - 14:10

#### COMPREHENSIVE EVALUATION OF MEDULLOBLASTOMA OUTCOMES IN LMICs: A REPORT FROM 4 COUNTRIES

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**Background and Aims:** Cure rates for medulloblastoma (MB) exceed 70% in high-income countries, where access to timely diagnosis, risk-stratified therapy, and comprehensive supportive care exists. Reports from low- and middle-income countries (LMICs) are scarce but describe lower survival rates. This retrospective study aimed to analyze outcomes for MB in 4 LMICs.

**Methods:** Patients <18 years-of-age with newly diagnosed MB treated between January 2014 and December 2018 were included. Clinical and biological characteristics and their association with outcomes were examined.

**Results:** Overall, 62 patients with a median age of 6.5 years were included. Ten patients (16%) were younger than 3 years and 41 (66%) were male. Forty (65%) patients had more than 4 weeks of symptoms at the time of presentation. Seventeen (31%) patients received a diagnosis more than 4 weeks after the first visit with a physician. Permanent CSF diversion procedure was done in 12 (19%) patients. Where information available ( $n=30$ ), 60% of resections were gross total. Five (8%) patients had post-operative infections. Thirteen (21%) patients had metastatic disease at diagnosis. On pathology reports, histologic subtype was not available in 37 (62%) cases. One (2%) patient had molecular subgroup identified. Radiotherapy was given in 35 (57%) patients. A median of 6 cycles of chemotherapy were given. The 5-year event-free survival was 37%, while the 5-year overall survival was 79%. Seven (11%) patients died, including 4 from disease, 2 from surgical complications, and 1 from infection. Twenty-two (35%) patients had disease relapse, 8 distant and 14 local. Eighteen (29%) patients abandoned treatment.

**Conclusions:** This multi-institutional cohort describes poor outcomes, mainly due to high death and relapse rates and frequent abandonment. Additional patient and family support and expansion of service delivery capacity would improve outcomes. Additional centers are being onboarded on this study to expand the number of included patients.

O241/#1345 | Poster Discussion Session

#### POSTER DISCUSSION 01: BEST OF GLOBAL PAEDIATRIC ONCOLOGY

14-10-2023 13:10 - 14:10

#### A LOW PROPORTION OF CHILDREN WITH SUSPECTED BRAIN TUMORS UNDERGO ACTIVE TREATMENT: A PROSPECTIVE OBSERVATIONAL STUDY IN A LARGE TERTIARY CENTER IN PAKISTAN

Rahat Ul-Ain<sup>1</sup>, Alia Ahmad<sup>1</sup>, Shazia Riaz<sup>1</sup>, Laeeq Ur Rehman<sup>2</sup>, Rabia Aqeel<sup>3</sup>, Mahwish Hussain<sup>4</sup>, Amber Goraya<sup>3</sup>, Samina Zaman<sup>4</sup>,

Mahwish Faizan<sup>1</sup>, Zeena Salman<sup>5</sup>, Naureen Mushtaq<sup>6</sup>, Eric Bouffet<sup>7</sup>  
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**Background and Aims:** Pediatric brain tumors (PBT) are the most common solid tumor in children in high-income countries, but data on their incidence and issues in management in low- and middle-income countries (LMIC) are poorly documented. Existing literature suggests poor survival in LMIC. The objectives of this study were to document the trajectory of PBT patients at a tertiary-care hospital in Pakistan.

**Methods:** This prospective, analytic, cohort study recorded all new cases of PBT (birth to 16 years) that were seen over a 3-month period.

**Results:** A total of 52 new cases of PBT were seen in 3 months. The male-to-female ratio was 1.6:1. Fifty-two percent of tumors were supratentorial, 46% infratentorial, and 2% spinal. The median lag time from the first medical consultation to the first visit to our center was 1 month (0.1-96 months). The most common presenting complaint was headache and vomiting associated with a focal neurological deficit (35%). A background of consanguinity (36.5%) and a family history of brain tumors (11.5%) were frequent. Ten patients (19%) showed evidence of neurocutaneous syndrome. Four patients (8%) underwent VP-shunt, 16 (31%) were discharged without surgery, 8 (15%) expired without surgery, and 1 (2%) expired after surgery. Only 10 patients (19%) underwent surgical excision. The median lag time from presentation to surgery was two months (0.16-96 months). Five patients (10%) were lost to follow-up, and 2 (4%) left against medical advice. Currently, two patients are on palliative radiotherapy, one patient is receiving weekly Vinblastine, two patients are due for surgery, and two are for further investigations.

**Conclusions:** Our data suggest that, following the diagnosis of an intracranial mass through imaging, only a limited number of PBT patients undergo active treatment. The reasons for this attrition are still unclear and require further evaluation. We also observed a high number of patients with suspected underlying cancer predisposition syndromes.

O242/#741 | Poster Discussion Session

POSTER DISCUSSION 01: BEST OF GLOBAL PAEDIATRIC ONCOLOGY

14-10-2023 13:10 - 14:10

## ACUTE LYMPHOBLASTIC LEUKEMIA: RESULTS OF THE RANDOMIZED ALLIC-GATLA 2010 PROTOCOL IN ARGENTINA

Cecilia Riccheri<sup>1</sup>, Sergio Gomez<sup>2</sup>, Sandra Borchichi<sup>1</sup>, Constanza Drozdowski<sup>1</sup>, Monica Makiya<sup>1</sup>, Federico Manni<sup>1</sup>, Lorena Moran<sup>1</sup>, Pedro Negri<sup>1</sup>, Paola Reichel<sup>1</sup>, Loreto Senosiain<sup>1</sup>, Virginia Schuttenberg<sup>1</sup>, Alejandra Deana<sup>1</sup>, Jorgelina Santamaria<sup>1</sup>, Eduardo Dibar<sup>1</sup>

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**Background and Aims:** Background and Aims Acute Lymphoblastic leukemia is the most common cancer in childhood. The Argentine group for treatment of ALL (GATLA) is member of the International- Berlin-Frankfurt-Münster study group, ALLIC-GATLA-2010 is the second I-BFM protocol carried out. The primary objectives were to incorporate measurement of minimal residual disease (MRD) using flow cytometry (FCM) to stratify risk groups, to assess the role of early intensification with augmented-IB schedule and to compare 2gr/m<sup>2</sup> vs 5gr/m<sup>2</sup> methotrexate.(MTX)

**Methods:** This is a prospective, multicenter, interventional study. We included 2.150 patients (pts) <=18 years old. 61 pts (2.9%) were excluded: previous treatment 30, protocol violation 23, death prior to start treatment 3, missing data 5 pts) MRD at day 15th were incorporated to age, WBC, cytogenetics/molecular aberrations, and response to treatment, to define risk groups(RG). Pts were classified: standard (SRG), intermediate (IRG) and high risk (HRG), two randomizations were performed: IB vs augmented-IB in IRG and HRG and 2gr/m<sup>2</sup> vs 5 gr/m<sup>2</sup> MTX in precursor B-ALL in IRG.

**Results:** Complete remission rate was 98.6% (n=2076). (SRG 98.3%; IRG 98.9% HRG 98.0%). 5-year event free survival (EFS± standardized error[SE]) and overall survival (OS ± SE) rates were 70.5±0.7% and 75.6±0.8% respectively. SRG (n = 421), 82.9±1.1% and 88.26±1.4%; IRG, (n=1213), 72.9±1.4% and 79.4±2.2%; and HRG, (n=442), 51.6±0.6% and 53.5±0.9%, respectively. MRD was available 82.2%. With a median time of 5-years, the overall survival rate between IB and augmented IB protocol were 0.81%±0.13 and 0.80%±0.14 respectively, log rank test= 0.76 (NS), accordingly the overall survival of pts receiving MTX doses of 2 g/m<sup>2</sup> and MTX 5 g/m<sup>2</sup> was 0.835%±0.018 vs 0.827%±0.023, log rank 0.969

**Conclusions:** Treatment intensity and randomized intervention were not superior to standard treatment. Most pts were able to have MRD level assessment, pts had a better risk group classification

O243/#1726 | Poster Discussion Session

POSTER DISCUSSION 02: LYMPHOMA OUTCOMES IN L/MIC

14-10-2023 13:10 - 14:10

## COMPARISON OF OUTCOMES OF HODGKIN S LYMPHOMA IN CHILDREN IN TWO DIFFERENT SOCIOECONOMICAL BACKGROUNDS IN ARGENTINA

Cecilia Riccheri<sup>1</sup>, Claudia Ruiz<sup>2</sup>, Sergio Gomez<sup>3</sup>, Gina Gutierrez<sup>1</sup>, Pablo Lagrotta<sup>1</sup>, Cecilia Garbini<sup>1</sup>, Miguela Caniza<sup>4</sup>

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**Background and Aims:** Hodgkin's lymphoma (HL) is the most frequent B cell lymphoma. In High-income-countries, cure rates are +/-90% However in low-middle-income countries progression-free-survival range from 42-90%; reported reasons are advanced disease, delay in diagnosis, poor supportive care, and mostly treatments at public hospitals (PH).The primary objective of this review was to compare the outcomes of HL at a PH and at a private center(PC)

**Methods:** Retrospective-observational study. All patients had lymph node biopsy. PET/CT were performed at diagnosis and after second cycle. According to GATLA-LHP Protocol patients were classified : Group 1: stages I A, IIA, no bulky disease, no B symptoms; Group 2:patients not included in Group 1-3, and Group 3: stages II B, III B, IV A y IV B. Group 1: received ABVDx4 or ABVDx4 if Partial remission (PR) after 2nd cycle + 20 Gy involved field radiotherapy (IFRT). Group 2:ABVDx6 or ABVDx2 if PR+ABVDx4 and 20 Gy IFRT. Group 3: OEPAx 2 and COPDACx4+20 Gy IFRT 20 or OEPAx2 if PR + COPDACx4+25 Gy IFRT.

**Results:** From 9-2012 to 9-2022, 56 patients were admitted, 31 pts were from PH (55.4%) and 25 from PC (44.6%),median age was 13 y. o.(IQR 9-15); Male 62%;. Scleronodular subtype was 95.2%. 73% had PET/CT performed. There were no clinical differences concerning age, sex, B symptoms, histology, stages(I-II vs III-IV) or risk-groups between centers(P=NS); EBV was + in 100% in PH and 29% in PC (P=0.001) At a median time of 60 months the Survival were 95%(SE 0.049) and 100% at PC and PH respectively (log rank 0.37),EFS was 86% (SE 0.076) and 100% at PC and PH respectively. (log rank 0.08). Only three patients relapsed, (5%), two were rescued.

**Conclusions:** Centers did not influence outcomes in HL, results proved to be very excellent on both groups witch current protocols.

O244/#293 | Poster Discussion Session

POSTER DISCUSSION 02: LYMPHOMA OUTCOMES IN L/MIC

14-10-2023 13:10 - 14:10

## RETROSPECTIVE ANALYSIS OF PEDIATRIC PATIENTS WITH BURKITT LYMPHOMA TREATED IN MWANZA, TANZANIA; CHALLENGES AND OPPORTUNITY

Hutton Chapman<sup>1</sup>, Paul Shadrack Ntemi<sup>2</sup>, Heronima Kashaigili<sup>2</sup>, Kristin Schroeder<sup>1</sup>

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**Background and Aims:** Despite years of continued improvement in the outcomes for pediatric Burkitt lymphoma treated in high resource settings, outcomes achieved in LMICs remain incredibly disparate. A long-standing barrier to conducting research addressed at ending this disparity remains the lack of high-quality outcomes data, especially in sub-Saharan Africa. To help address this need at our study site, Bugando Medical Centre (BMC) in Mwanza, Tanzania, we conducted a 5-year retrospective cohort analysis with the goal of better understanding the response rate and outcomes achieved with the current standard of care chemotherapy.

**Methods:** Historical patient data for pediatric patients with BL treated at BMC between 2016 and 2021 were available for analysis via a prior IRB approved study. These patients were all treated per the Tanzania National Guidelines which prescribes 6 cycles of cyclophosphamide, vincristine, and low dose methotrexate (75mg/m2). Relevant patient data were curated in a REDCap database and statistical analysis was performed on aggregated cohort data.

**Results:** 94 patient records were analyzed. Patients were an average age of 7.5 years at presentation and a 2:1 male to female ratio was observed. Most patients, 91.5%, met high risk criteria per the International Network for Cancer Treatment and Research (INCTR) definition. Only 60% of evaluable patients achieved a first CR with front line therapy. The estimated 1-year EFS was 28.6% (95% CI, 19.4-38.4%), including abandonment as an event. The estimated 1-year OS, was 50.2% (95% CI, 38.5-60.9%).

**Conclusions:** Overall, there are poor outcomes for the treatment of pediatric BL at BMC, including a low CR rate to first-line therapy and a low EFS. Despite resource limitations, we hypothesize that these data support increased intensity chemotherapy will be necessary as part of improving outcomes for this disease moving forward. Future research should focus on understanding how to increase treatment intensity for BL in a safe manner in LMICs.

O245/#990 | Poster Discussion Session

POSTER DISCUSSION 02: LYMPHOMA OUTCOMES IN L/MIC

14-10-2023 13:10 - 14:10

## OUTCOMES IN CHILDREN AND ADOLESCENTS DIAGNOSED WITH CLASSICAL HODGKIN LYMPHOMA: EXPERIENCE FROM AMOHP. (MEXICAN ASSOCIATION OF PEDIATRIC ONCOLOGY AND HEMATOLOGY)

Alberto Olaya Vargas<sup>1</sup>, Deyanira Cortes<sup>2</sup>, Manuel Donovan<sup>1</sup>, Eduardo Baños-Rodríguez<sup>3</sup>, Luz Zúñiga Quijano<sup>4</sup>, Julia Colunga Pedraza<sup>5</sup>, Norma Araceli Lopez Facundo<sup>6</sup>, Daniel Ortiz Morales<sup>7</sup>, Lourdes Romero-Rodríguez<sup>8</sup>, Alfonso Reyes<sup>9</sup>, Adriana Sandoval<sup>10,11</sup>, Francisco Pantoja Guillen<sup>12</sup>, Victor Cabrera Garcia<sup>13</sup>, Selene Portillo<sup>14</sup>, Felix Gaytan<sup>9</sup>, Ana Vera Rodriguez<sup>15</sup>, Ricardo Gomez Martinez<sup>16</sup>, Nadia Mendez Alud<sup>17</sup>, Enrique Lopez Aguilar<sup>18</sup>, Liliana Velasco<sup>19</sup>

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**Background and Aims:** HL accounts for 6% of childhood cancers; its incidence is age-related and is highest among adolescents. Adolescents with cancer are a vulnerable group mainly due to psychosocial challenges and a lack of health insurance, a major presenting problem in Mexico. With approximately 90% to 95% of children with HL being cured, a higher incidence of complications (i.e., secondary cancers, endocrine disruption) has presented within long-term survivors. Its excellent prognosis reported in developed countries highlights that HL should be measured to assess pediatric cancer care quality in the Mexican healthcare system. This multicenter study aims to analyze the clinical and biological characteristics, toxicity, and outcomes of HL-diagnosed children in Mexico.

**Methods:** We conducted a retrospective multicenter study of patients aged  $\leq 18$  years, diagnosed with HL at 16 participating Centers in Mexico from January 2008 to December 2017.

**Results:** There was a total of 309 children with a mean age of 11 (range, 2 to 18 years) and a male to female ration of 1.9 to 1. Among partici-

pants, 70% presented with advanced-stage (stages IIB, III, IV) disease, 59% experienced B-symptoms, and 57% had nodular sclerosis type of HL. Multiagent chemotherapy was the mainstay of treatment. The 5-year overall survival (OS) was 91%. Based on age at diagnosis, the outcomes for 5-year were 94% for ages  $\leq 13$  years versus 88% for ages 13 to 18 years ( $p = 0.209$ ).

**Conclusions:** Results obtained from this study demonstrate an improvement in outcomes of young patients diagnosed with HL in Mexico compared with previous reports with an OS of 74.5%. However, the results continue to not be optimal, especially in adolescent demographics. There is a need to establish an academic collaboration to form strategies aiming to improve pediatric cancer care based on resources, especially in diseases with expected excellent prognosis.

O246/#1894 | Poster Discussion Session

### POSTER DISCUSSION 02: LYMPHOMA OUTCOMES IN L/MIC

14-10-2023 13:10 - 14:10

#### SURVIVAL OF PATIENTS WITH BURKITT'S LYMPHOMA (BL) AND TREATED ACCORDING TO THE GFAOP LMB09 PROTOCOL, IN THE PEDIATRIC ONCOLOGY DEPARTMENT OF CHU-YO IN BURKINA FASO

Viviane Bissyande<sup>1</sup>, Chantal Bouda<sup>1</sup>, Rolande Kabore<sup>1</sup>, Sandrine Kaboret<sup>1</sup>, Brenda Mallon<sup>2</sup>, Sonia Kaboret<sup>3</sup>, Caroline Yonaba<sup>1</sup>, Aimée Kissou<sup>4</sup>, Fla Koueta<sup>1</sup>, Catherine Patte<sup>2</sup>

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**Background and Aims:** GFAOP LMB09 protocol for BL treatment was evaluated and published in 2019. This observational study was conducted from 2009 to 2015 in 7 units including the pediatric oncology of the CHU-YO. These recommendations continued for another 5 years. We studied the survival of patients with BL, treated according to this protocol following its publication.

**Methods:** This retrospective study included patients  $<15$ y with confirmed BL, treated according to the GFAOP LMB09 protocol from September 2015 to December 2020. Kaplan-Meier method was used to estimate patient survival with a 95% confidence interval. OS was estimated from the date of diagnosis to the date of last news or death.

**Results:** In this period, 190 patients were included in the study. The median age was 8 years. There was a male predominance (sex ratio = 2.2). The diagnosis of BL was made by cytology (91.6%), by histology (5.8%) and both in 2.9%. Stage was according to Murphy classification: 1, stage I; 31, stages II including 27 Bulky, 81 stages III and 77 stages

IV including 56 with bone marrow involvement (45, <25% blasts; 9, between 25 and 70%; and 2, >70%). Patients who completed the full protocol represented 60%. The overall death rate was 9.5% (with 4.2% toxic deaths) and the abandonment rate was 26.3%. For all patients, the overall survival rate at 24 months was 59% and the Event (including abandonment)-free survival, 48%. OS of patients who received the second induction course before 35 days was 65% vs 43% for those who received it after 35 days ( $p=0.01$ ).

**Conclusions:** Compared with the first publication on GFA LMB09 protocol, OS was stable, although toxic death rate decreased, but abandonment rate was higher. Abandonment remains a huge challenge for the management of these patients.

O247/#761 | Poster Discussion Session

## POSTER DISCUSSION 02: LYMPHOMA OUTCOMES IN L/MIC

14-10-2023 13:10 - 14:10

### HODGKIN LYMPHOMA IN CHILDREN: A 16-YEAR EXPERIENCE AT THE CHILDREN'S WELFARE TEACHING HOSPITAL OF BAGHDAD, IRAQ

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**Background and Aims:** Hodgkin lymphoma (HL) is one of the most curable pediatric cancer, with long-term survival rates now exceeding 90%. Treatment is modulated according to the risk group, and, in particular, the reduction/omission of radiotherapy (RT) is made according to the early/late response. The aim of this study is to evaluate the results in children with HL treated at Children's Welfare Teaching Hospital (CWTH) in Baghdad over 16 years.

**Methods:** The diagnosis was based on a histopathological examination of a biopsy of an involved node/tissue. At admission, history (including B symptoms), physical examination, blood chemistry, chest X-ray, peripheral node-abdominal sonography, chest-CT scan, bone marrow

biopsy (stage III, IV, B symptoms), and cardiac functions were obtained. Therapy consisted of 4-8 COPP/ABV (in case of Dacarbazine unavailability) or ABVD cycles for most children. The response was evaluated with the same diagnostic techniques during and at the end of therapy. RT was not available.

**Results:** From December 2003 to November 2019, 305 children aged < 15 years (median age 7.8 years; range 1-14), were diagnosed and treated at the CWTH. Two-hundred eighty-nine (95%) are evaluable for the analysis (11 refused treatment; 4 misdiagnosed as non-Hodgkin's lymphoma and one as Langerhans cell histiocytosis). Among them, 207 (72%) were male, 189 (65%) presented with advanced-stage (IIB-IV) disease, 144 (50%) had B symptoms and 173 (60%) had mixed cellularity type. Treatment consisted of COPP/ABV (87 cases), ABVD (185 cases), and other regimens (17 cases). With a median follow-up of 5.4 years, the 5-year estimated overall survival (OS) is 92% for the entire population; 88% for COPP/ABV, and 95.7% for the ABVD group.

**Conclusions:** In our 16-year experience, more than 90% of children having HL, survived, in spite of the numerous limitations in diagnostic procedures, chemotherapy shortage, no radiotherapy facilities, absence of effective second-line treatments, and finally therapy abandonment for social and financial reasons.

O248/#87 | Nursing

## NURSING: QUALITY IMPROVEMENT AND RESEARCH ABSTRACT PRESENTATIONS

14-10-2023 13:10 - 14:10

### NATIONWIDE QUALITY IMPROVEMENT INITIATIVE BASED ON CHILDRENS VIEWS ABOUT CANCER SERVICES

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**Background and Aims:** NHS England (NHSE) committed to developing a bespoke survey to capture the views of children's experience of cancer care. The first Under 16 Cancer Patient Experience survey (U16 CPES) was run in 2019, with the survey results enabling identification of areas for improvement across England. Results of the first survey were used to inform the focus of the Cancer Experience of Care Improvement Collaborative (CIC), a structured quality improvement initiative. This session will share the development of the U16 survey and the first CIC to focus on children.

**Methods:** CYP and their parents, clinicians, commissioners, and charities came together with Picker Institute to develop the survey. The

U16 CPES is designed for, and tested with, children aged 0-15 years and their parents/caregivers. Using quantitative and qualitative findings derived from the 2021 U16 CPES, key themes were identified for the CIC. The CIC, led by NHSE, upskilled teams in Principal Treatment Centres (PTCs) in Quality Improvement (QI) methodology to facilitate service improvement based on nationally identified themes. Lived experience partners (LEPs) were core members of PTC project teams. Progress was monitored and evaluated using various project management tools and site visits.

**Results:** Eight PTCs benefitted from each upskilling a team in QI methodology and they developed a wide-range of projects. The value of including LEPs in QI is recognised and this learning will carry forward. The value of QI Teams networking for peer learning support and critique is recognised.

**Conclusions:** Service improvement must be grounded in listening to those who use the service. Age should not be a barrier to gaining meaningful service user feedback and this world first, nationwide, QI programme is evidence the views of children as young as 7 can play an important role in service improvement. LEPs add value and must be involved in co-creation of improvement work.

O249/#1006 | Nursing

#### NURSING: QUALITY IMPROVEMENT AND RESEARCH ABSTRACT PRESENTATIONS

14-10-2023 13:10 - 14:10

##### "IT JUST MADE ME FEEL BETTER": PERCEPTIONS OF THE NOVEL TEENS4TEENS VIRTUAL PSYCHOSOCIAL SUPPORT PROGRAM FOR TEENAGERS WITH CANCER DURING COVID-19 AND BEYOND

Alicia Kilfoy<sup>1,2</sup>, Chana Korenblum<sup>3,4,5</sup>, Sarah Alexander<sup>6,7</sup>, Elham Hashemi<sup>1</sup>, Prabdeep Panesar<sup>1</sup>, Tatenda Masama<sup>1</sup>, Myra Pereira<sup>1</sup>, William Liu<sup>1</sup>, Lindsay Jibb<sup>1,2</sup>

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**Background and Aims:** Cancer in adolescence is characterized by unique and often profound psychosocial disruptions including peer isolation, loss of independence, academic consequences, and body image concerns, which have been magnified during the COVID-19 pandemic. To address these issues, a novel, virtual, weekly psychoeducational and peer support group named Teens4Teens was developed. This study

aimed to assess the feasibility, acceptability, and impact of the program from the viewpoint of adolescents, program guest speakers and moderators.

**Methods:** Audio-recorded interviews were conducted with participants using a semi-structured interview guide. Interviews were conducted until data saturation, transcribed, coded in duplicate and analyzed using an inductive thematic approach.

**Results:** Twenty-one participants were interviewed for this study; eight female-identifying adolescents who ranged in age from 15-19 years with varying cancer diagnoses and stages and 13 guest speakers or moderators who were clinicians or survivors. We identified 4 themes, each with several subthemes: (1) Being an adolescent with cancer (loss of control, lack of teen-specific cancer care resources), (2) Teens4Teens program implementation feasibility (high acceptability of the program, recurring adolescent attendance, no technological issues, program day and timing approval, creating a safe space for adolescents, and challenges integrating the experiences of adolescents in different phases of their cancer trajectory into the program), (3) The perceived positive impact of Teens4Teens (adolescent psychosocial health improvement, adolescent disease self-management and clinician professional development), (4) Suggestions to enhance program utility (creating a hybrid in-person-virtual version, bolstering male recruitment and expanding the program to other hospitals across the country).

**Conclusions:** Teens4Teens was a widely endorsed and feasible intervention to support the psychosocial health of adolescents with cancer. The insights of key program stakeholders will be used as the basis of future Teens4Teens iterations and may provide guidance for the development of other psychosocial care interventions for adolescents with cancer.

O250/#1018 | Nursing

#### NURSING: QUALITY IMPROVEMENT AND RESEARCH ABSTRACT PRESENTATIONS

14-10-2023 13:10 - 14:10

##### EVALUATION OF THE IMPROVING CHILDREN'S ONCOLOGY-HEMATOLOGY NURSING (ICON) PROCESS BY THE RESEARCHERS AND THE PARTICIPANTS

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**Background and Aims:** The ICON project is a country-specific novel approach to design strategies for Improving Children's Oncology-Hematology Nursing. The first ICON project was launched in Brazil in February 2022 in collaboration with the local alliance group. This pilot of ICON initiative carried a myriad of opportunities for refining the approach for effective partnership with local nursing workforce. This study aims to evaluate the ICON process in Brazil from both the researchers' and the participants' perspectives.

**Methods:** We utilized a mixed-methods approach to gather data from two perspectives. We used a qualitative descriptive design to explore the researchers' perspectives and conducted a thematic analysis of the research team's meeting minutes. We used a quantitative cross-sectional descriptive survey to obtain participants' input on the content and delivery of the ICON findings. We collected data from the participants' evaluation survey filled during the two-day ICON workshop held in Brazil in September 2022. We analyzed data using descriptive statistics. We triangulated the results of both study arms to identify areas for refining ICON process.

**Results:** From the researchers' perspective, 31 meeting minutes were analyzed and revealed two emerging themes. The ICON process carried many implementation challenges. Simultaneously, this initiative facilitated personal growth and global exposure. From the participants' perspectives, 26 participants attended the ICON workshop, respectively, 92% and 65% completed the evaluation on the first and second day. More than 75% found the research findings easy or very easy to understand. They all highly rated the interactive activities used to define the gaps, goals, and measures. Participants shared suggestions for enhancing the workshop's logistics and content.

**Conclusions:** The ICON project is a promising approach for global pediatric oncology nursing. The pilot in Brazil revealed ways for ensuring smooth implementation. The combination of researchers' and participants' feedback provided a comprehensive evaluation and helped refining the process.

O251/#2383 | Nursing

#### NURSING: QUALITY IMPROVEMENT AND RESEARCH ABSTRACT PRESENTATIONS

14-10-2023 13:10 - 14:10

#### CLOSING REMARKS

O252/#1350 | Poster Discussion Session

#### POSTER DISCUSSION 03: IDENTIFYING AND REDUCING DISTRESS

14-10-2023 13:10 - 14:10

#### FEASIBILITY AND ACCEPTABILITY OF A STRUCTURED ACTIVE PLAY INTERVENTION FOR PRESCHOOLERS DIAGNOSED WITH CANCER: A STUDY BASED ON DATA FROM THE REPLAY TRIAL

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**Background and Aims:** Rehabilitation including structured active play for preschoolers (1-5 years) with cancer (RePlay), is a randomized controlled trial of physical activity as structured active play versus usual care. Since there is limited knowledge of children's and parents' willingness and ability to partake in structured active play, we aim to explore the feasibility of the study design.

**Methods:** Feasibility was assessed in the first 30 recruited children with cancer (1-5 years). Feasibility domains used were acceptability (percentage of eligible children accepting participation), attrition (percentage of children dropping out), completion (percentage of children completing the Peabody Developmental Motor Scales-2 (PDMS-2) (primary outcome) at 6 months (primary end-point)), and intervention adherence (percentage of structured active play sessions the children participated in during admission). Parents evaluated the intervention through a survey.

**Results:** The acceptance was 91% (30 of 33 eligible children were included), hereof 15 were randomized to the intervention group. None dropped out, but one died during the intervention period, resulting in an attrition rate of 3%. The completion rate of the PDMS-2 was 77% (23 of 30). Reasons for non-completion were health-related(n=2), logistic failure(n=2), mood/motivation(n=1), concentration(n=1), and death(n=1). During admission, adherence to the intervention was a median of 50% [80% range: 28-82%]. The main reasons for decreased adherence to sessions were treatment procedures(21%), treatment-related side effects(14%), and naps(3%). Eighty percent of parents in the intervention group answered the survey, 92% thought RePlay was relevant/very relevant for themselves and their child, and 75% stated that the intervention motorically challenged their child. The length of the intervention was considered appropriate by 83%.

**Conclusions:** The acceptable adherence rate and high completion rate of outcome measures indicate a feasible intervention design for preschool children hospitalized with cancer. The intervention had high relevance among the parents, which was ultimately reflected by a high acceptance.

O253/#473 | Poster Discussion Session

## POSTER DISCUSSION 03: IDENTIFYING AND REDUCING DISTRESS

14-10-2023 13:10 - 14:10

## REDUCING PROCEDURAL PAIN IN PEDIATRIC ONCOLOGY: ACQUISITION OF HYPNOTIC COMMUNICATION SKILLS FOLLOWING REL@X TRAINING

Margot Bedu<sup>1,2</sup>, David Ogez<sup>1</sup>, Anne-Frédérique Tessier<sup>2</sup>, Jennifer Aramideh<sup>1</sup>, Claude-Julie Bourque<sup>3</sup>, Christian Dagenais<sup>2</sup>, Michel Duval<sup>3</sup>, Andréa Laizner<sup>4</sup>, Sylvie Le May<sup>5</sup>, Ariane Levesque<sup>1</sup>, Ahmed Moussa<sup>3</sup>, Argerie Tsimicalis<sup>6</sup>, Émélie Rondeau<sup>1</sup>, Serge Sultan<sup>1</sup>

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**Background and Aims:** Children with cancer typically undergo repeated painful procedures. Hypnotic communication techniques can help reduce procedural pain and distress. Healthcare professionals can be trained to use these techniques with a manualised intervention called Rel@x. The current study aims to systematically evaluate the acquisition of objective skills by nurses following training in hypnotic communication.

**Methods:** Fifty-eight participants (54 nurses and 4 physicians, aged 39 ± 10 years) followed the Rel@x training (PMID: 36389009). Participants were evaluated using a video-recorded simulation of a venous puncture before, after training, and 3-month later. We selected five speech markers to evaluate changes over time: time-related effects (e.g., speech rate), lexical fields (e.g., medical terminology), language complexity, suggested affective experience (e.g., positive or negative), and questioning format (e.g., open-ended questions). Using full transcripts from the professional-patient interactions during simulations, we statistically describe speech indices in verbal material used by the professional. Comparisons across time-points are performed using linear mixed models.

**Results:** Preliminary results on a subset of ten professionals point to medium-large differences with pre-post increases in hypnotic communication specific lexicons ( $d=1.21$ ) and positive affective experience ( $d=0.79$ ), and pre-follow-up decreases in medical lexicon ( $d = 1.01$ ), and negative affective experience (Cohen's  $d = 0.68$ ). Moderators (e.g. seniority, age) of effect are being analysed.

**Conclusions:** We found strong support for the Rel@x training, as trainees use hypnotic communication techniques after training and at follow-up. These favorable results support future trials on the clinical impact of the training.

O254/#1311 | Poster Discussion Session

## POSTER DISCUSSION 03: IDENTIFYING AND REDUCING DISTRESS

14-10-2023 13:10 - 14:10

## IMPROVING PALLIATIVE CARE AND END-OF-LIFE COMMUNICATION WITH ADOLESCENTS AND YOUNG ADULTS WITH CANCER: AN INTERNATIONAL EXAMINATION OF CLINICAL GAPS AND TRAINING NEEDS

Ursula Sansom-Daly<sup>1,2,3</sup>, Holly Evans<sup>1,2</sup>, Lori Wiener<sup>4</sup>, Anne-Sophie Darlington<sup>5</sup>, Hanneke Poort<sup>6</sup>, Abby Rosenberg<sup>7,8,9</sup>, Meaghann Weaver<sup>10</sup>, Antoinette Anazodo<sup>2</sup>, Jennifer Mack<sup>11</sup>, Fiona Schulte<sup>12,13,14</sup>, Celeste Phillips<sup>15</sup>, Karen Wernli<sup>16</sup>, Ruwanthie Fernando<sup>17</sup>, Toni Lindsay<sup>18</sup>, Louise Sue<sup>19</sup>, Maria Cable<sup>20</sup>, Claire Wakefield<sup>1</sup>, The Global Adolescent And Young Adult Cancer Accord End-Of-Life Study Group<sup>1</sup>

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**Background and Aims:** For adolescents and young adults (AYAs) with uncertain cancer prognoses, equitable and inclusive access to age-

appropriate palliative care and end-of-life communication is critical. However, data suggests this quality of care is not widely implemented. The Global AYA Cancer Accord End-of-Life Study examined health-professionals' perspectives on barriers to this communication, to inform training for health-professionals to effectively support it. With health-professionals from Australia, New Zealand (NZ), and the United Kingdom (UK), and United States (USA), we aimed to: 1) examine perceived barriers to end-of-life communication and 2) determine the training needs of health-professionals.

**Methods:** Stage 1 involved a cross-sectional survey of barriers to end-of-life communication among Australian, NZ and UK health-professionals. Stage 2 used a two-round Delphi survey establishing (i) content needed in training, and (ii) preferred training models internationally.

**Results:** Stage 1 included 105 health-professionals from Australia/NZ/UK. Our sample included 23% oncologists/haematologists, 33% nursing professionals, 28% allied-health professionals and 16% palliative care physicians, with 16 years' clinical experience on average (range 1-43, SD=9.5). Sixty six percent of health-professionals indicated that the greatest barrier to palliative care conversations was not knowing how to introduce the topic. In Stage 2, 77 health-professionals from Australia, NZ, UK and USA identified that structured training programs (28.6% endorsing a mode of 8 out of 10) and learning from bereaved family members (27.3% endorsing mode of 10/10) were the preferred training models to upskill in this area. Timing (37.7% endorsing mode of 9/10) and family processes (36.4% endorsing mode of 8/10) were suggested to be the most important topics for training.

**Conclusions:** Health-professionals identified communication skills as a key barrier to delivering gold-standard end-of-life care with AYAs. Our data identifying health-professionals' training modality and topic preferences will directly contribute to developing sustainable training resources to underpin quality care for all AYAs with cancer.

O255/#948 | Poster Discussion Session

### POSTER DISCUSSION 03: IDENTIFYING AND REDUCING DISTRESS

14-10-2023 13:10 - 14:10

#### ADDRESSING NEEDLE-BASED PROCEDURAL PAIN FOR CHILDREN WITH CANCER IN LOW- AND MIDDLE-INCOME COUNTRIES

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**Background and Aims:** Children with cancer experience significant pain and anxiety from needle-based procedures. Undertreated pain in children has long-lasting consequences and reduces the efficacy of subsequent analgesic efforts. A validated quality improvement (QI) intervention known as the "Children's Comfort Promise" includes 1) topical anesthetics, 2) sucrose or breastfeeding for infants, 3) comfort positioning, and 4) distraction techniques, and is effective in addressing procedural pain in children. However, there is limited data about these interventions in low- and middle-income countries (LMICs).

**Methods:** A pilot project of the "Global Comfort Promise" was implemented in 4 global sites (Lima, Peru, Barretos, Brazil, Pietermaritzburg, South Africa, and Manila, Philippines.). Between August 2021 and December 2022, the pilot sites identified a specific aim, designed the measurement strategy, adapted, and implemented the project at their individual sites.

**Results:** A total of 2,185 different procedures were recorded. Most patients were less than 10 years old (60.5%) and solid tumors (37.9%) were the most common diagnosis. Healthcare professionals (98.3%) were satisfied overall with the procedures. Parents and patients reported that only 33.7% of patients experienced pain during the procedure. All (100%) parents and patients felt the healthcare teams adequately addressed their child's pain. Median self-reported adherence to  $\geq 2$  interventions was 98.0%. Challenges to implementation of the QI initiative included lack of training, turnover of the medical staff, maintaining staff enthusiasm, and inconsistent access to topical anesthetics. Each site had unique change ideas to implement the initiative.

**Conclusions:** This multi-site, multi-country QI initiative was feasible and successfully adapted to the LMIC context to improve procedural pain in children. Additionally, this intervention resulted in high satisfaction of both the healthcare professionals and patients/families. Further work is needed to overcome challenges of topical anesthetic access, and education of the workforce. Additional plans, include expansion to additional sites and further refinement of the implementation strategy.

O256/#277 | Poster Discussion Session

### POSTER DISCUSSION 04: NOVEL THERAPEUTICS AND TARGETS

14-10-2023 13:10 - 14:10



## PHASE-2 FIRST-IN-INDIA INDUSTRY STUDY OF VARNIMCABTAGENE AUTOLEUCEL (IMN-003A) IN RELAPSED REFRACTORY B CELL MALIGNANCIES: B-ALL PEDIATRIC SUBANALYSIS (IMAGINE STUDY)

Sunil Bhat<sup>1</sup>, Raja Thirumalairaj<sup>2</sup>, Revathi Raj<sup>2</sup>, Pooja Mallya<sup>3</sup>, Ravi Joshi<sup>3</sup>, Sudarshan Chougule<sup>4</sup>, Deepak Mb<sup>4</sup>, Sudeshna Dhar<sup>5</sup>, Arun Kumar Mg<sup>5</sup>, Jeetendra Kumar<sup>5</sup>, Sunil Yadav<sup>6</sup>, Pallavi Arasu<sup>6</sup>, Sri Ramulu Elluru<sup>6</sup>, Mohammed Manzoor Akheel<sup>6</sup>, Rahul Nahar<sup>5</sup>, Anil Kamat<sup>6</sup>

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**Background and Aims:** Varnimcabtagene autoleucel(IMN-003A) is an autologous CD19-directed CAR-T with murine A3B1-binder, manufactured in India for phase-2 study in patients with relapsed/refractory B-cell malignancies(CTRI/2022/03/041162). Target dose (B-ALL:  $1 \times 10^6$  CAR+cells/kg) was infused as 3-fractions(10%,30%,60%) after Fludarabine-Cyclophosphamide lymphodepletion. This is B-ALL paediatric subanalysis. Primary objectives were safety and overall-response-rate(ORR:CR+CRi; NCCN) at Day+90.

**Methods:** Patients  $\geq 3$ -45years with relapsed/refractory B-ALL, detectable MRD and ECOG 0-1 were eligible. IMN-003A persistence was evaluated by ddPCR. Manufacturing was in CliniMACS Prodigy.

**Results:** Of 23-patients in study, 8-patients with B-ALL(median-8years,range3-14) underwent apheresis with 100%manufacturing success(median time 11.5days; range10-15). Mean%transduction was 39.1%(range23.50-52.58) with median transgene copies/genome of 3.04(range1.63-3.59). Mean CD4/CD8ratio was 0.38(apheresis);0.91(final product-FP);1.84(Day-0) and 0.82(Day+90) with reversal post-infusion. Mean proportion of naïve cells(CCR7+RA+) was  $>50\%$  in FP. Median Product-Doubling-Time was 1.04days(range0.83-4.20) and Apheresis-to-Infusion-Time was 20days(range16-22). Maximum IMN-003A expansion(Tmax) was at median10days(range 10-14) with median Cmax 191,718CAR-copies/ $\mu\text{g}$  gDNA(range113,658-413,968). IMN-003A persistence was 80% at Day+28 and 50% at Day+90(range 21-NR) with concurrent B-cell-aplasia(range42-NR). CD4+Tcell count recovery( $>200/\mu\text{L}$ ) was seen at median 10days(range4-NR) post-infusion. Of 7-patients infused, 4(57.1%) needed bridging-therapy. Median follow-up was 210 days(range12-310). Overall-response-rate(ORR) was 85.7%(6/7;MRDneg 77.8%(5/7)) at Day+28 and 80%(4/5;MRDneg 80%(4/5)) at Day+90. Median time-to-first-response was 28days. Median progression-free-survival(PFS) and overall-survival(OS) were not reached. AESIs reported were Cytokine-Release-Syndrome

CRS(Grade [G] 1 57.1%;G3+ 14.3%;overall 71.4%); Immune-Effector-Cell-Associated-Neurotoxicity-Syndrome ICANS(G1 14.3%;G3+ 0%;overall 14.3%); hypogammaglobulinemia(5/7, 4 received IVIg); cytopenia(G3+ 85.7%). CRS median onset was Day+6 and duration 3 days. No Grade3+ ICANS was reported. Tocilizumab usage was in 42.9% patients (majority for persistent Grade-1 CRS). Treatment related mortality was one patient(n=1/7;CRS).

**Conclusions:** This First-In-India Industry study (IMAGINE) for varnimcabtagene autoleucel(IMN-003A) in B-ALL has demonstrated 100% manufacturing success with excellent safety and efficacy outcomes and durable responses including absence of severe neurotoxicity. This offers a significant benefit for patients in India.

O257/#1761 | Poster Discussion Session

### POSTER DISCUSSION 04: NOVEL THERAPEUTICS AND TARGETS

14-10-2023 13:10 - 14:10

#### A NOVEL ANTI-CANCER VACCINE APPROACH FOR THE EFFECTIVE TREATMENT OF REFRACTORY LEUKEMIA IN CHILDREN

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**Background and Aims:** Relapse-related morbidity and mortality are the most devastating consequences of childhood leukemia. Hence, novel therapeutic approaches and innovative multicenter clinical trials are urgently needed for these children. Most cancer cells generate mutant proteins that are unique and not expressed in normal healthy cells. These distinct molecules, known as neoantigens, may allow the generation of highly efficient immune activation and anti-cancer vaccines for these patients. In this set of studies, we show that using applicable bioinformatics and molecular modelling tools relevant synthetic mutant peptides can be generated to stimulate the expansion of tumour-specific T-cell populations leading to safe and effective anti-leukemic activity.

**Methods:** Mutational analyses of pediatric leukemia samples to identify actionable variants were carried out using PedcBioPortal. The protein sequences identified were further refined for HLA binding affinity, proteasome processing and TAP binding capacity using the bioinformatics programs NetMHCpan 4.0, SYPEITHI, and NetCTL1.2. The high-affinity peptides were then synthesized and tested in vitro for T-cell activation against leukemia cells as targets, using ELISpot assays for interferon- $\gamma$  release.

**Results:** In contrast to previous studies using personalized sequence data, this study investigated public neoantigens shared among high-risk pediatric leukemia patients using a large database approach. The proportion of subjects covered by the top three missense variant genes, NRAS, KRAS and FLT3 were 18%, 11% and 5%, respectively. A combination of selected neoantigen peptides showed a statistically significant increase in the number of spots in ELISpot assays, compared to no-peptide treatment controls, indicating the potential of such peptides as anti-cancer vaccines. We describe the findings in detail including the methodology to generate neoantigen vaccine peptides and their validation.

**Conclusions:** Results obtained in this study provide the critical initial groundwork for future studies to evaluate the efficacy of the neoantigen peptides, particularly in combination with other immune therapies for refractory pediatric leukemia.

O258/#911 | Poster Discussion Session

#### POSTER DISCUSSION 04: NOVEL THERAPEUTICS AND TARGETS

14-10-2023 13:10 - 14:10

##### CLAUDIN 6 AS A NOVEL IMMUNOTHERAPEUTIC TARGET FOR CHIMERIC ANTIGEN RECEPTOR (CAR)-T CELLS IN THE TREATMENT OF PEDIATRIC SOLID TUMORS

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**Background and Aims:** Chimeric antigen receptor (CAR)-T cells directed against the oncofetal tumor antigen claudin 6 (CLDN6) have shown preliminary efficacy against CLDN6+ tumors as monotherapy or in combination with a CLDN6-encoding CAR-T cell-amplifying RNA vaccine (CARVac) in a Phase I trial (NCT04503278; Mackensen 2022 ESMO abstract LBA38). While CLDN6 expression has been well characterized in adults, data in pediatric tumors and healthy tissues are limited. First, we will present a large comprehensive analysis of CLDN6 expression in pediatric ( $\leq 18$  years) tumors (n=536) and healthy tissues (n=153). Second, atypical teratoid/rhabdoid tumor (ATRT) and chor-

doma xenograft mouse models have been developed to assess efficacy of CLDN6-CAR-T cells (Madsen 2022 SNO abstract EXTH-85), and we will show novel data on antitumor activity and CLDN6 expression.

**Methods:** Immunohistochemical analysis of membranous CLDN6 expression was performed using CLAUDENTIFY and assessed by two board-certified pathologists using an intensity score from 0 (negative) to 3+ (strong). Positivity was defined as  $\geq 50\%$  of tumor cells displaying weak (1+) to strong (3+) staining. For in vivo analysis, mice bearing orthotopic tumors received CLDN6 or control CAR-T cells Q4D. Bioluminescence imaging was used to measure tumor burden.

**Results:** CLDN6 expression was absent in 147/153 healthy samples (96%), and faint expression (1+) was detected in single cells from 6/153 samples (4%). Strong CLDN6 expression was observed in tumor samples, with 100% testicular, 67% ovarian, 42% liver, and 22% kidney tumors being CLDN6+. When analyzing by tumor type, 65% germ cell, 25% malignant rhabdoid, 25% neuroblastoma, 18% ATRTs, and other rare tumors were CLDN6+. In xenograft models, CLDN6-CAR-T cells induced tumor regression resulting in increased survival. Immunohistochemical analysis is ongoing.

**Conclusions:** CLDN6 is expressed across several pediatric tumors with limited expression in normal tissue. CLDN6-CAR-T cell treatment ( $\pm$ CARVac) could be feasible for CLDN6+ pediatric tumors, especially in the relapsed/refractory setting.

O259/#189 | Poster Discussion Session

#### POSTER DISCUSSION 04: NOVEL THERAPEUTICS AND TARGETS

14-10-2023 13:10 - 14:10

##### DEVELOPMENT OF A NOVEL CELLULAR IMMUNOTHERAPY FOR NEUROBLASTOMA USING ANTI-GD2 ANTIBODY-PRODUCING MESENCHYMAL STEM CELLS

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**Background and Aims:** High-risk neuroblastoma (NB) remains a clinical challenge with the 5-year survival rate still less than 50%, despite the development of various treatment modalities. Our research group developed engineered mesenchymal stem cells (MSCs) secreting anti-GD2 antibodies (anti-GD2-MSCs) as a novel therapeutic approach, focusing on the characteristics of MSCs that aggregate to tumors in vivo, and verified their anti-tumor effects.

**Methods:** We generated an anti-GD2 antibody construct (14.G2a-Fcx2-GFP) incorporating FLAG-tagged single-chain fragment variable against GD2 fused to a linker sequence, a fragment of the constant portion of IgG, and GFP protein. The construct was lentivirally introduced into mMSCs. The secretion and binding capacity of antibodies were verified by Western Blotting and flow cytometry. Antibody dependent cellular cytotoxicity (ADCC) activity was evaluated by co-culturing of NB cell lines and human NK cells with or without the antibodies. A syngeneic mouse model was established by subcutaneous transplantation of tumor tissue fragments from TH-MYCN transgenic mice. The homing effect of anti-GD2-MSCs was verified by an in vivo imaging system. The syngeneic model was divided into three groups injected with anti-GD2-MSCs containing IL-2, IL-2, and PBS. Natural killer (NK) cells in tumor tissue were counted after treatment.

**Results:** Antibodies were secreted into the culture supernatant of anti-GD2-MSCs, and these molecules efficiently bound to NB cells. The ADCC assay revealed a significant increase in the cytotoxic activity of NK cells against NB cells following the addition of antibodies secreted by anti-GD2-MSCs. Anti-GD2-MSCs showed homing effects in syngeneic models. The growth rate of subcutaneous tumors was significantly suppressed by anti-GD2-MSCs with IL-2 ( $p < 0.05$ ). Subcutaneous tumor immunostaining showed an increased NK cell infiltration in the same group ( $p < 0.01$ ).

**Conclusions:** Anti-GD2-MSCs based cellular immunotherapy has the potential to be a novel therapeutic option for intractable NB.

O260/#777 | Poster Discussion Session

#### POSTER DISCUSSION 05: STEM CELL TRANSPLANTATION

14-10-2023 13:10 - 14:10

##### STEM CELL MOBILIZATION WITH PEGFILGRASTIM IN PEDIATRIC PATIENTS FOR AUTOLOGOUS INFUSION: SAFE AND EFFECTIVE

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**Background and Aims:** Worldwide, filgrastim is used for stem cell mobilization in pediatric oncology patients. Few data is available using PEGfilgrastim in this population for successful stem cell mobilization, whilst the single administration of PEGfilgrastim is a lot more patient friendly. Here we describe our single center experience with PEGfilgrastim for stem cell mobilization across different oncological diagnoses.

**Methods:** Data of 149 mobilizations with PEGfilgrastim and subsequent engraftment data of 95 autologous stem cell transplantations were retrospectively analyzed from January 2019 until December 2022. PEGfilgrastim (dose 150 mcg/kg) was administered >24<48 hours after completion of chemotherapy.

**Results:** Median mobilization time -from PEGfilgrastim administration until stem cell apheresis- was 8 (range 3-18) days. In 71 of 149 mobilizations (48%), filgrastim had to be added to achieve a sufficient number of CD34+ cells to obtain the intended yield. Filgrastim was administered for median 3 (range 1-8) days. 11 of these 71 mobilizations required additional Plerixafor, median 2 doses (range 1-4 doses). In 134 mobilizations (= 90%) the intended yield was collected in one apheresis procedure. Result of mobilization was median 87.4 (range 9.4-1069) CD34+ cells per microliter. PEGfilgrastim was well tolerated, no side effects nor toxicity was seen. Neutrophil engraftment was median 11 (range 5-15) days, platelet engraftment was median 15 (0-59) days.

**Conclusions:** PEGfilgrastim for stem cell mobilization was successful in all cases in our cohort. Nevertheless a substantial number of patients needed additional Filgrastim and/or Plerixafor. Therefore the protocol has been adjusted by increasing the dose of PEGfilgrastim (up to max. 250 mcg/kg) for certain patients. Engraftment of stem cells obtained after mobilization with PEGfilgrastim was within normal range.

O261/#1091 | Poster Discussion Session

#### POSTER DISCUSSION 05: STEM CELL TRANSPLANTATION

14-10-2023 13:10 - 14:10

##### BUSULFAN WITH 400 CENTIGRAY OF TOTAL BODY IRRADIATION AND HIGHER DOSE FLUDARABINE. AN ALTERNATIVE REGIMEN FOR HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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**Background and Aims:** Hematopoietic stem cell transplantation can be curative for children with difficult to treat leukemia. The conditioning regimen utilised is known to influence outcomes. We report the outcomes of a conditioning regimen used at the Alberta Children's Hospital, consisting of Busulfan (with pharmacokinetic target of 3750 $\mu$ mol\*min/day for 4 days), higher dose (250 mg/m<sup>2</sup>) Fludarabine and 400 centigray of Total Body Irradiation.

**Methods:** This was a retrospective study involving children who received transplant for acute lymphoblastic leukemia (ALL). It compared children who fell within the target range for Busulfan with those who were either not measured or were measured and fell outside this range. All other treatment factors were identical.

**Results:** Twenty-nine children with ALL were transplanted, with 17 subjects within the targeted group. We noted similar demographic characteristics except for more children transplanted due to high-risk disease in CR1 after 2010. All children engrafted with a median (IQR) time to neutrophil engraftment of 14 days (8-30 days). The cumulative incidence of acute graft versus host disease at day 100 was 44.8% (95% CI 35.6 – 54.0%). Chronic graft versus host disease was noted in 16.0% (95% CI 8.7% - 23.3%) after one year of follow up. At two years, the overall survival was 78.1% (95% CI 70.8% - 86.4%) and event free survival was 74.7% (95% CI 66.4% - 83.0%). Cumulative incidence of relapse was 11.3% (95% CI 5.1% - 17.5%) and the non-relapse mortality was 15.4% (95% CI 8.3% - 22.5%). There were no statistically significant differences in overall and event free survivals between the group that received targeted busulfan compared with the untargeted group.

**Conclusions:** The current regimen used in children with ALL results in outcomes comparable to standard treatment with acceptable toxicities and significant reduction in the dose of irradiation. Targeting Busulfan dose did not result in improved outcomes in this cohort.

O262/#1877 | Poster Discussion Session

#### POSTER DISCUSSION 05: STEM CELL TRANSPLANTATION

14-10-2023 13:10 - 14:10

#### DEPLETION OF CD45RA+ NAÏVE T CELLS FOR DONOR LYMPHOCYTE INFUSION TO TREAT REFRACTORY VIRAL INFECTION AFTER ALLOGENIC HSCT

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**Background and Aims:** Viral infections refractory to antiviral therapy are a life-threatening complication following allogeneic hematopoietic stem cell transplantation (HSCT). Depletion of alloreactive CD45RA<sup>+</sup> naïve T cells produce the graft containing abundant pathogen-specific memory T cells which can be used as a therapeutic donor lymphocyte infusion (DLI) in patients with refractory viral infections after allogeneic HSCT. In this study, we evaluated the efficacy of CD45RA-depleted DLI for patients with refractory viral infection following allogeneic HSCT.

**Methods:** Between April 2022 and March 2023, 8 pediatric patients received CD45RA-depleted DLIs using CliniMACS device at Asan Medical Center Children's Hospital. Of the 8 patients, 5 had hematologic malignancy (ALL 3, AML 1, MDS 1) and 3 had severe aplastic anemia.

Donors were mismatched related in 1 patient, unrelated volunteer in 1 and haploidentical family members in 6.

**Results:** Overall CD3<sup>+</sup> T cells were depleted at a median of 0.7 log (range, 0.5-0.9) with > 99% purity of CD45RO<sup>+</sup> T cells. CD45RA depletion procedure resulted in 4.1-6.4 log (median 5.8) reduction of CD45RA<sup>+</sup> T cells. Of the 8 patients, 6 patients received CD45RA-depleted DLI for refractory cytomegalovirus (CMV) reactivation even with antiviral treatment including ganciclovir and foscarnet. Of the remaining 2 patients, 1 received DLI for adenovirus (ADV) infection, the other for ADV and HHV-6. The median day of the first CD45RA-depleted DLI was 67 days (range, 44-797) post-HSCT at a dose of 5 $\times$ 10<sup>4</sup> - 1 $\times$ 10<sup>6</sup> T cells/kg from their original donor with the median number of 3 (range, 1-7 times). Of the 8 patients, 5 cleared their viremia at a median of 70 days (range, 38-89) after first DLI. No patients developed GVHD after DLIs.

**Conclusions:** CD45RA-depleted DLI is feasible with a low risk of GVHD. Therefore, infusion of naïve T cell-depleted graft should be offered in patients with refractory viral infection after allogeneic HSCT.

O263/#318 | CCI

#### CCI: SUPPORTING FAMILIES AND ORGANISATIONS

14-10-2023 13:10 - 14:10

#### COLLABORATIVE MULTI-STAKEHOLDER ACTION AND ADVOCACY TO SUPPORT PARENTS IN SUB-SAHARAN AFRICA WITH OUT-OF-POCKET COSTS TO ENABLE THEM TO COMPLETE CANCER TREATMENT OF THEIR CHILD

Junious Sichali<sup>1</sup>, Neil Ranasinghe<sup>2</sup>, Glenn Mbah Afungchwi<sup>3</sup>, Cecilia Mdoka<sup>1</sup>, Tim Hodgkinson<sup>4</sup>, Daniel Mackenzie<sup>5</sup>, Piera Freccero<sup>6</sup>, Nagm Azar<sup>7</sup>, Elizabeth Molyneux<sup>1</sup>, George Chagaluka<sup>8</sup>, [Trijn Israels](#)<sup>1</sup>

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**Background and Aims:** Failure to complete treatment for non-medical reasons is the most common and a largely preventable cause of childhood cancer treatment failure in sub-Saharan Africa. Poverty and families' inability to pay for out-of-pocket costs are overriding causes of reduced survival for patients with common and curable cancers for whom treatment is available, catastrophic costs for already impoverished families and create extremely challenging situations and impossible choices for parents. Our aim has been to develop a collaborative, multi-stakeholder initiative to support parents with out-

of-pocket costs in a sustainable fashion to enable their children to complete treatment.

**Methods:** CANCaRe Africa – the Collaborative African Network for Childhood Cancer Care and Research initiated a programme called ‘Zero Abandonment from Start to Finish’. We developed a ‘positive cycle’ in which the currently available evidence is used to advocate for family support, including support with out-of-pocket costs. The aim is to evaluate impact and (cost) effectiveness of such family support interventions to create new and more robust evidence. This evidence can then be used to strengthen and improve the advocacy to support families.

**Results:** We launched a programme called ‘Zero Abandonment from Start to Finish’ at SIOP Barcelona. Multiple stakeholders have joined the project including the Wilms Cancer Foundation and representatives from CCI. A governance structure has been created to guide the project planning. Funds are being raised with two grant applications submitted. A social scientist has been hired, based in Malawi, to coordinate the project activities and facilitate implementation science informed research. Advocacy is continued to attract more stakeholders for better collaboration.

**Conclusions:** Together we are stronger. Collaborative multi-stakeholder advocacy and well-planned interventions to support families are expected to sustainably improve and increase family support in sub-Saharan Africa, contributing to a significant increase in survival for children with common and curable WHO Index childhood cancers.

O264/#759 | CCI

#### CCI: SUPPORTING FAMILIES AND ORGANISATIONS

14-10-2023 13:10 - 14:10

#### DEFINING A NOVEL FRAMEWORK OF FINANCIAL HARDSHIP FOR CHILDHOOD CANCER GLOBALLY USING GROUP CONCEPT MAPPING: A ST. JUDE GLOBAL AND CHILDHOOD CANCER INTERNATIONAL (CCI) COLLABORATION

Julie Ritter<sup>1</sup>, Joao Braganca<sup>2</sup>, Carmen Auste<sup>3</sup>, Alejandra Mendez<sup>4</sup>, Emily Baum<sup>1</sup>, Lane Faughnan<sup>1</sup>, Patricia Loggetto<sup>1</sup>, Troy Quast<sup>5</sup>, Russell Kirby<sup>5</sup>, Nickhill Bhakta<sup>1</sup>

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**Background and Aims:** While widely acknowledged to contribute to poor health outcomes, financial hardship in childhood cancer glob-

ally is not fully understood. Existing methods are heterogenous and designed using high-income country (HIC), adult perspectives. This project aimed to construct a novel framework of financial hardship tailored to the needs of children with cancer.

**Methods:** Participants, recruited through the St. Jude Global and CCI networks, engaged in a two-step process using group concept mapping, a participatory mixed-methods approach. A small representative panel brainstormed and refined a comprehensive list of how financial hardship manifests in childhood cancer. Subsequently, study participants individually sorted items and rated each for impact using a 4-point Likert scale. Activities were completed in the groupwisdom® platform (English/Spanish) and via a Qualtrics survey (Portuguese). Sorted data underwent multi-dimensional scaling and hierarchical cluster analysis to identify themes. For impact ratings, descriptive statistics were calculated.

**Results:** 21/80 (26.3%) parents or caregivers and childhood cancer survivors completed at least one activity. 44/80 (55.0%), 27/80 (33.8%) and 13/80 (16.3%) of participants reported working in clinical, charity/volunteer or non-clinical environments, respectively. 42 countries were represented, of which 78.6% (33/42) were low- and middle-income countries (LMICs). Conceptual themes of financial hardship centered around six distinct clusters: medical costs, non-medical costs, assistance and support, treatment impact, family impact, and caregiver impact. Caregiver impact (mean 3.39) and treatment impact (mean 3.29) were the highest rated clusters, though rating patterns varied between HICs and LMICs with overall higher impact ratings for every cluster in LMICs compared to HICs.

**Conclusions:** We have developed a novel framework for financial hardship in childhood cancer that is distinct from traditional frameworks and, for the first time, reflects the voices of global stakeholders, including parents and caregivers. This is a foundational step for developing tools to assess financial hardship among children with cancer and identify effective policies and interventions.

O265/#1472 | CCI

#### CCI: SUPPORTING FAMILIES AND ORGANISATIONS

14-10-2023 13:10 - 14:10

#### CCI ANCHOR ORGANISATION IN AFRICA PAYING IT FORWARD TO MOZAMBIQUE

Adri Ludick

CHOC Childhood Cancer Foundation SA, Programme Development, Rivonia, South Africa

**Background and Aims:** There is only one paediatric oncology unit serving all the patients in Mozambique, Africa with no comprehensive child and family support available. Frederico Congola’s twin son was diagnosed with bi-lateral retinoblastoma and was referred for

specialised treatment to Groote Schuur Hospital in South Africa - 2000 kilometers away from home. With no resources available, he was referred to CHOC Childhood Cancer Foundation in South Africa where he was introduced to the best practices of care and support.

**Methods:** The bereaved father decided to pay it forward and after the death of his son, started a parent support group called Associação de Pais e Amigos da Criança com Cancro em Moçambique (APACC). With no knowledge and just the experience of CHOC's services in SA, he reached out to CHOC for assistance. CHOC, as the anchor organisation for Childhood Cancer International, answered his plea by knowledge sharing and capacity building. CHOC visited APACC and the hospital in Maputo and paid it forward by supporting the group.

**Results:** CHOC reached out to Acreditar, the Portuguese Parent Group who supported APACC with CCI membership fees, CHOC introduced APACC to Alsac for technical support and guidance, and introduced them to and international donor for support. The group was officially launched, opened their own bank account and is in the process to build the first accommodation facility in Mozambique

**Conclusions:** CHOC learnt many lessons through international collaborations, conferences and networks and was privileged to pay it forward, just as the father who benefitted from best practices to a group who just started and is now excelling to make a difference in a low-income country.

O266/#1719 | Poster Discussion Session

#### POSTER DISCUSSION 06: MOLECULAR AND BIOLOGICAL PROGNOSTIC MARKERS

14-10-2023 13:10 - 14:10

#### DEFINING NOVEL MOLECULAR SUBTYPES OF OSTEOSARCOMA BASED ON INTEGRATIVE GENOMIC ANALYSIS

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**Background and Aims:** Treatment modalities for osteosarcoma have remained unchanged for the past 30 years<sup>1</sup>. Here, we investigate the genomic and cellular heterogeneity within a cohort of 202 osteosarcoma samples to identify novel molecular subtypes of osteosarcoma and which subtypes are likely to respond to genome-informed therapies. We incorporate advanced genomic approaches, such as network

heat diffusion strategy, to identify perturbed regulons that may suggest tumor-specific vulnerabilities.

**Methods:** We apply an innovative unsupervised clustering method, called Hydra, to explore the genomic landscape of osteosarcoma, using an extensive osteosarcoma cohort we assembled with our collaborators at UCSF. We demonstrate Hydra's ability to identify tumor subtypes, surpassing widely-used gene set enrichment approaches for detecting multimodal expression signatures.

**Results:** Applying the Hydra analysis framework to the patient cohort of 202 osteosarcoma samples identified expression signatures associated with changes in the tumor microenvironment. Notably, Hydra analysis of 164 primary osteosarcoma tumors revealed subtypes characterized by changes to infiltrating immune and stromal expression signatures.

**Conclusions:** Uncovering differential pathway expression and molecular subtypes within our osteosarcoma cohort has enabled us to begin to identify gene signatures for predictive biomarkers, explain tumor behavior, and suggest subtype-specific drug targets. Success in utilizing these advanced genomic analysis methods will enable the application of this framework to other difficult-to-treat, heterogeneous cancer subtypes. <sup>1</sup> Sayles LC, Breese MR, Koehne AL, et al. Genome-informed targeted therapy for osteosarcoma. *Cancer Discovery*. 2019;9(1):46-63.

O267/#259 | Poster Discussion Session

#### POSTER DISCUSSION 06: MOLECULAR AND BIOLOGICAL PROGNOSTIC MARKERS

14-10-2023 13:10 - 14:10

#### INTRATUMOR-INFILTRATING NATURAL KILLER CELLS PREDICT FAVORABLE PROGNOSIS AND RESPONSE TO PD-1 BLOCKADE IN NEUROBLASTOMA

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**Background and Aims:** T/NK cell-based immunotherapy has achieved remarkable success in adult cancers, but has limited efficacy in pediatric malignancies including high-risk neuroblastoma (NB). Immune defects of NB tumor microenvironment are poorly understood compared with adults.

**Methods:** The spatial distribution of T-cells (CD8<sup>+</sup>), NK-cells (NKp46<sup>+</sup>), and cells expressing programmed death 1 (PD-1) and its ligand (PD-L1) were comprehensively examined in a large-scale of patients with NB. The correlations of various cell populations in relation to the spatial distribution (intratumoural or peritumoural) of

T and NK cells and positive expression of PD-L1 on immune or tumor cells, with patient survival, *MYCN* amplification, INSS stage, and COG risk classification were analyzed. The phenotype and activity of T and NK cells, as well as their combination with PD-1 blockade were also investigated in vitro and in vivo.

**Results:** Only intratumoral T and NK cells and PD-L1<sup>+</sup> immune cells associated with increased survival in patients with NB. PD-L1<sup>+</sup> immune cells were a favorable prognostic factor in patients with intratumoral T or NK cells. Intratumoral NK cells was a prognostic biomarker independent of T cell infiltration, PD-L1/PD-1 expression, INSS stage, *MYCN* amplification, and COG risk classification. NK cells combined with PD-1 blockade showed potent antitumor activity against both *MYCN*-amplified and non-amplified NBs.

**Conclusions:** Our results suggest that compared with T cells, NK cells may play a predominant role in the antitumor immunity of NB. Intratumoral NK cells may be a promising biomarker for defining risk stratification and predicting survival and response to PD-1 blockade. These findings also explain why single PD-1 blockade may not be successful in NB and provide insights for the design of biologically stratified and personalized combination immunotherapy strategies, highlighting the combination of NK cell-adoptive cellular therapy and PD-1 blockade as a potentially effective strategy for relapsing/refractory NB.

O268/#929 | Poster Discussion Session

#### POSTER DISCUSSION 06: MOLECULAR AND BIOLOGICAL PROGNOSTIC MARKERS

14-10-2023 13:10 - 14:10

#### THE IMPACT OF COMPARATIVE GENOMIC HYBRIDIZATION MICROARRAY VERSUS CONVENTIONAL CYTOGENETICS IN RISK STRATIFICATION OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA: A SINGLE-INSTITUTION EXPERIENCE

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**Background and Aims:** Leukemia genetics are essential in modern risk stratification of childhood acute lymphoblastic leukemia (ALL).

Comparative genomic hybridization (CGH) microarray analysis was introduced as part of routine cytogenetic assessment of ALL at Sainte-Justine Hospital in 2016. This study aims to assess the concordance and added value of CGH in ALL risk stratification compared with conventional methods.

**Methods:** This retrospective study included pediatric ALL patients diagnosed at Sainte-Justine Hospital between 2016 and 2021. Results used in risk stratification from conventional cytogenetic and molecular analyses [G-banding karyotype, fluorescence in situ hybridization (FISH) and reverse transcriptase polymerase chain reaction] and flow cytometry for DNA index (DI) were collected and compared to those of CGH. Clinical data including patient characteristics, treatment details and outcome were collected and analyzed.

**Results:** from 135 ALL patients were analyzed: 117 B-ALL (87%) and 18 T-ALL (13%). Sample failures or non-diagnostic analyses occurred in 25/135 (18.5%) by G-banding karyotyping vs. 2/135 (1.5%) by CGH ( $P < 0.0001$ ). The mean turnaround time was significantly faster for CGH than karyotype, 6.9 vs. 10.7 days,  $P < 0.0001$ . In ploidy assessment, CGH-derived DI and flow-based DI demonstrated strong concordance ( $r = 0.9466$ ,  $P < 0.001$ ). Karyotype did not detect additional clinically-relevant aberrations that were already identified by the combined analysis of CGH and FISH. The most common aberrations detected by CGH were deletions involving *CDKN2A/B* ( $n = 48$ , 36.1%), *ETV6* ( $n = 42$ , 30.1%), *PAX5* ( $n = 27$ , 20.3%) and *IKZF1* ( $n = 17$ , 12.8%). In univariate analysis, *ETV6* or *PAX5* deletions were associated with superior EFS; however, only *ETV6* deletion retained significance in multivariate analysis (HR 0.12; 95% CI 0.007-0.647,  $P = 0.04$ ).

**Conclusions:** CGH provided faster, reliable and highly concordant results to conventional cytogenetics. Karyotype did not identify additional clinically-relevant alterations when compared with CGH and FISH's combined analysis. CGH identified recurrent gene deletions in pediatric ALL, among which *ETV6* deletions conferred prognostic significance.

O269/#940 | Free Paper Session (FPS)

#### FPS 21: BRAIN TUMORS - CLINICAL STUDIES

14-10-2023 15:00 - 16:00

#### A PHASE 2 STUDY OF TRAMETINIB FOR PATIENTS WITH PEDIATRIC LOW GRADE GLIOMA WITH ACTIVATION OF THE MAPK/ERK PATHWAY

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**Background and Aims:** BACKGROUND: Pediatric low-grade gliomas (PLGG) are the most frequent brain tumors in children. It is known that the majority of PLGG have activation of the MAPK/ERK pathway.

**Methods:** This ongoing multicenter phase II trial includes three recurrent/refractory PLGG groups: NF1 PLGG, KIAA1549-BRAF fusion PLGG and PLGG with other MAPK/ERK pathway activation (excluding BRAF V600E). The primary objective was to evaluate the overall response rate based on RANO criteria after daily oral trametinib administration for 18 cycles, each cycle lasting 28 days. Secondary objectives include the assessment of progression-free survival, tolerability of trametinib, serum levels of trametinib and quality of life evaluation during treatment.

**Results:** As of September 30, 2022 recruitment was completed with 68 PLGG patients enrolled (NF1: n=12; KIAA1549-BRAF fusion: n=42; other: n=14 including 7 patients with FGFR alterations). Median age at enrollment was 9.6 years (range 1.8-25.4). Median follow-up was 23.2 months (range 0.9-47.6). Fifty-nine patients were evaluable to assess response based on modified RANO criteria. The overall responses include: 1 complete response (1.7%), 9 partial response (PR) (15.3%), 15 minor response (MR) (25.4%), 28 stable disease (47.5%), 6 progressive disease (10.2%). Median time to response was 5.5 months (range 2.4-13.8) with a median duration of response of 14.5 months (range 2.7-44.6). Progression-free survival at 18 months was 76.2 % (95% CI 65.9-88.1%) and the median progression-free survival was 29 months. Treatment was discontinued for 61 patients: including 35 (57.4%) after completing 18 cycles as planned, 8 (13.1%) for progressive disease and 7 (11.5%) for adverse events. Fourteen (20.6%) patients progressed after discontinuation of treatment at a median time of 7.4 months (0.1-18 months). Eleven patients needed to restart treatment at progression, including three patients with MEK inhibitors and four with chemotherapy.

**Conclusions:** Trametinib can be an effective and well tolerated therapy for patients with recurrent/refractory PLGG.

O270/#1743 | Free Paper Session (FPS)

FPS 21: BRAIN TUMORS - CLINICAL STUDIES

14-10-2023 15:00 - 16:00

### A MODIFIED METRONOMIC ANTIANGIOGENIC REGIMEN (MEMMAT) INDUCES SURVIVAL BENEFIT IN EARLY RECURRENT MEDULLOBLASTOMA

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**Background and Aims:** Patients with recurrent medulloblastoma (MB) have a poor prognosis, irrespectively of used therapy approaches including conventional and high-dose chemotherapy, surgery and/or re-irradiation. Progression free survival (PFS) and overall survival (OS) are normally worse in patients with early recurrence (recurrence  $\leq$ 18 months after primary diagnosis). An alternative treatment approach is an antiangiogenic metronomic combination therapy (MEMMAT).

**Methods:** This is a retrospective survival and safety analysis of multicenter experience in the German HIT-REZ Register, a registry for relapsed pediatric brain tumors including medulloblastomas.

**Results:** Between January 2015 and December 2022, 29 patients with first MB relapse received the original or modified MEMMAT combination treatment. For modified MEMMAT oral cyclophosphamide and etoposide were replaced by oral temozolomide and topotecan. The 24 months PFS rates in children with early recurrence for original or modified MEMMAT or different regimens were 21%, 46% and 11% with a 24 months OS rate of 53%, 72% and 32%, respectively. In late MB relapses the 24 months PFS rates were 37%, 30% and 42% and the OS rates 100%, 86% and 70% using original or modified MEMMAT or different regimens, respectively. Most grade 3 or 4 treatment-related adverse events were hematologically with severe myelosuppression in 43% of patients, grade 3 or 4 infections with febrile neutropenia in 3% and, grade 3 or 4 polyneuropathy in 10%. In 70% of patients a significant dose reduction due to MEMMAT related adverse events was necessary.



**Conclusions:** The modified MEMMAT regimen has promising clinical activity in early recurrent MB with well manageable toxicity. It lead to comparable survival rates with original MEMMAT in late recurrent MB patients using a multimodal approach. A prospective randomized clinical trial comparing original and modified MEMMAT is warranted.

O271/#1180 | Free Paper Session (FPS)

## FPS 21: BRAIN TUMORS - CLINICAL STUDIES

14-10-2023 15:00 - 16:00

### ACT001 AND CBL0137: A VIABLE COMBINATION THERAPEUTIC FOR DIFFUSE INTRINSIC PONTINE GLIOMAS

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**Background and Aims:** Diffuse Intrinsic Pontine Gliomas (DIPG) are a subset of Diffuse Midline Gliomas (DMG) and are an incurable childhood brain tumour. We previously identified parthenolide as active against DIPG in vitro, but inactive in vivo due to limited brain penetration. ACT001 is a parthenolide derivative, that is in clinical development and is blood-brain-barrier permeable. We hypothesized that ACT001 will be active as a single agent against DIPG and that the development of rational combination therapy, may increase its efficacy.

**Methods:** As a single agent, ACT001 demonstrated potent cytotoxic activity against a panel of DIPG neurospheres, inhibiting colony formation and inducing apoptosis. Additionally, RNA sequencing and concomitant qPCR and western blot data from ACT001 treated DIPG neurospheres demonstrated upregulation of both genes and proteins related to oxidative stress, ROS production and activation of the unfolded protein response. These data suggest that ACT001 acts to inhibit DIPG cell proliferation through increased ROS generation.

**Results:** In vivo testing of ACT001 in a highly aggressive DIPG-orthotopic model showed that ACT001 was well tolerated and significantly improved survival. ACT001 treatment led to a reduction in intratumoral proliferating DIPG cells, with significantly increased H3K27me3 staining. Given the significant effects on H3K27me3, we evaluated the combination of ACT001 with a known, clinically available epigenetic modifier, CBL0137. CBL0137 is a quinacrine derived anti-cancer compound that targets FACT, a chromatin remodelling complex involved in transcription, replication, and DNA repair. Combination

treatment significantly decreased colony formation in vitro and significantly enhanced survival in vivo using two independent orthotopic DIPG models. ACT001 is currently in a Phase 1 paediatric trial for children with DIPG/DMG and has demonstrated clinical activity.

**Conclusions:** These combined preclinical and clinical results suggest that ACT001 is a viable therapy for patients with DIPG/DMG and preclinical combination therapy testing may guide further clinical trials.

O272/#445 | Free Paper Session (FPS)

## FPS 22: UNDERSTANDING AND MITIGATING TOXICITY

14-10-2023 15:00 - 16:00

### GENETIC VARIATIONS RELATED TO NERVE MYELINATION AND SYNAPSE ASSEMBLY ARE ASSOCIATED WITH THE RISK OF VINCRIStINE-INDUCED PERIPHERAL NEUROPATHY

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**Background and Aims:** Vincristine is a very effective chemotherapy that is commonly used for the treatment of different types of pediatric and adult cancer. However, its clinical utility is severely limited by the presence of vincristine-induced peripheral neuropathy (VIPN), which is highly debilitating toxicity often requiring dose reduction, potentially affecting quality of life and survival. Although previous studies have demonstrated several genetic variants are associated with VIPN risk, the relevance of identified variants for clinical use is limited by small sample sizes in most of the studies and weak associations with VIPN risk. This study aims to identify pharmacogenomic risk factors of VIPN in a large and well-characterized cohort of pediatric cancer patients.

**Methods:** A case-control genome-wide association study (GWAS) was conducted on 1,352 pediatric patients recruited through the Canadian Pharmacogenomics Network for Drug Safety (CPNDS) in ten Canadian pediatric oncology centers. VIPN was defined according to the Common Terminology Criteria for Adverse Events (CTCAE v5.0). The analysis included 669 cases [CTCAE grade  $\geq 2$ ] and 683 controls [CTCAE grade 0], patients with CTCAE grade 1 (n=155) were excluded to improve the case/control phenotypic discrimination. Genotype data was generated from DNA samples using custom Illumina GSA array, and priori power calculations were performed to ensure adequate statistical power.

**Results:** The analysis revealed 3 novel associations ( $p < 5.0 \times 10^{-8}$ ) near/within *NRG3* (OR=0.15, 95% CI: 0.07-0.33), *LRRTM3* (OR=0.14, 95% CI: 0.06-0.32) and *MCM3AP* (OR=5.95, 95% CI: 2.91-12.14) genes with the risk of VIPN.

**Conclusions:** These results suggest that genetic variations in genes related to nerve myelination (*NRG3*), pre-synapse assembly (*LRRTM3*) and Charcot-Marie-Tooth neuropathy (*MCM3AP*) play an important role in the overall susceptibility of VIPN in pediatric oncology patients.

O273/#41 | Free Paper Session (FPS)

## FPS 22: UNDERSTANDING AND MITIGATING TOXICITY

14-10-2023 15:00 - 16:00

### ORAL-ROUTE SUPPORTIVE CARE REGIMEN DURING HIGH-DOSE METHOTREXATE ADMINISTRATION IN CHILDREN WITH HEMATOLYMPHOID MALIGNANCIES - IS IT FEASIBLE?

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**Background and Aims:** Administration of high-dose methotrexate (HDMTX) requires strict intravenous hydration, urine alkalinization, and timely leucovorin (LV) rescue thereby contributing to significant length of hospital stays. An oral-route supportive care regimen (OSCR) after ensuring satisfactory methotrexate clearance can cut short the length of hospital stay required for safe administration of HDMTX and allow optimal health care resource utilization in developing nations. The aim of the study is to test the feasibility of an OSCR in the in-hospital setting during HDMTX administration. The primary objective is to identify the proportion of HDMTX courses completed on OSCR in children started on OSCR after documentation of an initial safe serum methotrexate level.

**Methods:** Children with hematolymphoid malignancies aged 5-18 years, that received high-dose methotrexate with initial intravenous alkaline hydration and have a safe initial methotrexate level were started on OSCR including oral hydration, oral bicarbonate, and oral LV after the family was counseled regarding need for strict compliance. Oral fluid intake and urine output were documented in monitoring sheets by parents. Inpatient monitoring to ensure adherence to the OSCR was done periodically by nursing team. Children were changed

to the intravenous supportive care regimen if pre-defined withdrawal criteria were met, to ensure safety.

**Results:** OSCR was tested in a total of 20 HDMTX courses, involving 12 children. OSCR was completed in 18 (90%) of the 20 HDMTX courses. 2 courses had to be withdrawn from OSCR and started on the intravenous regimen due to requirement of more than 2 oral bolus doses of bicarbonate for maintaining urine pH. All but the 2 withdrawn courses, had a safe 2<sup>nd</sup> methotrexate level. The mean adherence rate to oral fluid intake was 96% among the courses that completed OSCR. No grade 3/4 adverse events were noted.

**Conclusions:** OSCR in the inpatient setting is safe and feasible during HDMTX administration in children with hematolymphoid malignancies.

O274/#1879 | Free Paper Session (FPS)

## FPS 22: UNDERSTANDING AND MITIGATING TOXICITY

14-10-2023 15:00 - 16:00

### SEVERE MALNUTRITION AND HEMATOLOGICAL MALIGNANCY POSED HIGHER RISK OF EARLY DEATH IN CHILDREN WITH CANCER TREATED IN RESOURCE-LIMITED PEDIATRIC ONCOLOGY SETTING

Nur Melani Sari<sup>1</sup>, Jeanne Depi<sup>2</sup>, Nur Suryawan<sup>1</sup>, Susi Susanah<sup>1</sup>, Kurnia Wahyudi<sup>3</sup>, Mulya Ardisasmita<sup>3</sup>, Gertjan Kaspers<sup>4,5</sup>

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**Background and Aims:** Despite significant advances in pediatric care in recent decades, early death remains the biggest challenge treating childhood cancer in most Low Middle-Income Country (LMIC) regions. May be caused by inadequacies in early detection and proper referral, as well as suboptimal supportive care. The aim of this study was to identify risk factors of early death in pediatric cancer patients diagnosed in a large teaching and referral hospital in Java, Indonesia.

**Methods:** This retrospective cohort study used data from Indonesian Pediatric Cancer Registry (IP-CAR) from 1 January 2020 to 30 November 2022. Among the 884 patient records, a total of 373 patients met the inclusion criteria which was pediatric cancer patients who died during the diagnosis and early therapy period given at the Dr. Hasan Sadikin Bandung Hospital. We classified the group as the early death if the patient died within 30 days after diagnosis. We describe the char-

acteristics of 371 eligible patients and performed bivariate chi-square and multivariate cox regression tests to identify risk factors for early death, a p-value  $\leq 0.05$  statistically indicated significant results.

**Results:** The percentage of early death was still high within the study population 144/371 (38.8%) with hematological malignancies being the most common cancer among early death patients. Malnutrition was identified in 192 patients, 80 (55.6%) of them had early death. Nutritional status and cancer types were found to be risk factors for early death in childhood cancer patients, as shown in cox regression analysis both severe malnutrition (Hazard Ratio [HR]:1.601, 95% Confidence Interval [CI] :1.136-2.497, P:0.009) and hematological malignancies (HR:1.417, 95%CI :1.018-1.971, P:0.039) made a statistically significant result.

**Conclusions:** Severe malnutrition and hematological malignancies were significant risk factors of early death in a large group of children with cancer treated in Indonesia, a LMIC country.

O276/#48 | Free Paper Session (FPS)

FPS 23: SUPPORTIVE CARE AND EPIDEMIOLOGY

14-10-2023 15:00 - 16:00

#### THE IMPACT OF READY-TO-USE-THERAPEUTIC-FOOD (RUTF) ON MICRONUTRIENT LEVELS IN UNDERNOURISHED CHILDREN WITH CANCER: A RANDOMIZED OPEN-LABELLED CONTROLLED STUDY

Maya Prasad<sup>1</sup>, Shyam Srinivasan<sup>1</sup>, Rajul Gala<sup>1</sup>, Girish Chinnaswamy<sup>1</sup>, Elena Ladas<sup>2</sup>, Ronald Barr<sup>3</sup>

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**Background and Aims:** Emerging evidence suggests that micronutrient deficiencies are predictive of poorer outcomes in children with cancer. We assessed the prevalence and clinical impact of micronutrient deficiencies, as well as the change in micronutrient status after RUTF supplementation in undernourished children with cancer.

**Methods:** Undernourished children with cancer were randomized 1:1 to receive either standard nutritional therapy (SNT) or SNT+ RUTF for 6 weeks. The primary outcome was weight gain, and secondary outcome was improvement in micronutrient status from study entry to 6 weeks including serum copper, zinc, iron, B12 and 25-OH vitamin D3. Standard cut-offs for deficiency were applied. The micronutrient composition of RUTF was as per WHO norms. Clinical outcomes assessed were significant infection, grade 3-4 mucositis and treatment delay >1 week.

**Results:** Between July-2015 and March-2018, 260 subjects were enrolled; 249 were evaluable. The prevalence of deficiency at diagnosis and 6 weeks (respectively) were iron -18%,15.1%; copper-2%,1.2%; zinc - 38 %,37%; D3-44%,33%; and B12 -12.3%,12.5%. Serum levels of iron and zinc at diagnosis were lower amongst females (median mcg/dL 87 vs 129,p=0.07 and 63.6 vs 75.8,p=0.05 ), equally distributed among both arms. Children supplemented with RUTF had an increase in B12 levels (28.6% vs 13.6%,p=0.052) at 6 weeks compared to controls although a similar proportion continued to be deficient. We observed a trend between zinc deficiency and increased incidence of grade 3-4 mucositis (15% vs 7.5%,p=0.06) and treatment delay (23.6 % vs 12.6%,p=0.03) and higher treatment delay with B12 deficiency (60% vs 15.2%,p=0.032). No statistically significant association of micronutrient status and toxicity.

**Conclusions:** Micronutrient deficiencies, specifically zinc, iron and vit D3 are highly prevalent in undernourished children with cancer. RUTF supplementation had a beneficial effect only on B12 levels; possibly the 6-week supplementation is inadequate. The clinical impact of micronutrient deficiencies spectrum in children with cancer should be the focus of future interventional trials.

O277/#509 | Free Paper Session (FPS)

FPS 23: SUPPORTIVE CARE AND EPIDEMIOLOGY

14-10-2023 15:00 - 16:00

#### AN INTERNATIONAL SURVEY OF PEDIATRIC ONCOLOGY NUTRITIONAL PRACTICES IN HIGH INCOME COUNTRIES

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**Background and Aims:** Optimal nutrition in pediatric oncology can influence cancer related outcomes; however, there lacks evidence-based nutrition guidelines to direct care in this population. To establish understanding of current practice, we investigated nutrition practices among institutions providing pediatric oncology care in high-income countries.

**Methods:** An electronic, multi-disciplinary, cross-sectional survey of nutrition practices was conducted in 2022. Final analysis included 110 surveys from 72 unique institutions and included practitioners from Europe (42), the United States (22), the United Kingdom (20), Canada

(9), Australia/New Zealand (6), South America (5), and the Middle East/Asia (4).

**Results:** All institutions reported having dietitians; 72% have designated oncology dietitians. On average, institutions staffed 3.2 full time dietitian equivalents for inpatient settings and 2.1 full time equivalents for outpatient settings; 47% of practitioners reported feeling their institutions were adequately staffed. The majority (81%) of institutions completed nutrition risk screening but there was no consensus on specific screening tools used. Half (50%) of institutions who screened for nutrition risk did so in both inpatient and outpatient settings. The majority (75%) of institutions completed a nutrition assessment close to the time of diagnosis. Those that did not cited lack of staff, burden of tests at diagnosis, and consult only level of nutritional care as primary barriers. No practitioner reported having guidelines for starting parenteral nutrition, one (<1%) reported having guidelines for starting enteral nutrition. Leading topics of nutrition education provided to patients/families were symptom management (68%), nutrition support (64%) and general food safety (63%).

**Conclusions:** While the majority of institutions report having access to pediatric oncology dietitians, there continues to be a lack of standardized practice for nutrition screening, nutrition assessment, and nutrition interventions to guide specialized care in this patient population. Further work is needed to develop practice guidelines to optimize clinical outcomes for pediatric oncology patients around the world.

O278/#953 | Free Paper Session (FPS)

### FPS 23: SUPPORTIVE CARE AND EPIDEMIOLOGY

14-10-2023 15:00 - 16:00

#### INCREASED PROBABILITY OF RELAPSE ASSOCIATED WITH THROMBOEMBOLISM AND BLOODSTREAM INFECTIONS DURING PRIMARY CANCER THERAPY IN CHILDREN: RESULTS OF A PROVINCIAL PROSPECTIVE STUDY

Louise Guolla<sup>1,2</sup>, Leonardo Brandao<sup>3</sup>, Jacqueline Halton<sup>4</sup>, Laura Wheaton<sup>5</sup>, Soumitra Tole<sup>6</sup>, Trishana Nayiager<sup>1,2</sup>, Gary Foster<sup>2</sup>, Lehana Thabane<sup>1,2,7,8</sup>, Uma Athale<sup>1,2</sup>

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**Background and Aims:** Prior retrospective studies in pediatric cancer patients have demonstrated an adverse impact of thromboembolism

(TE) and central venous line dysfunction (CVLD) on survival. We undertook a province-wide prospective study to evaluate the impact of TE, CVLD, and blood culture-positive infection occurring during primary cancer therapy on the risk of relapse and death in children.

**Methods:** Children (<18 years) treated for non-CNS cancer (n=486; 56.4% male, 53.1% with acute lymphoblastic leukemia [ALL]) were followed from diagnosis until 5 years after completing therapy. We used Kaplan-Meier curves to calculate relapse-free (RFS) and overall survival (OS) and extended Cox modeling with competing-event analysis to assess the impact of CVLD, TE, and infection on outcomes while adjusting for other factors, including those associated with poor outcomes: age and high-risk cancer diagnosis (acute myeloid leukemia, neuroblastoma, sarcoma).

**Results:** With a median follow-up time of 4.4 years, 90 relapses and 62 deaths were recorded. For the entire cohort, 5y-RFS was 79.3% (95% confidence interval [CI]: 75.3-83.2) and OS 84.8% (95%CI: 81.0-88.6). Older age and high-risk cancer diagnosis were confirmed as poor prognostic factors (data not shown). Infection, but neither CVLD nor TE, independently decreased OS (HR: 1.76 95%CI: 1.05-2.96). After adjusting for competing risk of death, there was an increased risk of relapse with both infection (HR: 1.69, 95%CI: 1.05-2.70) and TE (HR: 1.71, 95%CI: 0.92-3.18); this effect was more pronounced for patients with ALL (infection HR: 2.62, 95%CI: 1.27-5.42; TE HR: 2.11, 95%CI: 0.95-4.67).

**Conclusions:** Adjusting for age and high-risk cancer diagnosis, blood-culture positive infection during primary cancer therapy was independently associated with a higher probability of relapse and death. TE was associated with an increased probability of relapse, though this cohort lacked statistical power to achieve significance. Future studies should evaluate strategies to prevent infection and TE to reduce risk of relapse and improve survival.

O279/#1322 | Free Paper Session (FPS)

### FPS 23: SUPPORTIVE CARE AND EPIDEMIOLOGY

14-10-2023 15:00 - 16:00

#### SEX DISPARITY IN TREATMENT ABANDONMENT OF CHILDHOOD CANCER - A RETROSPECTIVE SINGLE INSTITUTIONAL ANALYSIS FROM INDIA

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**Background and Aims:** Sex disparity is conspicuous in childhood cancer care in areas of societal sex bias and resource limitations. This study aimed to systematically analyse sex disparity in treatment abandonment (TA) of childhood cancer from India.

**Methods:** All children diagnosed with cancer, aged 0-19 years, registered at our centre between January 2017-July 2022 were included. Any deferred scheduled treatment  $\geq 4$  weeks at any point during therapy, irrespective of intent of therapy, was considered as treatment default (TD). The primary objective was to assess sex disparity in TA, which was defined as defaulting during a curative-intent therapy. The secondary objectives were to analyse sex disparity in TA at upfront diagnosis versus at disease relapse, TD during palliative-intent therapy and to evaluate the independent impact of sex on TA and TD, along with other socio-demographic and clinical factors.

**Results:** Data of 3,820 children were screened out of which 3284 [MFR: 2.08 (1.94-2.24)] were analysed. Total 559 children (14.6%) had TD with higher proportion of females as compared to males (19.1% vs 16.1%;  $p=0.031$ ) with adjusted MFR of 0.84 (0.71-1.00). Out of 2906 children treated with curative-intent, TA was observed in 415 (14.3%) children. A higher proportion of females had TA as compared to males (16.4%vs13.3%;  $p=0.029$ ) with adjusted MFR of 0.80 (0.66-0.98). The adjusted MFR of TA at upfront diagnosis was 0.73 (0.59-0.91), while at relapse, it was 1.19 (0.68-2.06). On multivariable analyses, sex independently predicted TA ( $p=0.019$ ) along with type of malignancy (TA in hematological malignancies 14.9% vs 8.6% in solid cancer;  $p=0.004$ ). Children whose mother had an education  $\leq$ high school also had more TA (10.1%vs6%;  $p=0.010$ ). The adjusted MFR of TD in palliative-intent therapy was 0.96 (0.68-1.35) with no factors including sex predictive of TD in this setting.

**Conclusions:** Sex disparity drives TA in childhood cancer with significantly more female abandonment, especially in upfront setting

O280/#275 | Free Paper Session (FPS)

FPS 24: PSYCHO-ONCOLOGY - WHEN IS YOUR HELP NEEDED AND EFFECTIVE ONLINE INTERVENTIONS

14-10-2023 15:00 - 16:00

EFFECTIVENESS OF OP KOERS ONLINE, AN ONLINE PSYCHOSOCIAL GROUP INTERVENTION FOR PARENTS OF CHILDREN WITH CANCER: RESULTS OF A RANDOMIZED CONTROLLED TRIAL

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**Background and Aims:** Parents of children with cancer are impacted by their child's disease. They have to face multiple challenges, such as uncontrollability and uncertainty and are at risk for developing psychosocial problems. The present study aims to evaluate the effect of an online group intervention (Op Koers Online, in English: On Track Online) on psychosocial wellbeing and coping skills.

**Methods:** The intervention focuses on specific issues that play a role in parents coping with a child with cancer. In six protocolled sessions in an online chat room, trained psychologists and social workers teach coping skills using cognitive behavioral techniques and acceptance and commitment techniques, while providing parents with the opportunity for peer support. Per group, four-six parents participate. Parents living with a child with a cancer (diagnosis <5 years ago) participated in a randomized controlled trial comparing an intervention group to a waitlist-control group, after open recruitment. Online questionnaires assessed anxiety and depression (PROMIS, computer adaptive tests) and coping skills (Op Koers Questionnaire). Regression analyses were performed to test differences in outcomes at T1, shortly after the intervention, between intervention and waitlist-control group, controlling for baseline score, age, gender, time since diagnosis and treatment status (on and off treatment).

**Results:** 100 parents participated (mean age 41.7 years, 86% female, mean time since diagnosis 1.8 years), of which 87 filled out follow-up questionnaires. The intervention group ( $n=42$ ) reported significantly ( $p<.05$ ) less anxiety ( $\beta=-.36$ ), less depression ( $\beta=-.38$ ) and more relaxation ( $\beta=.44$ ) compared to the waitlist-control group ( $n=45$ ) at T1. No differences were found for coping skills open communication, positive thinking and predictive control.

**Conclusions:** Short-term effects of participating in Op Koers Online are promising and in line with previous positive findings of research into Op Koers for other groups. Analyzing additional outcome measures and determining long-term effects are the next steps of the study.

O281/#907 | Free Paper Session (FPS)

FPS 24: PSYCHO-ONCOLOGY - WHEN IS YOUR HELP NEEDED AND EFFECTIVE ONLINE INTERVENTIONS

14-10-2023 15:00 - 16:00

RANDOMIZED CONTROLLED TRIAL TO EVALUATE THE EFFECT OF ONLINE COGNITIVE BEHAVIOIRAL THERAPY FOR INSOMNIA AFTER CHILDHOOD CANCER

Hinke Van Der Hoek<sup>1</sup>, Shosha Peersmann<sup>1,2</sup>, Martha Grootenhuis<sup>1</sup>, Esther Van Den Bergh<sup>1</sup>, Heleen Maurice-Stam<sup>1</sup>, Annemieke Van

Straten<sup>3</sup>, Wim Tissing<sup>1,4</sup>, Floor Abbink<sup>2</sup>, Andrica De Vries<sup>1,5</sup>, Jacqueline Loonen<sup>6</sup>, Leontien Kremer<sup>1</sup>, Gertjan Kaspers<sup>1,2</sup>, Raphaële Van Litsenburg<sup>1,2</sup>

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**Background and Aims:** Insomnia is common after childhood cancer (prevalence 26-28%) and associated with negative health outcomes and impaired quality of life. The first-line treatment is cognitive behavioral therapy for Insomnia (CBT-I), but research shows the vast majority of adolescents and young adults after childhood cancer do not receive treatment for their sleep problems. The present study aimed to investigate the effectiveness of the online CBT-I intervention *i-Sleep* in improving sleep efficiency and decreasing insomnia.

**Methods:** Patients (12-30 years) with insomnia complaints (Insomnia Severity Index score  $\geq 8$ ), <10 years after diagnosis of childhood cancer, and  $\geq 6$  months since end of treatment, were invited to participate in a randomized controlled trial. Participants were randomized to the intervention group or waiting-list control group. *i-Sleep* consists of 5 online sessions supported by an online coach. Outcomes were sleep efficiency (7-day actigraphy) and insomnia complaints (Insomnia Severity Index). Differences between intervention and control group after the intervention, three months from baseline, were preliminary assessed with linear regression analysis, controlled for baseline score, age, sex and time since diagnosis.

**Results:** Fifty-four (response rate 47.0%) patients participated: 68.9% females, mean age 18.3 years (SD 3.2), 15.6% CNS tumors, 31.1% solid tumors, 53.3% hemato-oncology, mean time since diagnosis 4.8 years (SD 2.5). After *i-Sleep*, there was no difference in sleep efficiency (standardized beta 0.17,  $p=0.43$ ). However, the intervention group reported significantly fewer insomnia complaints than the control group (Mean 8.1, SD 4.2 vs 13.1, SD 4.7; standardized beta -0.84, indicative of a large effect,  $p 0.009$ ).

**Conclusions:** The positive results of *i-Sleep* on insomnia are promising, and suggest that an online intervention can facilitate access to treatment for adolescents and young adults with insomnia after childhood cancer and should be implemented. Further research will focus on long-term effects of *i-Sleep* and on effects on psychosocial outcomes.

O282/#1193 | Free Paper Session (FPS)

## FPS 24: PSYCHO-ONCOLOGY - WHEN IS YOUR HELP NEEDED AND EFFECTIVE ONLINE INTERVENTIONS

14-10-2023 15:00 - 16:00

### FEASIBILITY, ACCEPTABILITY, AND PRELIMINARY EFFECTS OF AN ONLINE GROUP PSYCHOTHERAPY INTERVENTION FOR ADOLESCENTS AND YOUNG ADULTS WITH CANCER

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**Background and Aims:** A novel, virtually-delivered group psychotherapy intervention was developed to address the unique psychosocial needs of adolescents and young adults (AYAs; ages 15-29 years) with cancer. The aim of this study was to evaluate the feasibility, acceptability, and preliminary effects of the intervention.

**Methods:** The intervention is a manualized 8-week virtual group psychotherapy program led by registered psychologists. Thirty-three patients ( $M_{age} = 20.88$  years,  $SD = 3.70$ , range = 15-29 years) formed four groups ( $n = 5-11$  AYAs per group). Participants primarily identified as female (73%) and were diagnosed with a hematologic malignancy (67%). Patients were recruited from adult (67%) and pediatric (33%) oncology settings. Feasibility was assessed based on recruitment and retention data. Acceptability and preliminary effects were assessed using questionnaires that examined the perceived value of the intervention and psychosocial outcomes that were measured pre- and post-intervention. Descriptive statistics summarized feasibility and acceptability measures. Exploratory repeated-measures t-tests examined preliminary effects on psychosocial outcomes.

**Results:** The intervention completion rate was 85% ( $n = 28$ ). Reasons for non-completion included scheduling conflicts (6%), group not a good fit (6%), and change in medical status (3%). Three quarters (73%) of participants attended  $\geq 6/8$  of the sessions. All participants "strongly agreed" (88%) or "agreed" (12%) that they were satisfied with the group. The most highly rated sessions (rated as "very" or "somewhat" useful) were the sessions focused on "planning for the future"

(96%) and “relationships and body image” (92%). Improvements in participants’ emotional ( $t(20) = 2.64, p < .05, d = .58$ ) and functional ( $t(20) = 3.19, p < .01, d = .70$ ) wellbeing from baseline to immediately post-group were significant and had medium effect sizes.

**Conclusions:** Results demonstrate that the intervention is acceptable, feasible, and shows promise for improving psychosocial outcomes in AYAs. Future research is needed to evaluate the intervention and establish efficacy with a larger sample.

O283/#1724 | Free Paper Session (FPS)

#### FPS 24: PSYCHO-ONCOLOGY - WHEN IS YOUR HELP NEEDED AND EFFECTIVE ONLINE INTERVENTIONS

14-10-2023 15:00 - 16:00

#### IN UKRAINE: THE WAR OUTSIDE THE WINDOW OR THE WAR FOR THE LIFE OF A CHILD WITH CANCER. THE PSYCHOLOGICAL FACTOR

Liudmyla Baletska<sup>1</sup>, Vladyslava Andrushchenko<sup>2</sup>, Marianna Nych<sup>3</sup>, Liliia Sirokha<sup>4</sup>, Olesya Horlenko<sup>5</sup>, Olga Pushkarenko<sup>6</sup>, Liubov Pushkash<sup>5</sup>, Viktor Pushkarenko<sup>5</sup>, Anastasia Pushkarenko<sup>5</sup>  
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**Background and Aims:** The lives of Ukrainians have changed dramatically over the past year. There are difficult realizations and collective reflection ahead. This study aims to make a current snapshot of the situation in order to realize the factor of psychological impact on the lives of all those who are trying to preserve the childhood health of a child with cancer in times of war.

**Methods:** The survey was conducted during 2022 and covered children’s specialized hospitals in three key cities of Ukraine: Kyiv, Lviv, and Kharkiv. Data from four groups of respondents were collected and analyzed: pediatricians (48), psychologists (12), parents (255), and children themselves (112). The main indicators were dynamism and changes in the psychological state (emotions, coping behavior); access to psychological support services or development of self-help skills; changes in living and working conditions compared to before and during the war; contacts and professional networking.

**Results:** The level of sensitivity to complaints from parents has increased among doctors (83%), and they have a hard time dealing with palliative care situations among children (67%). 58% of doctors have to live in the hospital with their families because their own homes

were destroyed. 32% report a longer recovery and acute reaction to constant alarms and prolonged stay in shelters.

95% of oncological psychologists have acquired additional skills in dealing with crisis management, but there is no professionally oriented training related to the specifics of the work.

Parents, there is an increase the frequency of panic attacks (62%), episodes of PTSD by the experience of occupation and other factors of war (45%), and exposed to long-term stress due to financial difficulties (89%).

The number of children with multi-trauma (45%) and early depression (38%) has increased.

**Conclusions:** Given the situation in the country and the ongoing migration processes, it was extremely difficult to summarize the data.

## POSTER ABSTRACTS

EP001/#1766 | Poster Topic: AS01 Surgery - IPSO

#### SURGICAL MANAGEMENT OF PRIMARY MALIGNANT BONE TUMORS IN CHILDREN

Anas Abouelkheir, Mohammed Arihi, Mohamed Cherqaoui, Abdelmounaim Cherqaoui, Chafik Bjitro, Mustapha Aboumaarouf Ibn Rochd University Hospital center, Pediatric Surgery, Casablanca, Morocco

**Background and Aims:** Primary malignant bone tumors in children are general diseases due to an abnormal proliferation of pathological cells with a bone starting point. They represent 5% of all pediatric malignancies, dominated by osteosarcoma and Ewing’s sarcoma, which account for 90% of all these tumors.

**Methods:** We carried out an analytical descriptive retrospective study, between 2013 to 2019, about 41 patients. The objective of our work, is to share the surgical experience of our center of pediatric traumatology and orthopedics department with primary malignant bone tumors.

**Results:** Our study concerned 24 cases of osteosarcoma, 16 cases of Ewing’s tumor and one case of lymphoma. The average age of the patients was 10.1 years, the sex ratio was 2.1 with a male predominance. The time elapsed between the onset of symptoms and the diagnosis was 4 and a half months on average. The clinical symptomatology was dominated by pain and swelling. The lesion was found mainly in the long bones in (80.48%) including all locations, predominantly in the knee in 58.53% of cases. Therapeutically, 36 patients (87.80%) had received preoperative chemotherapy. Among the operated patients (32 cases), the surgery was conservative in 27 cases (84.37%) and it consisted of amputation in 5 cases (15.62%). There were 4 patients lost to follow-up, including 2 cases of discontinuation of treatment for refusal of amputation. Local and/or distant recurrence was found in 7 patients, ie (17.07%). There are 24 patients in complete remission, of which only 7 cases reached 5 years of follow-up with an average follow-up of 17 months at the date of the study.

**Conclusions:** This report will provide an overview of the current treatment options and discuss bone tumor genomics, current challenges, surgical modalities and emerging drug targets, in primary malignant bone tumors for the pediatrician caring for a child with these problems.

EP002/#1428 | Poster Topic: AS01 Surgery - IPSO

### MANAGEMENT AND OUTCOME OF BILATERAL WILMS TUMOR (BWT) TREATED UNDER AIIMS WT-99 PROTOCOL AT A SINGLE TERTIARY CENTRE OVER A 22 YEAR PERIOD

Sandeep Agarwala<sup>1</sup>, Vishesh Jain<sup>1</sup>, Anjan Dhua<sup>2</sup>, Sameer Bakhshi<sup>3</sup>, Ahitagani Biswas<sup>4</sup>, M. Srinivas<sup>5</sup>, Devendra Yadav<sup>1</sup>, Prabudh Goel<sup>1</sup>, Manisha Jana<sup>6</sup>, Devasenathipathy Kandasamy<sup>6</sup>

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**Background and Aims:** Wilms tumor (WT) is bilateral in 5-8% of cases. Outcome of these patients is not as good as unilateral WT. This study evaluates the management and outcome of children with bilateral WT (BWT).

**Methods:** Prospective study of all BWT patients between October 2000 and June 2022 treated. These were evaluated for presentation, treatment, type of resection and outcome. Kaplan Meir analysis for 4-year event free survival (EFS) and overall survival (OS) was done. Events being death, recurrence and progression.

**Results:** Of the 577 WT patients registered in this period, 31(5.4%) were BWT. Six left without any treatment so the remaining 24 were included. The age ranged from 4-48months. Ten (41.7%) were  $\leq 12$  m of age. All were favourable histology WT. Five (20.8%) had metastatic disease and 1(4.2%) had IVC thrombus. All received three drug (VCR+ACD+DOX) neoadjuvant chemotherapy for 6-10 weeks followed by staged surgical resection in 22 of the 24. Two could not be operated and there was spill in 5(5/22=22.7%). Post-operative radiotherapy was administered to 8(33.3%). Recurrence was observed in 9 of 22(40.9%) operated (3 on chemotherapy and 6 after completion of chemotherapy). Of these 9, three could be salvaged. Overall 18(75%) were alive with 14 of them in complete remission (CR). Six had died (2 of sepsis after having achieved CR). Overall 8(33.3%) did not achieve CR (2 not operated; 1 incomplete resection; 5 recurrence). Fourteen patients had events giving a 4-year EFS of 31.6% (95 CI 9.6 - 53.6) and OS of 68.6% (95 CI 45.8 - 91.4).

**Conclusions:** The prevalence of BWT was 5.5% with it being commoner in males and children above 12 months. After neoadjuvant chemotherapy 92% could undergo resection and bilateral NSS was the commonest

procedure (%). The 4-year EFS (32%) and OS (69%) was lower than that reported for unilateral WT.

EP003/#668 | Poster Topic: AS01 Surgery - IPSO

### LONG-TERM EFFECTS OF CISPLATIN ON HEARING AND RENAL FUNCTION IN SURVIVORS OF PAEDIATRIC SOLID TUMOURS

Sandeep Agarwala<sup>1</sup>, Vishesh Jain<sup>1</sup>, Mansi Chadha<sup>1</sup>, Anjan Dhua<sup>1</sup>, Prabudh Goel<sup>1</sup>, Devendra Yadav<sup>1</sup>, Mehak Sehgal<sup>1</sup>, Rakesh Kumar<sup>2</sup>, Alok Thakar<sup>3</sup>, S.C. Sharma<sup>3</sup>, Sameer Bakhshi<sup>4</sup>, Mani Kalaivani<sup>5</sup>, Tanvir Kaur<sup>6</sup>

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**Background and Aims:** The adverse effects of cisplatin drug on the kidney and the inner ear are well known. The aim of the present study was to assess the long-term ototoxicity and nephrotoxicity of survivors of solid malignant tumours treated with cisplatin.

**Methods:** Survivors of Hepatoblastoma (HB), Malignant Germ Cell (MGCT) and Neuroblastoma (NB) tumours from a paediatric surgical oncology clinic from a tertiary care hospital from 1994 to 2023 were included. The ototoxic effects of cisplatin were assessed in these survivors by the means of Pure-Tone Audiometry (PTA). The severity of loss of hearing was graded using the SIOP and the Brocks' Ototoxicity Scale. Nephrotoxicity was assessed with Glomerular filtration rate (GFR) calculated by dual sample Tc99-DTPA. Normal GFR was defined as  $>90$  ml/min/1.73m<sup>2</sup>.

**Results:** 259 children were assessed of which 103 received cisplatin. Of these 45 (43.69%) patients had Malignant Germ Cell Tumours, 33 (32.04%) had Hepatoblastoma and 24 (23.30%) had Neuroblastoma. The median age of the survivors was 11 years. PTA was performed in 83 survivors of which 67 (80.7%) and 44 (53%) were reported to have high-frequency hearing loss as per SIOP and Brock's scale respectively. As per the SIOP scale, 35 (42.17%) had grade 3 or 4 hearing loss whereas on Brock's scale only 9 (10.6%) patients had grade 3 or 4 ototoxicity. GFR was assessed for 78 survivors. Normal GFR was noted in 37 patients whereas 41 (52.56%) patients had GFR $<90$ . Age at diagnosis, dose of cisplatin, Age at Audiometry & GFR and the time between diagnosis and date of assessment did not correlate with hearing loss and nephrotoxicity. Age, Gender and type of tumour had no effect on ototoxicity or nephrotoxicity.

**Conclusions:** Ototoxicity and nephrotoxicity is prevalent in patients who receive cisplatin though it is subclinical in most cases. Considering the small sample size, no predisposing factors were noted.



EP004/#207 | Poster Topic: AS01 Surgery - IPSO

### PERIOPERATIVE OUTCOMES OF LIVER RESECTION SURGERY IN CHILDREN- EXPERIENCE FROM A TERTIARY CANCER CENTRE IN INDIA

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**Background and Aims:** Anesthesia management for pediatric liver resections is challenging mainly due to the hemodynamic instability and major blood loss during the surgery. Aim of this study was to review the anesthesia management and perioperative outcomes of pediatric liver resection in a tertiary cancer hospital in India.

**Methods:** This was a retrospective audit from Jan 2011 till Dec 2022. After approval from the hospital ethics committee data was collected from the electronic medical records of all patients  $\leq$  18yrs of age undergoing liver resection. Postoperative complications  $\geq$  grade 3 (Clavien Dindo classification) was considered as morbidity.

**Results:** Data was analyzed from 189 children with a median age 2 years (1 month-15 years) and median weight of 10 kg (5-45kg) who underwent liver resections. 95% resections were for malignant tumors. All children received general anesthesia with epidural analgesia. Average surgical duration was 4:30 hours (1-10:30 hours) with a median blood loss of 25ml/kg (2 ml/kg-311ml/kg). Median intraoperative fluid balance was 7ml/kg/hr (1-32ml/kg/hr). Median post anesthesia care unit (PACU) stay was 41hours [IQR 23-54 hours] and median hospital stay was 7 days [ IQR 6-9 days]. Overall morbidity was 25 % (N=47). There were no complications due to epidural analgesia. On univariate analysis age  $<$  1year ( $p=0.03$ ), resection of  $>$  3 segments ( $p=0.01$ ), duration of surgery ( $p=0.03$ ), blood loss ( $p=0.03$ ) and intaroperative fluid balance ( $p=0.008$ ) was associated with morbidity. On multivariate analysis resection of  $>$  3 segments (OR 2.4[1.0-5.7];  $P=0.05$ ) fluid balance of  $>$  7ml/kg/hour (OR 2.3[1.1-4.6];  $P=0.04$ ) and age  $<$  1 year (OR 2.0[1.0-4.2];  $P=0.04$ ) significantly increased the morbidity.

**Conclusions:** Our overall morbidity rate was 25 % with no mortality. Epidural analgesia is safe and effective in providing adequate analgesia following liver resections in children. Judicious fluid management and improved surgical techniques to minimize blood loss can help in reducing the morbidity and hospital stay.

EP005/#1657 | Poster Topic: AS01 Surgery - IPSO

### THE MANAGEMENT OF PARATESTICULAR RHABDOMYOSARCOMA: EXPERIENCE OF TUNISIAN INSTITUTE WITH 20 CHILDREN

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**Background and Aims:** Paratesticular rhabdomyosarcoma is a rare and aggressive embryonic tumor in children and young adolescents. It develops at the expense of connective tissues, including genito-urinary localizations. The primary paratesticular location of the tumor represents 7% of all rhabdomyosarcomas, all locations combined. The aim of this study were to determine the epidemiologic characteristics of Tunisian pediatric population and elicit overall survival prognostic factors.

**Methods:** We collected the data of patients diagnosed with paratesticular rhabdomyosarcoma in pediatric department in Salah Azaiez Institute between January 1994 and December 2019. We reviewed patients' characteristics and overall survival with regards to prognostic factors.

**Results:** Median age was 13 years (2-18). One patient had a medical history of hydrocele. Presentation was dominated by scrotal swelling in 16 patients while 3 patients consulted for pain and one for urinary symptoms. At diagnosis, 15 patients had a localized disease and 5 were metastatic. Eight patients received neoadjuvant chemotherapy. Surgery was performed in 12 patients. The surgery was R0 in 10 patients, R1 in one patient and R2 in one patient. The primitive tumor's median greater length was 90mm (22-180). Pathology revealed embryonic type in 16 patients and alveolar type in 4 patients. Fifteen patients were classified as Intergroup Rhabdomyosarcoma Study (IRS) group I, 2 as group II, and 3 as group IV. Adjuvant therapy was based on chemotherapy in all patients and radiotherapy in 3 patients. With a median follow-up of 30 months (1-206), 2 years-overall survival was 50% and 3 years-overall survival was 30%. Three years progression free survival was 34%. The prognostic factors influencing OS were the IRS group ( $p=0.025$ ) and resection margin ( $p=0.006$ ), while the factor influencing PFS was the IRS group ( $p=0.027$ ).

**Conclusions:** The outcome for patients with localized paratesticular rhabdomyosarcoma is excellent, despite the reduction in chemotherapy over the years. the IRS group and resection margin significantly influence survival.

EP006/#1698 | Poster Topic: AS01 Surgery - IPSO

### MANAGEMENT AND OUTCOME OF PEDIATRIC CHONDROBLASTIC OSTEOSARCOMA

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**Background and Aims:** Osteosarcoma is the most frequent bone tumor for children and adolescents. The chondroblastic subtype is aggressive and accounts for 25% of cases of high-grade osteosarcoma. The aim was to assess the clinico-epidemiologic profile, prognostic factors, and treatment outcome of chondroblastic osteosarcoma.

**Methods:** A monocentric retrospective study was conducted between 1995 and 2020 including 16 patients with chondroblastic osteosarcoma at the pediatric oncology department of Salah Azaiz Institute.

**Results:** We included 16 patients. The mean age was 14 years old. The most common sites involved were femur (n=10) and tibia (n=5). The initial symptoms were bone pain (n=16) and swelling (n=14). The average size was 4.4 cm. At diagnosis, 70% of patients had localized disease. Eleven patients had neoadjuvant chemotherapy. Multiple combinations were used and protocols included etoposide and ifosfamide duet alternating with either methotrexate or adrimaycin and cisplatin duet. Progressive disease was noted in 56% of patients. Surgery was performed for 10 patients. We have found that 44% were poor responders to chemotherapy. Despite having a localized disease, 64% of the patients experienced relapse. Two patients had local recurrence and five patients had distant metastases. Median overall survival was 33 months. Overall survival (OS) at 2 years was 60%. For patient treated with methotrexate in the neoadjuvant protocol, median overall survival was 27 months compared to 7 months for the rest (p=0.003). The absence of radiological response was also a prognostic factor influencing OS (p=0.01).

**Conclusions:** Chondroblastic osteosarcoma is an aggressive neoplasm with a high risk of relapse. The use of methotrexate and the radiological response to neoadjuvant chemotherapy can predict a better OS.

EP007/#12 | Poster Topic: AS01 Surgery - IP SO

#### ABDOMINAL MALIGNANT NON-HODGKIN'S LYMPHOMA IN CHILDREN REVEALED BY SURGICAL EMERGENCY. IS PROGNOSIS PEJORATIVE?

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**Background and Aims:** Primary abdominal Non-Hodgkin Lymphoma NHL revealed by surgical emergency in children is a very rare entity. This study aims to describe the clinical presentation and to evaluate the outcome of children with abdominal NHL diagnosed following a surgical complication.

**Methods:** We retrospectively reviewed a series of patients who were hospitalized in a pediatric oncologic unit with the diagnosis of abdominal NHL from January 1998 to January 2023. Patients are staged and treated according to adapted LMB protocol regimens. Survival rate is studied by Kaplan-Meier method.

**Results:** Among 86 patients identified with NHL, 39 presented with abdominal location including 7 who were diagnosed during surgical exploration. Three patients presented with acute appendicitis and four had intussusception. No patient exhibited intestinal perforation. All patients had a resection of the tumor. Histopathologic study revealed Burkitt's lymphoma into the entire series. Only one patient presented

secondarily with local relapse. Five patients were staged 3 while two were stage 2 of Murphy's classification. Chemotherapy was conducted according to LMB protocol regimens with achievement of complete remission. Overall survival is 100% with a follow up ranging 8 to 17 years.

**Conclusions:** Despite the alarming circumstances of the discovery of NHL in children, the tumor prognosis remains favorable apart from postoperative complications. Does surgery allow early revelation of this tumor?

EP008/#883 | Poster Topic: AS01 Surgery - IP SO

#### PAEDIATRIC MALIGNANT PERIPHERAL NERVE SHEATH TUMOURS – A PICTORIAL REVIEW

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**Background and Aims:** Malignant peripheral nerve sheath tumours (MPNST) are rare in children. Overall outcomes rely on complete surgical resection but are often poor. We reviewed our paediatric cases and imaging to identify common features to aid early diagnosis.

**Methods:** Retrospective case note and imaging review of all children diagnosed with MPNST at a tertiary UK children's hospital between 2001 - 2018.

**Results:** Eight patients (2F, 6M) were identified, mean age at presentation was 12y [IQR 9.2-12.8y]. Main symptoms were pain, swelling, palpable lesion. 50% (4 patients) had a family or personal history of NF1 (Neurofibromatosis 1). Initial imaging was by ultrasound (US) in 3 cases: heterogenous appearance, cystic spaces, internal vascularity and rapid growth were common concerning findings. Magnetic resonance imaging (MRI) was performed in 7 cases and was the primary investigation in 3 cases due to the location of the lesion. On MRI all lesions were isointense to T1 with heterogenous high intensity T2 signal. Tumour location was lower limb/pelvis (n=4), upper limb/axilla (n=2), retroperitoneum (n=1), temporal region (n=1). Four patients had initial biopsy as core needle (n=2) or open biopsy (n=2), followed by surgical resection. Four patients had upfront resection, in 2 patients this was incomplete. One patient had lung metastases at presentation, 1 patient had suspicious lung nodules which subsequently developed into metastases. Three patients underwent chemo-/radiotherapy with curative intention. Four patients developed recurrence. Five patients are alive to date, median time since diagnosis 178m [IQR 141-228.25m]. Three patients passed away (median time from diagnosis 36m [IQR 30-36m]).

**Conclusions:** Although overall rare in children, MPNST is one of the commonest non-rhabdomyosarcoma soft tissue sarcomas in children. Heterogenous appearance with high internal vascularity and rapid growth are concerning US features. MRI is the investigation of choice.

Depending on location of the tumour, MRI should be considered as upfront investigation to expedite further management.

EP009/#871 | Poster Topic: ASO1 Surgery - IPSO

### SURGICAL CHALLENGES IN PELVIC RHABDOMYOSARCOMA

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**Background and Aims:** Rhabdomyosarcoma, the most common soft tissue sarcoma in children, can arise from various sites with an invasive growth pattern. Pelvic rhabdomyosarcoma not originating from bladder or prostate is rare. It causes specific surgical challenges due to its proximity to vital structures in a location difficult to access. We aimed to review such cases of pelvic rhabdomyosarcoma (P-RMS) and surgical approaches used to achieve best outcome.

**Methods:** Multi-centre retrospective case review between 2014-2022. Only true pelvic tumours (non-bladder/prostate) were included.

**Results:** Eight patients with complex P-RMS (6F, 2M). Median age at diagnosis was 3.6yrs [IQR 2.5-4.8yrs]. Symptoms at presentation: palpable mass (100%), abdominal pain (50%), urinary retention (50%). The patients in retention required ureteric stenting upfront. Three patients had metastatic disease at presentation. Histology from biopsy at diagnosis (75% transcutaneous, 25% laparoscopic) was embryonal rhabdomyosarcoma in 100% cases. Fusion status was negative in 50%, and unknown in 50%. All patients underwent neoadjuvant chemotherapy. In all cases the exact site of origin was difficult to determine. Location was in the lower retroperitoneum and pelvis, adherent to the abdominal or pelvic side wall (n=8), urachus/ bladder wall (n=7), sigmoid/ rectum (n=5). Half of cases either infiltrated or encased the ureter and iliac vessels. Partial organ resection was required in 5 cases to achieve R1 clearance: Ligation of ureter (n=3), internal iliac vessels (n=3), dome of bladder (n=2), common iliac vein (n=1), oophorectomy (n=1). Urological and vascular reconstruction were required in 50% cases. Major haemorrhage occurred in 2 cases. One patient died 12 months following surgery.

**Conclusions:** P-RMS poses a unique challenge for surgical resection. A multi-surgical-specialty intraoperative approach may be required to achieve macroscopic complete resection. The potential requirement

for organ resection should be discussed during the consent process. Long term follow-up of these cases will be required to determine OS, EFS and surgical morbidity.

EP010/#1612 | Poster Topic: ASO1 Surgery - IPSO

### RECURRENCE, REMNANTS AND TUMOR PROGRESSION IN WILMS TUMOR: SURGICAL RISK FACTORS

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**Background and Aims:** Wilm's tumor is the most common renal tumor in children. It is potentially curable in most patients. Despite the advances in Wilms tumor management, recurrent tumors still have unfavorable prognosis. Surgical procedure is among prognostic factors. The aim of this study is to identify the main risk factors, related to surgery, involved in recurrence and progression of Wilms' tumor.

**Methods:** This is a descriptive, retrospective, cross-sectional study conducted in the pediatric oncology unit of the Bechir Hamza children's hospital of Tunis, over a period of 17 years (January 2004-December 2020). It involved 14 patients with recurrent or progressing Wilms. The surgical risk factors studied were: intraoperative tumor rupture and lymph node sampling.

**Results:** The mean time to tumor progression during postoperative chemotherapy was 2.8 months. The mean time to tumor recurrence after complete remission was 13 months. Tumor recurrence and progression was diagnosed on imaging data during postoperative monitoring in 12/14 patients. Five patients had only distant lymph node resection. One of them had lymph node involvement on histological examination. He had a tumor progression postoperatively with hepatic, lymph node and pulmonary metastases and peritoneal carcinosis. The other four had no lymph node involvement. Local recurrence was noted in one patient, pulmonary recurrence in two patients and local and pulmonary tumor progression in one case. Tumor rupture was found in two patients on pathological examination. It was reported in only one patient as incidental during surgery. Of these two patients, the first had local tumor progression immediately postoperatively despite radiation therapy. The second had a local recurrence after 3 months of complete remission.

**Conclusions:** Surgeons must avoid rupture while removing wilm's tumors. Remote lymph node sampling does not exempt the surgeon from local lymph node sampling, because this situation could lead to "understaging", inappropriate treatment and thus cause avoidable recurrences.

EP011/#1409 | Poster Topic: AS01 Surgery - IPSO

### BREAST INFANTILE TUMOR ANALYSIS AT THE NATIONAL CANCER INSTITUTE BRAZIL/RJ

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**Background and Aims:** Breast lesions are rare in children and adolescents, and, in most cases, they are benign lesions. Malignant breast cancer in adolescents corresponds to 0.1% of all cancers in this age group and to 1% of all pediatric cancers.<sup>1</sup> It is important to recognize the stages of normal breast development to recognize congenital anomalies in your development and differentiate them from other changes, both in males and females. This study aims to evaluate the characteristics of children with breast nodules based on the clinical, histopathological, radiological, and surgical findings of these patients treated at the National Cancer Institute, from January 1, 2010, to March 20, 2020.

**Methods:** This is an analytical, retrospective, and cross-sectional study, in which data were obtained through electronic and physical records, collected by the authors.

**Results:** Data from 53 patients seen at the service were evaluated, with a mean age of 15 years, ranging from 2 to 18 years. 98% of the patients were female. In the initial imaging exam, 8% had a hypoechoic nodule in the breast ultrasound. Of these, 58% had a nodule smaller than 5 cm, 64% did not undergo other exams. In the ultrasound examination for the evaluation of BIRADS, we observed that they had no classification in 42% of the cases, grade II in 2%, grade III in 15% and grade IV in 42%. Analyzing the crossing of BIRADS with the USG of breast size, it is observed that 28% have no classification and have a nodule smaller than 5 cm. In 81% of the cases, the biopsy was performed, and classified by fibroadenoma in 68% of the cases

**Conclusions:** Further research is needed to clarify the best management in pediatric patients with breast nodules, although with a limited incidence of cases, large-scale studies are probably not feasible

EP012/#297 | Poster Topic: AS01 Surgery - IPSO

### EFFICACY OF VIRTUAL REALITY FOR PAINFUL PROCEDURES IN CHILDREN WITH CANCER: A PILOT STUDY

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**Background and Aims:** Virtual reality (VR) has been shown to be a useful technique for assisting people in overcoming a number of anxiety conditions. In this pilot study, we investigated the potential use of VR as a distraction during an invasive medical treatment for children with cancer.

**Methods:** We prospectively collected data about oncological patients (over the age of 7) treated at Bambino Gesù Children's Hospital from July 2022, who underwent painful procedures (i.e. venipuncture, thoracentesis, thoracic or abdominal drainage removal) with [Group A] or without VR [Group B], based on their personal requirements and attitude. Behavioral signs of discomfort by the researcher and reports of pain and anxiety by the patient, parent, and nurse were taken before and during the procedure, using Visual Analogue Scale (VAS) and Children's Hospital of Eastern Ontario Pain Scale (CHEOPS) scales. The child's pulse was monitored throughout the procedure.

**Results:** 40 patients with oncological diseases were included in the study; among them 14 (35 %) underwent painful procedures with the auxilium of VR. The median age was 12.9 years (range 7.48 - 17.72) for Group A and 12.5 years (range 7.34 - 18.03) for Group B. In the analyzed population, lower rating of pain and pain-related behaviors were reported in Group A, on both CHEOPS and VAS scale. Furthermore, the patient's pulses during the procedures were significantly lower in Group A, compared to Group B.

**Conclusions:** The results from this pilot study suggest benefit from using VR distraction, as indicated by lower pain and anxiety ratings, reduced pulse, and fewer observed behavioral indices of distress. The need for larger scale studies and application of VR with younger children is mandatory, especially in pediatric oncology.

EP013/#1339 | Poster Topic: AS01 Surgery - IPSO

### CLAVIEN-DINDO CLASSIFICATION IN PEDIATRIC SURGICAL ONCOLOGY- IS IT UNDER-UTILISED?

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**Background and Aims:** Clavien-Dindo classification has been used as a standardized reporting system in adults. The utility of Clavien-Dindo classification in pediatric surgical-oncology is less explored. We aimed to apply Clavien-Dindo classification in pediatric surgical-oncology.

**Methods:** Prospective study of all children < 16 years of age who underwent surgery from October 2022 to February 2023, excluding the day care and vascular access procedures. Post operative morbidity and mortality were classified based on Clavien-Dindo classification. Post operative interventions and length of stay (defined as time from surgery to discharge) were documented. Grade  $\geq$  III were graded as severe. Non-parametric correlation tests were used for analysis.

**Results:** A total of 119 patients underwent surgery during the study period. Median age at surgery was 36 months (4-180). Abdominal and retroperitoneal surgeries formed the majority of procedures- 61.3% (n=73) followed by thoracic surgeries- 15% (n=18). Overall complication rates were 29.4% (n=35); of which grade <III was 22.7% (n=27) and severe grade (>III) was 6.7% (n=8) with one mortality. The severity of morbidity correlated significantly with the duration of hospital stay (Pearson's  $r$  significance <0.001); mean duration of stay in grade <III= 6.6 days against 12.4 days in grade >III group. Other variables like acute or chronic malnutrition during surgery, duration of surgery or blood loss during surgery failed to show a significant correlation with the severity of morbidity. The application of the objective documentation streamlined the surgical audits.

**Conclusions:** Clavien-Dindo classification is a simple and standardized classification and can be applied in pediatric surgical-oncology. Objective standard documentation of morbidity forms an important tool for surgical audits and also may aid multi-institutional studies and meta-analysis and may prevent ambiguity and under reporting of complications, aids decision making.

EP014/#1348 | Poster Topic: AS01 Surgery - IPSO

#### MEDIASTINAL MUCORMYCOSIS. A SURGEON'S QUANDARY?

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**Background and Aims:** Mucormycosis is an invasive fungal infection that commonly affects the immunocompromised hosts. Most common anatomical sites involved are rhinocerebral, pulmonary, cutaneous, gastrointestinal and disseminated. Isolated mediastinal involvement is rare and poses challenge to diagnosis and management considering the vital structures involved.

**Methods:** Three year old girl, diagnosed with standard risk- acute lymphoblastic leukemia (SR-ALL), had repeated hospitalizations for respiratory distress compounded by febrile neutropenia however blood cultures were sterile. Contrast enhanced computed tomography (CECT) showed neo-onset mediastinal lymph nodal enlargement with invasion into SVC (superior Vena Cava) and upper lobe of right lung. CT guided biopsy showed fungal aseptate branching hyphae suggestive of mucormycosis.

**Results:** Child was started on liposomal Amphotericin B and posaconazole and planned for debridement; but as it was invading SVC planned for surgery with a CPB (cardiopulmonary bypass) circuit backup and the cardiothoracic surgery team. Lesion was approached by median sternotomy and wedge resection of lung with resection of involved pleura and pericardium done. Debridement done over the aorta distal to the origin of coronary arteries. Part of anterior wall of SVC

was resected under CPB, with debridement of luminal mass. SVC was reconstructed with pericardial patch. Child received liposomal Amphotericin B for 2 weeks and is on Posaconazole and asymptomatic and is receiving planned chemotherapy for primary illness.

**Conclusions:** Isolated mediastinal mucormycosis is a diagnostic challenge in the background of ALL or lymphoma. Treatment involves combination of surgical debridement and systemic antifungals for complete response. Due to invasive nature of the infection, extensive surgical planning involving multidisciplinary team is necessary for good outcomes.

EP015/#706 | Poster Topic: AS01 Surgery - IPSO

#### BILATERAL WILMS' TUMOR: 10-YEAR EXPERIENCE FROM A SINGLE CENTER IN CHINA

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**Background and Aims:** To describe our clinical experience with the different surgical approach for bilateral Wilms tumor and evaluate the outcomes of patients treated in our center.

**Methods:** The clinical data of bilateral Wilms' tumor admitted to our hospital from January 2010 to December 2020 were retrospectively analyzed, and the clinical symptoms, surgical approaches and prognosis were summarized.

**Results:** The retrospective analysis included 16 patients: 13 (81.3%) girls and 3 (18.7%) boys. The mean age of the patients was  $17.88 \pm 11.65$  months (range 6~42 months). Except for 1 case of metachronous bilateral lesions, the remaining 15 cases had synchronous tumors. Thirteen patients received neoadjuvant chemotherapy and only eight kidneys (30.8%) responded to chemotherapy. Except for 2 patients who gave up, all the others underwent radical resection, of which 2 patients underwent unilateral radical nephrectomy (RN); 7 patients and 5 patients underwent single-stage and two-stage operation for bilateral lesions, respectively. In all surgical patients, RN was performed on 5 kidneys, nephron sparing surgery (NSS) was performed on 21 kidneys. The positive margins after NSS were found in 6 kidneys (35.3%). After a median follow-up period of 26.3 months, local tumor recurrence and renal insufficiency occurred in 2 and one patients. The 5-year overall and event-free survival rates were 78.1% and 58.6%, respectively. In univariable analysis, the survival rate in the initial chemotherapy group (92.3%) was significantly higher than that in the initial surgery group (33.3%) ( $P=0.048$ ). But positive margin and staged operation ( $p > 0.05$ ) appeared no significantly associated with overall survival.

**Conclusions:** Preoperative chemotherapy has a low response rate for bilateral Wilms tumor but improves overall survival. The approaches and procedures of radical surgery can be selected according to the

condition of the affected kidney. Although NSS has the risk of positive margins and tumor recurrence, it has become a feasible and effective option with good oncologic outcomes.

EP016/#1843 | Poster Topic: AS01 Surgery - IPSO

### THROMBOCYTOPENIA IN PEDIATRIC PATIENTS WITH CANCER UNDERGOING TUNNELED CENTRAL LINE PLACEMENT: IS THERE AN INCREASED RISK OF BLEEDING?

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**Background and Aims:** Thrombocytopenia associated with pediatric cancer may increase the risk of bleeding from tunneled central venous catheter (CVC) placement. However, there is no clear understanding of the degree of risk or consensus on the ideal preoperative platelet level to minimize risk in children with cancer. The purpose of this study is to assess bleeding complications in pediatric patients with cancer who underwent tunneled CVC placement and the effects of perioperative platelet transfusions on the frequency of bleeding complications.

**Methods:** A retrospective cohort study of pediatric patients with cancer who underwent tunneled CVC placement from 1/2014 to 8/2022 (n=429). Bleeding complications were classified by Common Terminology Criteria for Adverse Events (Grades 1-4). Thrombocytopenia was defined as platelet count  $<150 \times 10^3 \mu\text{L}$ . Univariate analysis was used for descriptive statistics. Chi-squared tests assessed differences in outcomes between thrombocytopenic and non-thrombocytopenic patients.

**Results:** 9/429 (2.10%) had a post-operative bleeding complication (3 Grade 1, 1 Grade 2, 5 Grade 3). When comparing patients with thrombocytopenia versus without, thrombocytopenic patients were significantly more likely to have post-operative bleeding complications (7/141, 4.96% vs. 2/288, 0.007%;  $p=0.0033$ ). Platelet count in the patients with a bleeding complication ranged from 47-340 (median 72, Q1-Q3 63-125). 2/9 were not thrombocytopenic, 1/9 had platelets  $100-150 \times 10^3 \mu\text{L}$ , 5/9 had platelets  $50-100 \times 10^3 \mu\text{L}$ , and 1/9 had platelets  $<50 \times 10^3 \mu\text{L}$ . Thrombocytopenic patients who received preoperative platelet transfusions had no difference in bleeding complications compared to thrombocytopenic patients who did not ( $p=0.1805$ ).

**Conclusions:** Our study confirmed that overall bleeding risk is very low in pediatric patients with cancer undergoing tunneled CVC placement. Patients with preoperative thrombocytopenia are more likely to have bleeding complications and to receive transfusions, however, patients who underwent platelet transfusion did not have lower risk of bleeding. Therefore, further investigation to evaluate the efficacy of preoperative platelet transfusion in protection against bleeding complications is needed.

EP017/#705 | Poster Topic: AS01 Surgery - IPSO

### LONG-TERM OUTCOMES OF INFANTILE SACROCOCCYGEAL TERATOMA: RESULTS FROM JAPAN NATIONWIDE SURVEY

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**Background and Aims:** Although sacrococcygeal teratoma (SCT) is often considered to have good prognosis, there are cases of tumor recurrence, bladder and bowel dysfunction, and lower limb dysfunction during long term follow-up. In this study, a nationwide questionnaire survey was conducted.

**Methods:** A questionnaire survey was conducted among all 192 facilities accredited by the Japanese Society of Pediatric Surgeons, covering patients who underwent radical surgery at  $<1$  year of age from 2000 to 2019 and who survived for at least 180 days after birth. Collecting data were investigated and analyzed.

**Results:** Eventually, 355 cases were included in the analysis after exclusion of duplicates and ineligible cases. Median gestational age was 38.6 weeks (26.0-42.3), median birth weight was 3026 g (1020-5344), Altman classification type I-II was 248, type III-IV was 107, mature teratoma was 269, immature was 69, and malignant was 10. Surgical procedures were total in 325 cases, subtotal or partial resection in 27 cases, and perioperative complications were noted in 54 cases. The median postoperative follow-up was 6.6 years (0.5-21.7). 83 patients (23.4%) had functional disability, including 62 (17.5%) with bowel dysfunction, 56 (13.0%) with urinary dysfunction, and 15 (4.2%) with lower limb motor dysfunction. Recurrence occurred in 42 (11.8%) with a median age of recurrence of 16.8 months (1.7-145.1). Risk factors for dysfunction included preterm delivery, maximum tumor diameter, Altman classification type I-II, degree of resection, and perioperative complications. Risk factors for recurrence included pathological findings of immature or malignancy, incomplete resection, and perioperative complications.

**Conclusions:** Postoperative dysfunction was not low, at 23.4%, and 11.8% of the patients had recurrence, which occurred more than 10 years after surgery, suggesting the need for periodic imaging and tumor markers in patients with risk factors. It is necessary to establish treatment guidelines for best practice monitoring for long-term quality of life.

EP018/#1115 | Poster Topic: AS01 Surgery - IPSO

### LONG-TERM OUTCOME OF SURGICAL MANAGEMENT OF HEPATOBLASTOMA: 22-YEAR EXPERIENCE WITH 120 PATIENTS IN A SINGLE CENTER

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**Background and Aims:** Hepatoblastoma (HB) occur mainly in pediatric patients. The treatment is based on resection of tumor as definite treatment in combination of chemotherapy and liver transplantation (LT). Five-year survival of HB was increased to 80% and to 90% in the low-risk group. We present our 22-year experience of surgical management of hepatoblastoma, including hepatectomy and LT.

**Methods:** We retrospectively reviewed patients diagnosed HB from 2000 to 2022. Of 128 patients, 120 patients got surgical management for HB. We analyzed outcome including tumor relapse. Factors affecting HB recurrence was also analyzed. Also, we compared outcome of hepatectomy and LT in advanced HB (PRETEXT III/IV).

**Results:** For recurrence, metastasis ( $p=0.04$ ), lymphovascular invasion in pathology ( $p=0.05$ ), and serum AFP level at operation ( $p<0.001$ ) were significant. Degree of necrosis of tumor (%), resection margin length (cm), and Glissonian capsule invasion were confirmed to have no effect on HB recurrence. For intrahepatic tumor recurrence, there was no significant factor except serum AFP level at operation. Degree of tumor necrosis, margin length, and invasion of Glissonian capsule and lymphovascular invasion were not related with intrahepatic tumor recurrence. When comparing outcome in all advanced HB patients, there was no statistical difference in recurrence outcome between hepatectomy and LT ( $p=0.83$ ). But after matching patients by age, LT has shown better outcome than hepatectomy in advanced HB in recurrence free survival ( $p=0.29$ ). We couldn't compare overall survival because all primary LT patients were survived.

**Conclusions:** In our experience, considering the recent treatment results, HB may be considered as a surgically manageable and curable disease when combined with chemotherapy. Control of tumor burden before operation was most important factor affecting recurrence. Resection margin was no significant effect on either systemic or local recurrence. As a treatment for unresectable HB, LT is conventional but can still be considered as an excellent alternative despite improved outcome of hepatectomy.

EP019/#1538 | Poster Topic: AS01 Surgery - IPSO

#### DIAGNOSIS AND TREATMENT OF ADRENAL MASSES IN CHILDREN: 10-YEAR EXPERIENCE AT A HIGH-COMPLEXITY PEDIATRIC HOSPITAL

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**Background and Aims:** Adrenal neoplasms constitute a wide spectrum of lesions. Despite minimally invasive surgery has gained relevance in the management of this type of tumors, experience in the pediatric population has not been widely documented. The aim of this study is to describe a case series of children with adrenal masses over a 10-year period.

**Methods:** Retrospective review of medical records and register of pertinent variables. Analysis of demographic, clinical, diagnostic and therapeutic data.

**Results:** Thirty cases were identified during the study period. The mean age at diagnosis was 6.92 years (1-16, SD 5.6) and the female-to-male ratio was 2:1. The most frequent symptom was a mass ( $n=18$ , 60%). More than half of the cases had metanephrines, catecholamine metabolites, and cortisol measured. Preoperative work-up mostly included ultrasound and computed tomography, with 73.3% left-sided lesions. The suspected diagnosis according to imaging findings was a neuroblastic tumor in 70% of the cases. Minimally invasive surgical resection was achieved in only 23.3% of the procedures, obtaining complete resection of the lesion in 80% of the cases. The mean operating time was 176 minutes (40-300, SD 64). The most frequent histopathological diagnosis was neuroblastoma in 50% of cases (L1 33.3%, L2 26.7%, M 40%, high risk 40%, 72.2% received systemic therapy), followed by adrenocortical tumors (7%) and pheochromocytoma (3%). Postoperative complications were documented in 23% of the cases (50% Clavien-Dindo I events). The mean follow-up time was 35.3 months (median 18.1, IQR 43.6), at which time 66.6% of the patients were asymptomatic. Three patients were diagnosed with a second neoplasm.

**Conclusions:** Adrenal tumors in children are rare. Despite the wide spectrum of existing lesions, surgical principles are similar. Minimally invasive approaches should be encouraged in selected cases.

EP020/#1488 | Poster Topic: AS01 Surgery - IPSO

#### AN ANALYSIS OF THE PERIOPERATIVE MANAGEMENT OF PAEDIATRIC ADRENAL NEUROENDOCRINE TUMOURS AT CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL, SOUTH AFRICA

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**Background and Aims:** Childhood adrenal neuroendocrine tumours (NETs): pheochromocytomas (PCCs) and neuroblastomas (NBLs) are problematic due to the catecholamine-secreting propensity that may lead to perioperative haemodynamic instability. This study aimed to analyse the perioperative behaviours and intraoperative methods employed in the management of PCCs and NBLs undergoing surgery.

**Methods:** A 10-year retrospective descriptive case series was conducted in children under the age of 18 years undergoing surgery for adrenal NETs at Chris Hani Baragwanath Academic Hospital (CHBAH) from 2011 to 2020. All individuals with a diagnosis of PCC or NBL who underwent surgery were included. Patient anaesthetic charts were retrieved for data capture.

**Results:** Twenty eight patients with adrenal neuroendocrine tumors comprising of 24 NBLs (85.7%) and 4 PCCs (14.3%) were included. Sex distribution was 54% males and 46% females. Hypertension and cardiac manifestations occurred in 25% and 12.5% of NBLs, and 75% and 50% of PCCs respectively. The median age of excision was 3 years for NBLs and 11 years 6 months for PCCs. Pre-excisional intraoperative NBL management included an alpha antagonists (4.2%, n= 1), magnesium sulphate (MgSO<sub>4</sub>) (4.2%, n= 1) and alpha<sub>2</sub> agonists (12.5%, n= 3). Pre-excisional intraoperative PCC management included alpha antagonists (25%, n= 1), beta blockers (25%, n= 1), nitro-glycerine (50%, n= 2) and MgSO<sub>4</sub> (25%, n= 1). Post-excisional management of NBLs included alpha agonists (25%, n= 6) and beta blockers (4.2%, n=1). Post-excisional management of PCCs included alpha agonists (25%, n= 1), adrenaline (50%, n= 2) and MgSO<sub>4</sub> (25%, n=1). Catecholamine inducing anaesthetic agents were avoided. There was no perioperative morbidity or mortality.

**Conclusions:** PCC required a larger proportion of sympatholytic agents prior to excision, and sympathomimetic agents post excision relative to NBLs to achieve haemodynamic stability. The excellent postoperative outcomes suggest that the perioperative management of PCCs and NBLs is highly effective in a South African setting.

EP021/#535 | Poster Topic: AS01 Surgery - IPSO

#### LAPAROSCOPIC RESECTION OF NEUROBLASTOMA WITH VASCULAR IDRFs: IS IT FEASIBLE?

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**Background and Aims:** The current recommendation for neuroblastoma resection by laparoscopy relies on a small size of the tumour

and the absence of image-defined-risk-factors (IDRF). The presence at preoperative images of vascular IDRF has so far precluded surgeons from trying to develop a minimally invasive approach. We present a preliminary experience of patients operated on by laparoscopy for neuroblastoma encasing major abdominal vessels.

**Methods:** Among patients with neuroblastoma resection in our institution in 2022, we collected all cases operated on by laparoscopy and presenting encasement of aorta and/or celiac trunk (CT) and/or superior mesenteric artery (SMA) and/or inferior vena cava (IVC) at preoperative assessment.

**Results:** Six girls and one boy with a median age at surgery of 2.5 years [1.3-12.5] presented with neuroblastoma (n=5), ganglioneuroma (n=1) and ganglioneuroblastoma (n=1). Neo-adjuvant chemotherapy followed HRNBL02 (n=3, 2 Rapid Cojec and one GPOH) or LINES group 8 protocols (n=3). The patient with ganglioneuroma was operated upfront. The tumour was from adrenal gland (three right and two left) or perivascular sympathetic chain (two around the aorta) and measured a mean of 11 cm at diagnosis [5.7-17] and 7 cm at preop [5.3-12]. Four patients lost IDRF with neo-adjuvant chemotherapy but encasement of CT and SMA remained in five patients, three of them having also aorta encasement. Four patients had IVC encasement. The mean operative time was 406 mn [366-453]. Conversion occurred in two patients, one because of very strong adherences to IVC and the other because of aorta rupture due to tumoral wall infiltration. Postoperative complications were one portal thrombosis with cavernoma, one chylous ascites and one re-operation for bleeding. All patients are alive except one at last follow-up.

**Conclusions:** Laparoscopic resection of neuroblastoma with encasement of major abdominal vessels is feasible but remains very demanding. Further experience is needed to confirm this preliminary experience.

EP022/#645 | Poster Topic: AS01 Surgery - IPSO

#### CLEAR CELL SARCOMA OF THE KIDNEY (CCSK): OUR EXPERIENCE!

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**Background and Aims:** Clear cell sarcoma of the kidney is the second most frequent paediatric kidney tumour after Wilms' tumour (WT). The present study aims to evaluate the overall survival, the event-free survival and the recurrence rate of children treated for Clear Cell Sarcoma of the Kidney (CCSK) patients.



**Methods:** Children treated for CCSK from 2000 through 2023 were included in the study. The staging was done as per NWTS-5 recommendations. The overall survival, event-free survival and recurrence rate were evaluated in these patients. Kaplan Meier Analysis was done for 4-year Overall Survival (OS) and 4-year event-free survival (EFS).

**Results:** Thirty-eight patients with CCSK were treated and followed up in the paediatric surgical oncology clinic. Out of which 35 were included in the study. There were 27 males (77.14%) and 8 females (22.86%). The median age of the patients at diagnosis was 38 months. The patients were staged and managed as per NWTS/ COG protocols. Metastases at presentation were present in 6 patients. All but one patient presented with a mass. The median size of the mass was 12 cm (7-20 cm). Pre-operative chemotherapy was given to 19 patients and the remaining underwent upfront surgery. Of the 35 patients, 16 had events (12 recurrences, 1 disease progression and 3 deaths). At the last follow-up at a median age of 26 months (0.5 to 195 months), 26 children were alive of which 21 patients were disease-free. The 4-year overall survival rate was 65% [CI 42% to 80%] and the 4-year event-free survival (EFS) rate was 50% [CI 31% to 66%].

**Conclusions:** Clear cell sarcoma has less favourable overall and event-free survival as compared to Wilms tumour. Recurrence was noted in one-third of our patients hence diligent follow-up is necessary.

EP023/#1763 | Poster Topic: AS01 Surgery - IPSO

#### SMALL CENTER, GOOD RESULT OF TOTAL THYROIDECTOMIES

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**Background and Aims:** The high volume centers providing better result in the surgical treatment of rare paediatric conditions such as thyroid cancer. What should do in a small country and the lack of giant hospitals? The disease specific centralization and specialized single surgeon experience maybe the solution.

**Methods:** Our 124 beds paediatric hospital is mainly specialized for paediatric tumours and endocrine diseases, multidisciplinary treatment provided. We listed our patients underwent total thyroidectomy from 2006-2022. All patients had been operating on by the same surgeon. All together 61 patients listed (2-17 y), M/F 20/41. 6 prophylactic thyroidectomies (MEN2A, MEN2B), 42 papillary cancer, 7 Thyroiditis and 6 Basedow diseases were the basic conditions. All the malignant patients underwent preoperative imaging and FNAB. 29/42 cases showed pathologic lymphnodes, to whom central lymphnode dissection attempted at the same time of thyroidectomy. Lateral dissection carried out after isotope treatment (7 cases) The thyroidectomy always done by Bliss method, with careful isolation of recurrent laryngeal nerve and parathyroid glands.

**Results:** None of the patients had LRN injury. All the patients got profylactic Calcium substitution until the endocrine check-up. Two patients need long term Calcium administration (1 year) all the others have normal parathyroid function. These patients underwent extended cervical lymphnode dissection due to advanced disease. These results seems comparable with the results of high volume centers.

**Conclusions:** If there is no available high volume center in the region, the disease specific centralization and the single surgeon experience may provide significantly good results.

EP024/#1579 | Poster Topic: AS01 Surgery - IPSO

#### ACCURACY OF 3D RECONSTRUCTION IN BILATERAL WILMS TUMOUR CASES, INITIAL EXPERIENCE

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**Background and Aims:** The 3D reconstruction is gaining an important role in the treatment of pediatric solid tumours. It's goal is to preserve the maximum amount of healthy tissue during the parenchymal sparing resections, like in case of bilateral Wilms tumour.

**Methods:** We retrospectively analyzed the accuracy of 3D reconstruction in our bilateral Wilms tumour cases. We used MRI for diagnostic. MRI sequences required T1W, contrast media enhanced arterial, venous and 5 minute nephrogenic phase, T2W SPAIR/TSE and MRI angiography We've used DICOM data sets, through Philips SmartCT software. Manual algorithms including "grow from seed" and "fill between slices" used in tumour and parenchyma imaging with 5 minute sequence nephrogenic MRI. Following the completion of tumour, parenchyma, vein, artery and urinary collecting system imaging; correction of under or over-segmentation is often required using the "scissor" tool and "smoothing out" of rigid structures to ensure accuracy. The difficulties are: moving artefacts (breathing) uncertain border, compressed surrounding structures, lack of difference of density of tumour and healthy tissue, poor arterial phase due to slow process of MRI. From 2013-2021. 5 patients with synchronous bilateral Wilms tumour found, M/F: 3/2. All received chemotherapy, (6-12 cycles VA) followed by surgery in two stages. Four patients underwent bilateral NSS, one nephrectomy and contraside NSS done. All the patients were tumourfree on the postop MRIs. One late nephrectomy carried out because of local relaps. We analyzed the correlation of 3D and the surgical findings. We classified the accuracy of 3D: Accurate, when surgical findings match with the preop 3D pictures; Acceptable, if different but surgically managed; Failed if tumour left behind or unexpected nephrectomy done.

**Results:** In 8 out of 10 kidneys the findings were accurate, in 2 cases acceptable. No failed 3D found.

**Conclusions:** This result seems more accurate than expected, especially since the 3D imaging is mostly a subjective handwork.

EP025/#727 | Poster Topic: AS01 Surgery - IPSO

### CLINICO-MORPHOLOGY, DIAGNOSIS, AND SURGICAL CHALLENGES WITH TROUBLE SHOOTING IN THE MANAGEMENT OF PHEOCHROMOCYTOMA -PARANGLIOMA

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**Background and Aims:** Pheochromocytomas (PCCs) and paragangliomas (PGLs) commonly referred together as PPGL are rare neuroendocrine tumors (NETs) and the clinical experience in pediatric age group is difficult to achieve due to their rarity. It secretes catecholamines and can mimic a wide range of medical disorder. Its diagnosis and management is challenging, especially the timing of surgery and perioperative medical management. The aim of our study is to review the clinic-morphological features, diagnosis, perioperative management, challenges in the surgical management with various approaches and its trouble shooting from a single tertiary care centre, India.

**Methods:** Retrospective data of PPGL treated at JIPMER, Pondicherry over last 10 years were collected from OT register, case records and hospital information system.

**Results:** Total 7 cases (3 pheochromocytoma, 3 paraganglioma and one had both pheochromocytoma and paraganglioma) were operated. The age ranges from 2 years -14 years with M/F ratio of 4:3. The common presenting symptoms were Hypertension - 85%(6/7) headache & vomiting -43%(3/7), palpitations - 28.5% (2/7). The plasma/ urinary catecholamines were elevated in 71.5% (5/7) cases. Four of 7 cases (57%) had grade III-IV hypertensive retinopathy. All patients had lesion detected on CECT scan and six (85.7%) had MIBG avid lesion. Three were operated via minimal invasive surgery (MIS), one case had laparoscopic converted to open due to IVC injury and three via open surgery. One had significant intraoperative bleeding and one had residual lesion in the contralateral side. Six of the 7 are doing well on follow-up and one with residual lesion is planned for redo surgery.

**Conclusions:** MIS is feasible in Pediatric PPGL, whether the lesion is adrenal or extra-adrenal in location, and the complication can be minimized by proper selection of cases and surgical approach, with bilateral lesion or multiple PPGL having higher risk of complications. Lifelong follow-up is needed to detect recurrence and metastasis.

EP026/#1528 | Poster Topic: AS01 Surgery - IPSO

### PRESENTATION AND CHALLENGES IN THE MANAGEMENT OF HIGH RISK HEPATOBLASTOMA AND ITS OUTCOME: EXPERIENCE OF RESOURCE CHALLENGED NATION FROM A TERTIARY CARE CENTRE

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**Background and Aims:** Hepatoblastoma (HB) is the most common primary malignant liver tumor in children and its management depends upon risk stratifications. The outcome of high risk HB varies and remains dismal in resource challenged nations where access for chemotherapy and liver transplantation is limited for poor. The aim of this study is to evaluate the outcome of children with high-risk hepatoblastoma treated at a tertiary referral centre in a resource-challenged country where pediatric liver transplantation is not easily available.

**Methods:** It is a retrospective study of Pretext high risk HB treated at JIPMER, Puducherry and the data were collected from January 2012-December 2022

**Results:** Of the 21 cases of HB treated over the last 10 years, 12 were high risk HB (7 girls and 5 boys) on the basis of pretext staging and various annotation factors, V (1), M (5), E (1), C (4), F (2) and three had multiple annotations. Three patients died before surgery due to chemotherapy related toxicity (1 -ADR toxicity, 1- febrile neutropenia and 1- unknown), one had immediate postoperative death (IVC and renal vein thrombosis) and two had death due to recurrence. Of the 9 cases who underwent surgery, 6 had standard hepatectomy, one had trisectionectomy, 2 had non-anatomical resection/segmentectomy and one each had cavotomy and atriotomy for IVC thrombosis removal under cardiopulmonary bypass and caudate lobe resection in addition to standard hepatectomy. Six of the 12 children were alive at last follow-up with overall survival of 50% with average followup of 15 months (range from 1 months-40months)

**Conclusions:** Management of high risk HB continues to be gloomy and limited by availability of pediatric liver transplantation and availability of experts in performing extreme resection resource challenged nations. The issue further aggravated by CT related toxicity and complications.

EP027/#572 | Poster Topic: AS01 Surgery - IPSO

**PELVIC EWING SARCOMA IN CHILDREN AND ADOLESCENTS**Rejin Kebudi<sup>1</sup>, Ülkü Miray Yıldırım<sup>1</sup>, Ayça Iribaş<sup>2</sup>, Bülent Zülfikar<sup>1</sup>, Bilge Bilgiç<sup>3</sup><sup>1</sup>Istanbul University Oncology Institute, Pediatric Hematology-oncology, İstanbul, Turkey, <sup>2</sup>Istanbul University Oncology Institute, Radiation Oncology, İstanbul, Turkey, <sup>3</sup>Istanbul University Oncology Institute, Pathology, İstanbul, Turkey**Background and Aims:** Pelvis is one of the primary sites of Ewing sarcoma (ES). Prognostic factors of pelvic ES remain controversial. This study aims to assess the demographic, clinical and therapeutic features, prognostic factors in children with pelvic Ewing Sarcoma.**Methods:** Files of 264 children/adolescents with Ewing sarcoma diagnosed and treated between 1990-2022 in our center were retrospectively reviewed, 42(15.9%) were located in the pelvis. All received a chemotherapy regimen of ifosfamide-etoposide, alternating with vincristin, adriamisin/actinomycinD and cyclophosphamide (IE/VAC). Variables were analyzed using the Kaplan-Meier method and log rank test.**Results:** The median age of the 42(23 male, 19 female) patients was 12.5(2-16) years. Seventeen (40 %) had metastasis at diagnosis. Radiotherapy (RT) was given to 36 patients (10 preoperatively, 5 post-operatively, 21 definitive dose), 19 underwent surgery (4 at diagnosis, 14 had additional RT). Surgical margins were positive in 6 and negative in 13. The histopathological necrosis was <90% in 6 and ≥ 90% in 9. The median follow-up was 55.5(10-370) months. At a median of 13 months (3-115), 22 had recurrence (9)/progression (13). The 3-year event free survival (EFS) and overall survival (OS) were 50.1% and 62.6%; in all; 62.2 and 75.3% in nonmetastatic; 31.9% ve %42.9% in metastatic patients ( $p=0.048$ ,  $p=0.028$ ) respectively. The 3-year EFS and OS were significantly higher in patients with negative surgical margins compared to ones with positive margins [(%83.9 vs 0 % ( $p=0.001$ ) and %91.7 vs %16.7 ( $p=0.001$ )]. The 3-year EFS and overall survival OS were higher in patients with ≥90% necrosis [76.2 vs 33.3 % ( $p=0.029$ ); 87.5 vs 50% ( $p=0.13$ ) respectively]. The mode of local therapy (surgery/RT/RT+surgery) was not prognostic.**Conclusions:** In our cohort 40% had metastasis at diagnosis. Metastasis, positive surgical margins, poor necrosis rate were poor prognostic factors for outcome. Patients with localized pelvic Ewing sarcoma had a successful outcome with multidisciplinary treatment approach.

EP028/#623 | Poster Topic: AS01 Surgery - IPSO

**INFANTILE FIBROSARCOMAS: CLINICAL FEATURES, TREATMENT AND OUTCOME**Rejin Kebudi<sup>1</sup>, Ülkü Miray Yıldırım<sup>1</sup>, Fikret Asarcıklı<sup>2</sup>, Banu Oflaz Sözmen<sup>2</sup>, Fatih Erbey<sup>2</sup>, Bülent Zülfikar<sup>1</sup><sup>1</sup>Istanbul University Oncology Institute, Pediatric Hematology-oncology, İstanbul, Turkey, <sup>2</sup>Koç University, Pediatric Hematology Oncology, İstanbul, Turkey**Background and Aims:** Resection with negative margins without morbidity is the mainstay of treatment of infantile fibrosarcoma (IFS). When primary surgery isn't possible, satisfying results can be obtained with surgery after neoadjuvant chemotherapy. Recently, targeted therapies have been used successfully. This study aims to evaluate the clinical features, treatment and outcome of patients with IFS.**Methods:** Files of children with IFS between 1990-2022 were retrospectively reviewed.**Results:** The median age of 10 patients (7 male, 3 female) was 88 days (7-360). Tumor localization was extremity in seven and scapula, cervical and thoracic region in one each. All were non-metastatic at diagnosis. Primary surgical excision was performed in five patients; three of them had positive margins and two of these experienced recurrence. Margins were negative in other two and recurrence occurred in one of them. Of the five patients treated with primary chemotherapy, two had complete response, surgery was not performed, both are under follow-up (138 months, 191 months). Surgical resection was performed in one patient progressed despite chemotherapy. Larotrectinib was initiated to a patient with an inoperable tumor at diagnosis and partial response to chemotherapy after NTRK1-LMNA fusion was detected. He responded very well to larotrectinib, was operated, but margin was positive. Tumor relapsed a year later. He was operated with a negative margin and larotrectinib was initiated again, he is under treatment. Another patient experienced progression under chemotherapy was operated. ETV6-NTRK3 fusion was detected and larotrectinib was started. Tumor was unresponsive, the family abandoned the treatment. Eight of ten patients survived disease-free for a median of 122.5 months (36-191).**Conclusions:** Surgical resection is important IFS if feasible. Recently, successful results have been reported with Larotrectinib. Use of targeted therapies can be increased by conducting molecular studies, especially in cases not suitable for surgery with a goal of avoiding side effects of conventional chemotherapy.

EP029/#1537 | Poster Topic: AS01 Surgery - IPSO

**WILMS TUMOR SURGERY WITH LOW COST IN-HOUSE 3D PRINTING MODELS: A PROMISING TOOL FOR SURGICAL PLANNING**Núria Adell-Gómez<sup>1</sup>, Arnau Valls-Esteve<sup>1</sup>, Albert Pasten<sup>2</sup>, Josep Munuera<sup>3</sup>, Lucas Krauel<sup>2</sup><sup>1</sup>Barcelona Children's Hospital Sant Joan de Déu, 3d For Health Unit, Barcelona, Spain, <sup>2</sup>Sant Joan de Deu Hospital, Oncology Pediatric Surgery, Esplugues de Llobregat, Spain, <sup>3</sup>Sant Joan de Deu Hospital, Diagnostic Imaging, Barcelona, Spain

**Background and Aims:** Wilms tumor (WT) is a type of kidney cancer that mainly affects young children. Among other clinical advances, 3D printing (3DP) has emerged as a promising tool for surgical planning. 3DP allows for the creation of patient-specific models of the affected kidney. These models are created from Computed Tomography (CT) or Magnetic Resonance Imaging (MRI) and provide a 3D representation of the kidney and tumor. Surgeons can better understand the tumor's location, size, shape, anatomical relations and plan a more precise surgical procedure. Our aim is to show out in-house 3D printing workflow and its possibilities.

**Methods:** We present three complex WT in which surgery was planned using 3D printed models manufactured in-house. The workflow has been: 1. Image Segmentation from DICOM combining both CT and MRI images using automatic and semi-automatic tools from the IntelliSpace Portal (Philips, Netherlands). 2. 3D virtual planning by using 3-Matic from Materialise® software (Belgium). 3. 3DP using a J5 Stratasys printer and multi-colour photopolymers. 4. Quality control.

**Results:** The 3DP models were produced by a combination of multi-colour, soft and rigid photopolymers for surgical planning discussion. The models presented different harnesses (from Shore 45A to Shore 90A). The mean printing time was 11h and a mean production cost of 210 € per model. Young surgeons were actively engaged on the surgical planning conference.

**Conclusions:** - 3DP of WT cases was feasible in a reasonable time frame period. - 3DP replicas were accurate and realistic. - 3DP allowed the manufacture of different aspects of the surgical planning such as tumor and kidney as a whole, tumor volume alone and kidney without tumor. - In house 3DP is affordable. - 3DP materials are still hard but new 3DP materials with different characteristics that mimic human anatomy will help to improve the surgeons surgical planning experience and simulation.

EP030/#1777 | Poster Topic: AS01 Surgery - IPSO

#### PROPOSING A NEW SURGICAL PLANNING TOOL FOR NEUROBLASTOMA USING 3D PRINTING AND VIRTUAL REALITY TECHNOLOGY: A QUALITATIVE STUDY ON A PATIENT-SPECIFIC MODEL

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**Background and Aims:** Neuroblastoma (NB) is one of the most common solid tumors in children. Surgery is a critical component of the treatment, and Image Defined Risk Factors (IDRF) in NB are a challenge for the surgeon. The use of 3D printing (3DP) and virtual reality (VR) technology has emerged as a promising approach for improving surgical planning and outcomes. Our aim is to evaluate the user experience

of 3DP and VR in comparison with standard biplanar imaging in a group of paediatric surgical oncologists.

**Methods:** After being exposed to an IDRF NB case using conventional medical imaging (CT), 3DP and VR, twenty paediatric surgical oncologists responded to a qualitative questionnaire. The questionnaire was prepared regarding the usefulness of the different techniques for surgical planning and contained three questions to be rated in a scale from 1 to 10. The 3D model was designed using 3-Matic from Materialise® software and produced by a combination of multi-colour, soft and rigid photopolymers 3D printed with PolyJet Technology using a J5 Stratasys printer. The VR model was segmented using IntelliSpace Portal (Philips) and 3-Matic from Materialise® software and visualized through a Oculus Quest 2 headset.

**Results:** The results show that the option that VR can be a good alternative to 3DP for the planning of complex NB was rated an average of 8. Additionally, in more than 50% of the opinions, both VR and 3DP were positioned as better options than conventional 2D medical imaging.

**Conclusions:** 3DP and VR technology allow for a detailed and accurate understanding of the patient's anatomy and can help to identify potential challenges that may not be apparent from traditional 2D imaging. VR can further enhance the planning process by providing a more immersive and interactive experience, while 3DP provides a unique tactile experience.

EP031/#1475 | Poster Topic: AS01 Surgery - IPSO

#### CHALLENGES IN THE MANAGEMENT OF NON-SYNDROMIC SYNCHRONOUS BILATERAL WILMS TUMOR WITH A RARE COMBINATION OF CARDIOTOXICITY AND INFERIOR VENA CAVA THROMBUS

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**Background and Aims:** Synchronous bilateral Wilms Tumor (WT) occurs in less than 10% of the cases of WT. Inferior vena cava (IVC) thrombus and cardiotoxicity due to anthracycline are also infrequently seen in WT cases. However a combination of all bilateral WT with IVC thrombus with cardiotoxicity in a small child, though very rare, presents a unique set of challenges and involves multidisciplinary management. The aim is to present the challenges in the management of such a unique case.

**Methods:** Retrospective review of a case of non-syndromic WT with a unique combination of bilaterality, IVC thrombus and cardiotoxicity.

**Results:** A one-and-a-half-year-old girl presented with distension of abdomen for a duration of one month. On evaluation patient was

found to have non-metastatic bilateral renal tumours with larger tumor on the right side. Syndromic evaluation was normal. The size of the tumours did not decrease despite twelve weeks of neo-adjuvant chemotherapy. The patient also had associated sub-hepatic IVC thrombus. The patient however developed anthracycline associated cardiotoxicity with severe left ventricle dysfunction. Haemodialysis catheter was placed pre-operatively. The patient underwent right nephrectomy and left nephron sparing surgery. A combination of diuretics, angiotensin-converting enzyme inhibitors and beta blockers were used in the peri-operative period with careful monitoring of the blood pressure. The patient did not require dialysis and had normal renal function in the post-operative period. Histopathology showed Wilms tumor with rhabdomyoblastic differentiation and received anthracycline-free adjuvant chemotherapy. The cardiac function improved post-operatively. The patient is currently on follow-up and has no recurrence.

**Conclusions:** The presence of IVC thrombus and cardiotoxicity in a case of bilateral WT requires individualised treatment with multi-disciplinary care, requiring close monitoring of the renal and cardiac function.

EP032/#507 | Poster Topic: AS01 Surgery - IPSO

#### IS MANDATORY COCCYECTOMY STILL APPROPRIATE FOR NEONATAL PERI-COCCYGEAL TUMOUR RESECTION?

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**Background and Aims:** Sacrococcygeal tumours are germ cell tumours within a diverse group of masses that may occur within the region of the pericoccygeal area. At the time of surgical resection the exact diagnosis is not always known. The UKCCLG guidelines for resection of sacrococcygeal teratomas mandates coccygectomy, either primary or delayed, due to risk of malignant recurrence. This paper aims to review practice and its implications.

**Methods:** In a tertiary paediatric surgical centre, a retrospective review was undertaken of all lesions resected from the pericoccygeal region to determine compliance with guidelines of mandatory coccygectomy for suspected or potential sacrococcygeal teratoma. Cases were identified from pathology reports and SNOMED codes for relevant topography and morphology across a 23 year period to 2023.

**Results:** There were 28 tumours excised. Coccygectomy was performed in 15 cases. There were 21 germ cell tumours resected; 18 mature teratomas and 3 immature teratomas. The remaining cases included retrorectal cystic hamartomas, fibrolipoma and lipoblastoma. To date there has been no tumour recurrence.

**Conclusions:** The evidence base for mandatory coccygectomy is controversial. Practice worldwide varies. This review shows poor compliance with UKCCLG guidelines with no adverse effects to date. The implications for surgery on undifferentiated tumours and wider literature review will be presented.

EP033/#1413 | Poster Topic: AS01 Surgery - IPSO

#### LIVER TRANSPLANTATION FOR POST-TEXT IV HEPATOBLASTOMA WITH TUMOR THROMBI INTO RIGHT ATRIUM, INFERIOR VENA CAVA, AND PORTAL VEIN: THE FIRST CASE IN MAINLAND OF CHINA

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**Background and Aims:** Pediatric hepatoblastoma (HB) with tumor thrombi extending into right atrium, inferior vena cava, and portal vein[A1] presents as a real clinical challenge. We report the first documented case in mainland of China of Liver transplantation for an advanced POST-TEXT IV HB with extensive tumor thrombi into right atrium (RA), inferior vena cava (IVC), and portal vein[A2]. **Methods:** We report a 6-year-old boy with pre-TEXT IV HB with tumor thrombi extending into right atrium, inferior vena cava, and portal vein[A3] in Shanghai children's hospital, Medicine school, Shanghai Jiaotong University.

**Methods:** The boy weighed 17 kg, with serum alpha-fetoprotein (AFP) at the level of 121000 ng/ml at diagnosis. After 6 cycles of COG chemotherapy, the tumor thrombus declined in the portal vein and thrombi in IVC and RA also regressed to subhepatic vena cava and suprahepatic vena cava. The hepatoblastoma shranked obviously but still involving 4 sectors of the liver. We performed tumor thrombectomy without cardiopulmonary bypass (CPB), liver transplantation (LT) from donation after cardiac death (DCD), and vascular reconstruction. The operation was completed successfully within 11 hours, and the liver's function and AFP levels gradually tended to normalize 2 weeks after the operation. The patient survived till now followed by 2 cycles of chemotherapy after LT.

**Results:** A 3-year postoperative follow-up revealed normal level of AFP and hepatic function with no sign of recurrence. The computed tomography (CT) scan revealed no signs of thrombi in the portal vein, inferior vena cava and atrium. None of the similar cases have been reported yet in the Chinese mainland

**Conclusions:** This case illustrates that LT is as the treatment option for the extremely advanced of the extensive tumor thrombi the right atrium, inferior vena cava, and portal vein[A1] with POST-TEXT IV hepatoblastoma.

EP034/#1474 | Poster Topic: AS01 Surgery - IPSO

#### OUTCOME OF PULMONARY METASTASECTOMY IN PAEDIATRIC SOLID TUMOURS PATIENTS

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**Background and Aims:** Lung is the commonest site of metastases in most pediatric solid tumors. This study evaluates the surgical management and outcome of these patients undergoing pulmonary metastasectomy.

**Methods:** Review of prospectively maintained data of patients operated for pulmonary metastases from September 2001 through June 2022 for their presentation, surgery and outcome. Kaplan Meir estimates for a 4-year event free survival (EFS) and overall survival (OS) was done.

**Results:** Sixty-eight patients underwent 106 thoracotomies for removal of 238 lung metastases (range 1-20 metastases). Primary diagnosis was Osteosarcoma (OSa) in 29; Wilms tumor (WT) 17, hepatoblastoma (HB) 11, malignant germ cell tumor (MGCT) 5 and Soft tissue Sarcoma 6(2 Ewing sarcoma (EW), 2 rhabdomyosarcoma (RMS) and 2 synovial sarcoma (SSa)). Fifty-eight thoracotomies were done for lung metastases that were already present at the time of primary diagnosis while 48 thoracotomies were done for pulmonary recurrence. Twenty-five patients (15 OSa, 5 HB, 4 WT and 1 MGCT) had bilateral metastases and 21 of them underwent bilateral staged metastasectomy. One patient died while another showed contralateral resolution after the first stage. Two others did not undergo contralateral surgery. Twelve repeat thoracotomies were required (8 OSa, 3 WT and 1 HB). The type of resection done included 48 lobectomies, 45 wedge resections (11 with additional sub-pleural resections) and 10 subpleural resections. Only biopsy was performed in one and two had negative thoracotomy. Twenty-four of 68 died and 38 had various events (including re-recurrence/progression). 4-year EFS was 35.4% (95 CI 21.8 - 49.0) and OS of 53.6% (95 CI 38.2 - 69.0) with a median survival time of 22.5 months.

**Conclusions:** Pulmonary metastasectomy, is a viable option for achieving survival in patients who have not achieved pulmonary clearance with chemotherapy. It leads to an acceptable 4-year EFS (35.4%) and OS (53.6%) in patients who would otherwise have progressed and died.

EP035/#85 | Poster Topic: AS01 Surgery - IPSO

#### THE ROLE OF PRE-OPERATIVE SPINAL ARTERIOGRAPHY IN ADDITION TO IDRFs (IMAGE-DEFINED RISK FACTORS) IN THE ASSESSMENT OF PATIENTS WITH LOWER MEDIASTINAL NEUROBLASTOMA: A PILOT STUDY

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**Background and Aims:** Patients with Lower Mediastinal Neuroblastoma (LMNB) are at higher risk of operative neurologic complications and sequelae for the possible lesions of the Adamkiewicz artery (AKA). This reduces the possibilities of complete resection. The role of pre-operative Spinal Angiography (POSA) has to be defined. The aim of our study was to investigate the role of POSA for patients with LMNB.

**Methods:** We conducted a retrospective analysis of patients with LMNB studied with POSA between November 2015 and February 2022 at our tertiary pediatric hospital, with particular emphasis on complications and outcomes of angiography and surgery.

**Results:** Six patients were identified. The tumor was thoracoabdominal in three cases. According to INRG, three patients were L2 and three were M. Two patients had N-MYC amplification. The surgery was evaluated after induction chemotherapy. The median number of IDRF was 2 (range: 1-8) at diagnosis, while pre-SA was 2.5 (range: 1-6). The POSA identified an AKA homolateral to the tumor in 4 cases, without periprocedural complications. Five (83%) patients underwent elective resection. One patient did not undergo surgery. Among the five surgical treated patients, two (33%) experienced intraoperative complications: one mild pulmonary laceration (sutured) and one aortic lesion (repaired). Three (60%) patients had a gross total resection at CT. After a median FU of 4.1 years (range: 2.6-8) from diagnosis, no patients developed neurologic sequelae for surgery. Five (83%) patients were alive and well at the end of the FU, while one deceased after a refractory recurrence.

**Conclusions:** In children affected by LMNB, the pre-operative SA is a safe procedure helpful to a correct identification of AKA in order to plan the best surgical approach that allow a radical surgery in more than 50% of LMNB with major IDRFs without neurological sequelae.

EP036/#1142 | Poster Topic: AS01 Surgery - IPSO

#### THE STUCK CATHETER: A RARE (BUT TRICKY) COMPLICATION OF CENTRAL VENOUS CATHETERS

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**Background and Aims:** The use of long-term central venous catheters (CVC) in specific pediatric settings is widely spread, still, complications can arise during both the insertion and the removal procedure.

**Methods:** In this study, we reviewed all cases treated in two Tertiary Pediatric Centers, between January 2011 and March 2023, in which long-term subcutaneously tunneled CVC were stuck at removal and, therefore, required a variation in the surgical approach.

**Results:** In the cited period, we removed 2367 subcutaneously tunneled CVC. In 16 cases (0.7%), the catheter was stuck at the time of removal. Removals were planned in 7 cases for catheter malfunction, in 7 patients for end of treatment and in 2 cases for catheter-related sepsis. Eight patients presented malignancies, while the others had non-oncological diseases (i.e. cystic fibrosis, low birth weight etc). Median age at removal was 9 years (0.25 – 33 years) and median time of stay was 2.5 years (1-6 years). Five CVC were placed surgically and eleven through US-guided technique. In 6 cases, the exit-site of the catheter was on the arm and in 10 on the thoracic wall. A counter incision to isolate the catheter at the site of insertion in the jugular vein was performed in 6 patients, while in one case a sternotomy was required. In one case, the vein was reconstructed with a heterologous pericardial patch. In 4 of the cited cases the cardiac surgeon was involved. The removal was staged in a second setting in 4 patients. In 1 case the patient is waiting for a second stage removal and in 2 cases the catheter was left in place.

**Conclusions:** One uncommon yet significant side effect of long-term tunneled catheter use is their retention. Surgeons should be aware of this complication, in order to be able to effectively adequate the surgical program.

EP037/#1085 | Poster Topic: AS01 Surgery - IPSO

#### TRAP-DOOR AND CLAMSHELL THORACOTOMY AS SURGICAL APPROACHES FOR CERVICOTHORACIC TUMORS IN CHILDREN

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**Background and Aims:** The surgical approach to cervicothoracic tumors represents a challenge in pediatric surgical oncology. The aim of this study was to evaluate trap-door and clamshell thoracotomy as surgical approaches for solid cervicothoracic tumors in children.

**Methods:** We retrospectively evaluated 22 children with solid cervicothoracic tumors who were treated at our institution between 2015

and 2023. Thirteen children had neuroblastic tumor, 3 children had rhabdoid tumor, 1 child had Ewing sarcoma, and 1 child had inflammatory myofibroblastic tumor. Two children had thoracic metastases from osteosarcoma, 1 child from clear cell sarcoma of the kidney, and 1 child from hepatoblastoma. Diagnostic work up consisted of cross-sectional imaging and was supplemented by plexus ultrasonography in 3 children and thoracic angiography in 8 children. The surgical approach was determined based on the location of the tumor.

**Results:** The mean age of patients (13 girls and 9 boys) at surgery was 173 months (range 20 - 534 months). Trap-door thoracotomy was performed in 13 and clamshell thoracotomy in 9 children. Successful resection (Local control) was achieved in 13/13 children by trap-door and in 8/9 children by clamshell thoracotomy. Mean operating time was 240 minutes for trap-door thoracotomies (range 122 – 424 minutes) and 192 minutes for clamshell thoracotomies (range 120 – 381 minutes). In 2 children grade IIIb complications according to Dindo-Clavien classification occurred after trap-door thoracotomy. After a mean follow-up of 20.5 months (range 0 – 150 months) event-free survival was observed in 12/13 children who had undergone trap-door thoracotomy and 7/9 children who had undergone clamshell thoracotomy.

**Conclusions:** Surgical removal of cervicothoracic tumors in children can be successfully performed with good surgical and oncological outcomes using trap-door and clamshell thoracotomy.

EP038/#602 | Poster Topic: AS01 Surgery - IPSO

#### CORRELATION OF CT SCAN RESPONSE TO NECROSIS AND VOLUME CHANGES WITH HISTOPATHOLOGY IN CHILDREN WITH WILMS' TUMOR

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**Background and Aims:** This study is to correlate the amount of necrosis and tumor volume change found in preoperative Contrast Enhance Computed Tomography (CECT) scan of abdomen with post-operative histopathological findings of Wilms Tumor (WT).

**Methods:** In this prospective study from January 2020 to December 2022, out of 33 patients, 15 patients with unilateral localized WT (stage I, II, and III) treated according to SIOP UMBRELLA protocol 2016 were included. Bilateral, syndromic, and stage IV WT were excluded. The radiological response was measured in preoperative CECT by estimation of the percentage of necrosis found in static images and compared with post-operative Histopathological findings. Tumor volume changes were measured by comparing CECT at diagnosis and following chemotherapy. Tumor volume change was also compared with histology.

**Results:** There was a correlation found between radiological response to necrosis and volume changes with histology. Pearson correlation was done for statistical analysis and found significant. Manner of necrosis found in CECT- scattered or central was also synchronous with the histopathology report.

**Conclusions:** Correlation between Preoperative CECT and histopathological findings to estimate necrosis and volume changes is of clinical importance and a further area of development for the management of Wilms Tumor.

EP039/#191 | Poster Topic: AS01 Surgery - IPSO

### LATERAL EXTENSION INCREASES SURGICAL RISKS IN WILMS TUMOR

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**Background and Aims:** Wilms tumor (WT) is sometimes found large and difficult to operate. Especially when it extends contralaterally, it may be difficult to dissect the renal hilum and ligate the renal artery and vein. Although there are some reports describe that increase in tumor size will increase surgical risk or tumor rupture, the relationship between lateral extension and surgical risk has not been investigated. In the present study, we analyzed the pre-operative image analysis in order to find the contribution of contralateral extension for surgical outcomes.

**Methods:** Twenty five patients with Wilms tumor resected in our institutions were enrolled in this study. Patients' clinical records were collected and retrospectively analyzed. In horizontal sections of CT or MRI before surgery, contralateral extension (CE) was classified in 3 groups; tumors are within the midline of the vertebral body (CE-, n=10), tumors extending beyond the midline of the vertebral body (CE+, n =11) and tumor extending beyond the lateral margin of the vertebral body (CE++, n=4). We examined the relationship between CE and operation time, blood loss, tumor rupture, and surgical complications.

**Results:** Four cases (3 in CE+ and one in CE++) had tumor spillage due to tumor rupture or extension beyond the tumor capsule. There were no complication related to surgery. Mean operation time was 223+-64min in CE-, 315+-72min in CE+ and 240+-149min in CE++. Mean blood loss was 159+-272ml in CE-, 458+-757ml in CE+ and 305+-545 in CE++.

**Conclusions:** Extension to the opposite side was significantly related with tumor rupture, operation time and blood loss during operation. Contralateral extension is considered to be useful to predict the surgical risks in the treatment of large localized Wilms tumor.

EP040/#647 | Poster Topic: AS01 Surgery - IPSO

### SHIFTING FROM OPEN TO MINIMAL INVASIVE APPROACH: CAN ROBOTIC SURGERY (RS) MAKE THE CUT?

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**Background and Aims:** The deployment of minimally invasive surgery (MIS) in oncology has always been complex, this is because the procedures require very long and precise dissections to achieve the desired results and, they are very variable, so performing with conventional MIS can be very difficult and very often dangerous. However, RS, with its well-known advantages, could overcome this limitation and make a difference. The purpose of our study is to evaluate the impact that RS has had, since its introduction in our Institute, in the oncology MIS.

**Methods:** We compared the number and type of procedures performed in MIS, open and RS surgery performed in the period between 2018-2020, before the introduction of the robotic system, and 2021-2022, after its introduction. Surgical indications and approach were discussed within the multidisciplinary tumor board. Descriptive statistics, data on type of procedure, approach, conversions, and complications are reported.

**Results:** Between 2018-2020, eighty-one patients were operated by open approach while twenty-three patients were operated by conventional MIS. In the period between 2021-2022, fifty-five patients were operated by open approach, eleven with conventional MIS, and forty-eight with RS. No conversions were reported in patients with conventional MIS, while thirteen conversions were reported in patients with RS. Nine postoperative complications reported in the group of patients operated with open approach (7x3b and 2x4a according to Clavien-Dindo classification), one complication in the group treated with conventional MIS (3b) and three in the RS group (2x3b and 1x4a).

**Conclusions:** The data collected so far do not allow us at this time to say with absolute certainty that RS can make a difference, however, we can say that the procedures completed with RS (thirty-five) would have been performed with open approach, thus RS allowed those patients a faster recovery and continuation of necessary oncologic care in a shorter time.

EP041/#1483 | Poster Topic: AS01 Surgery - IPSO

### WHO CARES ABOUT NEUROFIBROMAS? THE ROLE OF THE PEDIATRIC SURGEON IN TYPE-1 NEUROFIBROMATOSIS

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**Background and Aims:** Type-1 neurofibromatosis (NF-1) is a cancer-predisposition syndrome with a wide range of signs and symptoms, including neurofibromas (NF), that are characteristic and could be of concern because of malignant transformation, pain and esthetic disturbance. Our aim is to analyze the indications for surgery and its outcomes.

**Methods:** Cross-sectional observational design, analyzing patients with NF-1 under follow-up in a university referral hospital from February 1st, 2017, to February 28th, 2023, who have been operated by a pediatric surgical team with diagnosis of NF. Procedures performed in the orbital zone by the ophthalmology team aren't included.

**Results:** 28 patients (57.1% male - 42.9% female; 13.59 years of age, SD +/- 3.80) with 35 surgical procedures were included. Indications for surgery were: symptomatic (21, 60,0%), esthetic (7, 20,0%), rapid growth (4, 11,4%) and suspicion of malignancy (3, 8,6%). 71 NF were operated (mean size 33.51 mm, range 1-160 mm SD +/-41). Locations of NF were: scalp 12 (17%), face 5 (7,1%), neck 6 (8,4%), thorax 6 (8,4%), abdomen 1 (1,5%), pelvis or buttocks 5 (7,1%), back 9 (12,6%), superior extremity 18 (25,3%) and inferior extremity 9 (12,6%). Main symptoms were: Pain (24, 75,0%), paresthesia (3, 9,4%), movement impairment (1, 3,1%), deformity (3, 9,4%), and psychological disturbance (7, 21,9%). 6 patients (17,1%) were reoperated due to relapse.

**Conclusions:** NF-1 is a complex disease, with a broad spectrum of symptoms, and the inclusion of a pediatric surgeon in the multi-disciplinary team is important to make better decisions, performing better surgical procedures, and providing a better care, considering that neurofibromas usually appear and grow in childhood and adolescence.

EP042/#650 | Poster Topic: AS01 Surgery - IP SO

#### PRE-OPERATIVE THROMBOCYTOPENIA IN PATIENTS AFFECTED BY HIGH RISK NEUROBLASTOMA: IMPACT ON SURGICAL OUTCOME

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**Background and Aims:** Neuroblastoma is the most common solid extracranial tumor in children. Approximately one third of these

patients are stratified into high risk group. High-risk patients receive multimodal treatments, including chemotherapy, surgery and radiation therapy. Surgery should aim at complete macroscopic resection to improve patients' prognosis. Furthermore, these patients commonly experience thrombocytopenia, which can be associated with increased risk of surgical complications. The aim of the present study is to assess the impact of thrombocytopenia on the extent of surgical resection and on the rate of surgical complications in high-risk neuroblastoma patients.

**Methods:** The clinical notes of patients diagnosed with high-risk neuroblastoma from January 2013 to December 2022 were retrospectively reviewed. Patients were classified according to platelet count in the 24 hours before surgery, with a cut-off value of 100,000/mmc to define thrombocytopenia. Primary outcomes were the rate of complete macroscopic resection and the incidence of relevant surgical complications (i.e. Clavien-Dindo grade 2 or higher).

**Results:** In the analyzed period, 56 patients were diagnosed with high-risk neuroblastoma; fifty of them (89%) underwent surgical excision of the tumor, 47 of whom (94%) were operated after induction chemotherapy. Seventeen patients were thrombocytopenic immediately before surgery (36%). Complete macroscopic resection was achieved in 13 out of 17 thrombocytopenic patients versus 24 of 30 non-thrombocytopenic patients (76% vs 80%;  $p > 0.999$ ). Four thrombocytopenic patients experienced relevant surgical complications versus three non-thrombocytopenic patients (24% vs 10%;  $p = 0.235$ ). The difference was not statistically significant for either variables.

**Conclusions:** The occurrence of thrombocytopenia in the immediate pre-operative period in high-risk neuroblastoma patients does not seem to hamper complete macroscopic resection nor to increase the risk of post-operative complications. In selected patients in whom the timely excision of primary tumor is of paramount importance for local disease control, major elective surgery should be undertaken even in the setting of thrombocytopenia.

EP043/#1281 | Poster Topic: AS01 Surgery - IP SO

#### CONTRIBUTION OF 3D IMAGING IN THE SURGERY OF NEUROBLASTOMAS WITH HIGH SURGICAL RISK

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**Background and Aims:** 3D imaging is an innovative tool developed to improve preoperative assessment of high surgical risk tumors and decrease surgical morbidity, however these potential advantages need to be evaluated. The aim of this study was to evaluate the contribution of 3D imaging in the surgical management of abdominal neuroblastoma

with "Image Defined Risk Factors" (IDRFs) at high surgical risk after neoadjuvant chemotherapy.

**Methods:** This retrospective study included children operated between 2017 and 2022 for a neuroblastoma with encasement of the branches or origin of the superior mesenteric artery (SMA) and/or the celiac trunk (CT), with or without encasement of the aorta and/or the inferior vena cava (IVC). From 2021, a 3D reconstruction of the preoperative scanner (Visible Patient Software) was performed.

**Results:** Seven patients were operated with a median age of 52 months (32-126) and a median weight of 15kg (12.5-25). 3D reconstruction was performed in 4 patients (3D group). 7 presented an encasement of the CT (6 with encasement of all branches), 6 an encasement of the SMA and at least one renal artery. All 3D group patients presented all these vascular encasements, and 2/3 in the no-3D group. Postoperative tumor residue was less than 5 cm<sup>2</sup> in all patients. Intraoperatively, 1 complication was noted in 3D group (common bile duct wound; bile duct not reconstructed in 3D) and 3 in the no-3D group (aortic wound, IVC wound, bile duct wound). Postoperatively, 2 patients in 3D group presented a complication (embolized pseudoaneurysm of left hepatic artery, pancreatic fistula) and 2 in the no-3D group (pancreatic fistula + hepatic artery thrombosis + portal thrombosis; adrenal insufficiency). **Conclusions:** Preoperative 3D imaging seems beneficial for neuroblastomas retaining IDRFs after chemotherapy with high surgical risk to reduce complications and facilitate the surgery. This project was the pilot study of a larger multicenter prospective study.

EP044/#689 | Poster Topic: AS01 Surgery - IPSO

### OVARIAN-SPARING SURGERY FOR OVARIAN TUMORS IN CHILDREN: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background and Aims:** An increased number of children and adolescents with ovarian tumors have been managed with ovarian-sparing surgery in the last few years. However, comprehensive data on fertility outcomes and local relapse are scarce. In this study, we systematically describe the contemporary outcomes of ovarian-sparing surgery, as reported in the literature.

**Methods:** Using PRISMA guidelines, we analyzed studies reporting ovarian-sparing techniques for ovarian tumors in children and adolescents. from 1980 to 2022. Reports with fewer than three patients, narrative reviews, and opinion articles were excluded. Statistical analysis was performed for dichotomous and continuous variables.

**Results:** Of 283 articles screened, 16 papers (3057 patients) met inclusion criteria (15 retrospective/1 prospective) and were analyzed. The vast majority of studies had no long-term fertility follow-up data and direct comparison between ovariansparing surgery vs oophorectomy was reported in only a few studies. Ovarian sparing surgery was not associated with worse oncologic outcomes in terms of (i) tumour spillage or (ii) recurrence rates, and of key importance allowed a higher ovarian reserve at long term follow-up.

**Conclusions:** Ovarian-sparing surgery is a safe and feasible technique for benign tumours. Long-term outcome studies are needed to show efficacy and fertility preservation.

EP045/#665 | Poster Topic: AS01 Surgery - IPSO

### METHYLATION STATUS OF H19 LONG NON-CODING RNA IN PATIENTS OF WILMS TUMOR

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**Background and Aims:** To study the status of the methylation levels of H19 lncRNA in Wilms Tumor

**Methods:** This prospective study had included all consecutive cases of Wilms tumor from January 2020 to March 2021 at single centre. Patients with recurrent or residual tumors at the time of presentation were excluded from the study. The tumor specimen obtained after nephrectomy were used as test sample, while the controls were divided into two types; self-controls (normal renal parenchyma in the nephrectomy specimen) and normal controls (patients undergoing nephrectomy for non-malignant indications). The methylation status of H19 lncRNA was evaluated in the specimens using gel electrophoresis.

**Results:** A total of 31 patients were included in the study. The mean age at inclusion was 40.1 +/- 27.7 Months. Of these, 25/31 of the patients received neoadjuvant chemotherapy while the remaining 6/31 of the patients underwent upfront surgery. However, on comparing the methylation status of the Wilms Tumor samples with the self-control samples, there was no significant difference in the hypermethylation status of the H19 lncRNA promoter region in the tumor samples as compared to the self-control samples (p = 0.060). On comparison with controls (n=6), the tumor samples had significant hypermethylation of the H19 lncRNA.

**Conclusions:** In patients with Wilms Tumor, there is a definitive hypermethylation of the H19 lncRNA locus as compared to normal kidneys,

hence suggesting that epigenetic regulation H19 lncRNA plays an essential role in the tumorigenesis of Wilms Tumor.

EP046/#491 | Poster Topic: *AS01 Surgery - IPSO*

#### PRELIMINARY ANALYSIS OF NEPHRON-SPARING SURGERY FOR UNILATERAL WILMS TUMOR AFTER NEOADJUVANT

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**Background and Aims:** To investigate the preliminary therapeutic effect and experience of nephron sparing surgery (NSS) for unilateral Wilms tumor after neoadjuvant chemotherapy.

**Methods:** The clinical data of 7 children with unilateral nephroblastoma undergoing NSS in our hospital from January 2014 to December 2020 were retrospectively analyzed.

**Results:** Among the 7 patients, there were 4 males and 3 females, with an average age of  $38.86 \pm 18.23$  months (16-55 months). None of the patients had tumor related syndrome or hemi limb hypertrophy. None of the patients had tumor related syndrome or hemihypertrophy. The tumor involved one pole of the kidney in 1 case and located in the center of the kidney in 6 cases. After neoadjuvant chemotherapy, the tumor shrunk by  $66.4\% \pm 18.6\%$  (53.3%~93.9%) on average. Partial nephrectomy (PN) was performed in one patient whose tumor was located at the renal pole, and tumor enucleation (TE) was performed in the other six patients. Two patients had microscopical positive tumor margins. According to SIOP, there were 4 cases in stage II and 3 cases in stage III. All patients were followed for 27~64 months (mean  $38.42 \pm 10.17$  months), and no patients were dead. There were 6 cases of tumor-free survival and 1 case of tumor-bearing survival. Tumor recurrence occurred in 2 cases. The recurrence rate (28.6%) and 5-year survival rate (100%) after NSS were not significantly different from the recurrence rate (13.3%) and 5-year survival rate (86.9%) after radical nephrectomy (RN) in the same period.

**Conclusions:** Reasonable preoperative evaluation and neoadjuvant chemotherapy in unilateral Wilms tumor can increase the proportion of NSS surgery. In highly selected cases, NSS can achieve a therapeutic effect similar like that of RN. Moreover, sufficient margins (including under the microscope) should be ensured to reduce the recurrence of local tumors.

EP047/#979 | Poster Topic: *AS02 Radiation Oncology - PROS*

#### CLINICAL AND PROGNOSTIC ANALYSIS OF SARCOMA IN CHILDREN IN A SINGLE-RADIOTHERAPY TREATMENT CENTER

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**Background and Aims:** Sarcomas account for 6% of malignant tumors in children. We aim to summarize the clinical characteristics and prognostic factors of Sarcoma in children aged less than 20 years old, treated between 2015 and 2018, in The Mohamed VI centre for cancer treatment.

**Methods:** The clinical characteristics and Overall survival (OS), were analyzed retrospectively. Survival data was analyzed by Kaplan-Meier.

**Results:** The mean diagnostic age of 52 cases was 11.3 years. There were more males (57.7 %). Bone sarcoma was more frequent (57.7 %) than soft tissue sarcoma (42.1 %). Ewing sarcoma accounted for 34.6 %, Rhabdomyosarcoma (RMS) for 32.7 %, Osteosarcoma for 23.07%, Synovialosarcoma for 5.7% and there was 1 case of Dermatofibrosarcoma and another of Sclerosing Epithelioid Fibrosarcoma. For patients treated for localized Bone sarcoma (22 cases), 19 patients received neoadjuvant chemotherapy (CMT), 13 patients had surgical operations, and 17 patients received radiotherapy (RTH). The mean dose of RTH was 48.05 Gy. Seven patients received adjuvant CMT. For patients treated for localized Soft tissue sarcoma (22 cases), 14 received neoadjuvant CMT, 17 patients had surgical operations and 17 patients received RTH. The mean dose of RTH was 44.2 Gy. Fourteen patients received adjuvant chemotherapy. 8 patients were metastatic at diagnosis. The follow-up time was 21.5 months (ranged 1-108 months). There were 36% of patients with relapsed or progressed disease and 11.5% deaths. Patients treated with, an association of CMT, Surgery and RTH, had a better OS, with a median OS of 37.5 months (95%, 24.5 - 50.6).

**Conclusions:** A multimodal treatment combining Radiotherapy, chemotherapy and surgery, could be an important key factor in improving OS, for children treated with Sarcomas.

EP048/#1578 | Poster Topic: *AS02 Radiation Oncology - PROS*

#### CLINICAL CASE OF TOTAL BODY IRRADIATION IN PATIENT WITH RELAPSE ALL COMPLICATED PULMONARY ASPERGILLOSIS

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**Background and Aims:** Application of total body irradiation (TBI) as a type of myeloablative conditioning regimen prior to hematopoietic stem cell transplantation (HSCT) for patients with acute lymphoblastic leukemia (ALL). The 5-year overall survival ALL in Kazakhstan 72%. In this paper we presented case of TBI for patient with pulmonary aspergillosis.

**Methods:** TBI - in combination with chemotherapy, is widely used worldwide as a conditioning regimen before HSCT in patients with hematological malignancies and makes it possible to avoid graft vs. host disease.

**Results:** Male 16 years old, with ALL medium risk group in 2018, treated according to the AIEOP-BFM ALL 2009 protocol. In 2021, late combined bone marrow and right-sided testicular recurrence was diagnosed. Translocation ETV6/RUNX1 t (12;21). Local irradiation of the contralateral testicle was 15 Gy. Allogeneic HSCT was performed on 01.12.21, engraftment - 97,53%. In 2022 was diagnosed second an isolated bone marrow relapse treated according to the ALL-REZ-BFM 2002 protocol followed by allogeneic HSCT with TBI. The prescribed dose of TBI was 12 Gy (2 fractions of 2 Gy per day, with a break between sessions of at least 6 hours). The main criterion in creating a treatment plan was the delivery of a dose of 12 Gy to the entire target, as well as the minimum dose in the lungs of 6 Gy, but given the comorbidity pulmonary aspergillosis decided to remove the restriction on the minimum dose prescribed for the lungs. On Day +28 after HSCT, chimerism - 98%, which corresponds to complete engraftment.

**Conclusions:** TBI conditioning regimens in patients with relapsed ALL demonstrate sufficient tolerability and a low incidence of early and late toxicity despite comorbidity diseases particularly pulmonary aspergillosis.

EP049/#311 | Poster Topic: AS02 Radiation Oncology - PROS

#### ESTABLISHMENT OF TWINNING PARTNERSHIP TO IMPROVE PEDIATRIC RADIOTHERAPY OUTCOMES GLOBALLY

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**Background and Aims:** Pediatric radiotherapy is a necessary and challenging component of oncologic care for children in low- and middle-income countries (LMIC). Collaboration between institutions in LMIC and high-income countries (HIC) has been shown to be effective in improving oncologic treatment outcomes, however literature regarding pediatric radiotherapy twinning partnerships is limited.

**Methods:** Emory University has a long-standing twinning collaboration with Addis Ababa University (AAU) for certain medical specialties. After securing institutional funding, a faculty member and resident from Emory University Department of Radiation

Oncology set out to establish a twinning program with AAU for pediatric radiotherapy.

**Results:** Emory and AAU faculty and residents established initial communications virtually via email and video correspondence. AAU residents and faculty completed surveys regarding pediatric radiotherapy institutional and educational needs to outline goals of collaboration. Five lectures and case-based practicums were identified focused on Wilms' tumor, Medulloblastoma, Rhabdomyosarcoma, Hodgkin Lymphoma, and palliative radiotherapy. The Emory team then conducted a visit to AAU during which lectures and practicums were delivered. The Emory team directly observed and guided simulation and treatment planning procedures. AAU residents practiced decision-making, simulation, contouring and field placement for Wilms' tumor cases based on didactics and feedback provided by the Emory team. Additionally, a needs assessment regarding pediatric oncologic resources was completed. Clinical care pathways and standard operating procedures were drafted by collaborators. Virtual peer-review sessions were established to continue collaborations abroad and plan for next in-person visit.

**Conclusions:** Collaborative efforts by global experts have helped to establish and improve treatment protocols for childhood cancer. The presented twinning experience may serve as a model for other LMIC and HIC centers for establishing similar partnerships.

EP050/#965 | Poster Topic: AS02 Radiation Oncology - PROS

#### RADIOTHERAPY TECHNIQUES AND OVERALL SURVIVAL IN PEDIATRIC GLIOMAS: IMPLICATIONS FOR LOW AND MIDDLE INCOME COUNTRY

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**Background and Aims:** Childhood glioma (CG) is a rare tumor with a poor prognosis. Any tumor-directed surgical intervention is difficult. Magnetic resonance imaging forms the mainstay of diagnosis and radiation therapy has remained the backbone of therapy. In this study, we compare the outcomes of Volumetric Modulated Arc Therapy (VMAT) with 3D radiotherapy (3DRT) in the context of low and middle income country.

**Methods:** In this retrospective analysis, conducted between 2018 and 2022, all pediatric patients with a diagnosis of CG were analyzed. The survival data were calculated in months from the date of diagnosis. Survival differences between variables were compared using the Log-rank test and the risk of death was calculated using Cox regression analysis.

**Results:** A total of 22 patients (sex ratio M/F = 10/12) with a diagnosis of CG were included. Median age at diagnosis was 10.5 years. Diffuse brainstem glioma (dBSG) is the most common location (41%). High grade diffuse glioma is the frequent histology

(32% Glioblastoma). Seven patients underwent surgical resection, 3 received stereotactic biopsy. Six patients with dBSG received ventriculoperitoneal shunts without histological evidence. Seven patients with glioblastoma had Stupp regimens (31%), nine patients received radiotherapy alone (41%), four patients received chemotherapy alone (20%), and 2 patients received palliative care. Median overall survival (OS) was 7.17 months (95% CI 4.41–15.58). Children treated with radiotherapy had a longer OS than untreated children, however, the modality of radiotherapy employed or the addition of chemotherapy affect the OS (+20 months,  $P=0.069$ ). Thirteen patients who received VMAT modality (56%) had a longer OS (median OS 18 months 95% CI 9.23–26.76).

**Conclusions:** Radiotherapy, specially VMAT for better target volume coverage, increases the survival of children with Childhood glioma (CG) in resource-poor settings. In addition, socio-economic perspectives must be factored into the management of these tumors for optimal care.

EP051/#346 | Poster Topic: AS02 Radiation Oncology - PROS

#### MANAGEMENT OF HEAD AND NECK EWING'S SARCOMA IN PEDIATRIC PATIENTS

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**Background and Aims:** Ewing's sarcoma is a malignant bone tumor that usually affects children and young adults. Typically localized to the bones of the limbs, it can also occur along the axis, notably in the head and neck region. We aim to review our local experience with this particular site.

**Methods:** We studied the medical records of patients diagnosed with Ewing's sarcoma of the head and neck region and treated at the pediatric oncology department of Salah Azaiez Institute between 2013 and 2023.

**Results:** A total of three cases have been found: two girls and one boy, with a median age of 18. Occurrence sites included the orbit, the pterygoid process, and the frontal bone. The management of these tumors consisted of chemotherapy, radiotherapy and surgery. Chemotherapy was based on alternating courses of vincristine-doxorubicine-cyclophosphamide and Ifosfamide-Etoposide, before and after local control, according to Euro-Ewing 2012 protocol. Following induction chemotherapy, the frontal bone was the only site accessible for tumor resection. While local control was based on external beam radiotherapy (EBRT) in inoperable patients, which resulted in a partial response. Inevitably, a metastatic relapse occurred in each of the three patients, after a median event-free interval of 13 months. Metastases affected several axial bone structures, such as the clavicle, iliac wing, and dorsal vertebrae. Metastatic sites received focal EBRT at doses ranging from 10 to 28G. In addition, decompressive FLASH radiotherapy was

delivered at a dose of 14Gy for patients with symptomatic vertebral metastases with endocanal extension. Salvage chemotherapy was based on irinotecan-temozolomide duet. Despite undergoing a multimodal therapy, all three patients have died of disease after a median overall survival of 19 months.

**Conclusions:** Due to the inaccessibility of the tumor, disease control of Ewing's sarcoma of the head and neck remains challenging. Moreover, the outcome of metastatic relapses remains poor, even having undergone salvage chemoradiation.

EP052/#1688 | Poster Topic: AS02 Radiation Oncology - PROS

#### RADIATION THERAPY FOR RETINOBLASTOMA

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**Background and Aims:** Retinoblastoma (Rb) is the most common ocular malignancy in childhood, it carries a poor prognosis. However, the treatment of Rb has improved significantly recently with an increasing trend to use conservative treatment modalities. Nevertheless, challenges remain, especially for developing countries. Our aim is to describe clinical characteristics and therapeutic results of childhood Rb in a Tunisian population.

**Methods:** Retrospective study of 11 Rb patients treated in the department of oncological radiotherapy of the Farhat-Hached Hospital, Sousse, Tunisia between 1995-2020.

**Results:** The median age was 24 months [13-72], with a sex-ratio=0.37. The majority of the patients presented with either leukocoria (74.7%) or strabismus (24.9%). There were 10 unilateral (90.9%) and one bilateral case (9.1%). Patients were stratified by: the International Intraocular Retinoblastoma Classification (IIRC), all tumors were classified as group E and the Reese and Ellsworth classification; 2 tumors were group III (16.7%), 9 group IV (75%) and 1 group V (8.3%).

Upfront systemic chemotherapy (CT) was only done in 18.2% of cases and all tumors were treated by enucleation. Adjuvant CT was administered in 54% of cases. 45% of patients received post-operative radiotherapy (RT), with a dose of 39.8-45Gy, using three-dimensional-conformal RT in 40% of cases.

After a median follow-up of 24 months [12-204], 4 patients were in complete remission (23.5%), 6 patients had local recurrence (54.54%); treated by CT associated with surgery in 50% of cases and salvage-RT in 66.6%, with a dose of 44-54Gy, and 2 patients had metastatic relapse (11.7%) treated by CT.

Event-free-survival and overall-survival rates at 5 years were 27.27% and 36.36%, respectively.

**Conclusions:** Our study highlights that delayed presentation and inaccessibility to recent treatment options are major obstacles in achieving high cure rates in our country. Strengthening medical facilities for diagnosing and treating Rb is required in order to reduce mortality and morbidity.

EP053/#1723 | Poster Topic: AS02 Radiation Oncology - PROS

**RADIATION THERAPY FOR THE MANAGEMENT OF WILMS TUMORS**

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**Background and Aims:** Wilms tumor (WT) is childhood's most common renal tumor, accounting for approximately 90% of all paediatric tumors of the kidney. Its prognosis has improved dramatically in response to the advent and use of current multimodal therapy.

Our aim is to elucidate the contribution of radiotherapy in the treatment of wilms tumor.

**Methods:** Retrospective study of 23 patients with wilms tumor, treated in the department of radiotherapy of the Farhat Hached Hospital, Sousse, Tunisia between 1995-2020.

**Results:** The median age was 54 months [15-216 months], with a sex ratio=0.6. The tumor was localized in 13 patients and metastatic in 10. Treatment was based on the SIOP9 and SIOP93-01 protocols. All patients received upfront chemotherapy followed by radical nephrectomy.

The histology was of low risk in 4.3% of cases, intermediate risk in 69.6% and high risk in 26.1%. The stage distribution of the tumors was stage I in 4.3% of patients, stage II in 13%, stage III in 39.1% and stage IV in 43.8% of patients.

Flank radiotherapy (RT) was indicated in 20 cases, one patient was lost of sight before RT, the average dose was 25.2Gy [14.4-36Gy], using three-dimensional conformal RT (3D) in most cases (63.15%). Two patients, who had lung metastases with postoperative residue, had bipulmonary irradiation, with a dose of 15 Gy, using 3D RT. Overall tolerance was good.

After a median follow-up of 54 months; we had 2 cancer progression, 1 local relapse and 3 metastatic relapses. The overall survival at 2 years is 87.5%.

**Conclusions:** Wilms tumor is a highly radiosensitive and even radiocurable tumor. RT is reserved for advanced stages or unfavorable histology. In our population, the therapeutic results of WT are mostly similar to those reported in the literature. Thus, with appropriate treatment, an excellent outcome can be achieved in most cases.

EP054/#1731 | Poster Topic: AS02 Radiation Oncology - PROS

**WHOLE ABDOMINAL IRRADIATION IN WILMS TUMOR: CASE REPORT**

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**Background and Aims:** Wilms tumor (WT) rupture is rare, constituting 3% of all the cases of WT. Pre-operative rupture is rarer and could be either post-traumatic or spontaneous. It is a potentially significant event triggering tumor dissemination which raises the classification to

stage III. Then chemotherapy (CT) should be more intensive and whole abdominal radiotherapy (RT) is added.

**Methods:** We present a girl who had a whole-abdominal RT for pre-operative rupture of her WT, in the department of oncological radiotherapy of the Farhat Hached Hospital, Sousse, Tunisia

**Results:** A 5-year-old female, presented with abdominal pain evolving for the last six months. Renal ultrasound demonstrated a mixed-echo renal mass at the higher pole of the right kidney. The computed tomography (CT) demonstrated an heterogeneous-density mass, locally advanced in the right kidney. Chest imaging was negative. She had a CT-guided biopsy, which confirmed the diagnosis of nephroblastoma, that was complicated by tumor spillage with sub-capsular, intra-tumoral and peritoneal bleeding on imaging.

Given the minimal clinical signs and limited abdominal bleeding, she underwent neoadjuvant-CT with 4 courses of vincristine-actinomycin D, followed by radical nephrectomy. Histopathology revealed triphasic nephroblastoma, measuring 15 cm. Surgical margins were negative. All lymph nodes were negative. The local stage was considered stage III, intermediate risk.

Postoperatively, secondary liver lesions were discovered which completely disappeared with adjuvant CT. Whole-abdominal RT was performed in a 1.5Gy fractioning up to a dose of 21Gy, using three-dimensional-conformal RT.

She has been followed 29 months after surgery and complete remission of the tumour was achieved.

**Conclusions:** Wilms tumor is a rapidly growing tumor, and usually attains an enormous size before diagnosis, making it prone to rupture. Although rare, it is a complication that has been reported for a long time.

Most of these patients receive abdominal RT which is associated with both acute and delayed toxicity.

EP055/#1564 | Poster Topic: AS02 Radiation Oncology - PROS

**COMBINED APPROACH FOR CRANIOPHARYNGIOMA IN CHILDREN WITH CONSERVATIVE SURGERY AND PROTON THERAPY: LONG-TERM ANALYSIS OF A PHASE II STUDY TO EXAMINE FEASIBILITY OF DOSE ESCALATION**

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**Background and Aims:** Optimal treatment for paediatric cranio-  
pharyngioma remains controversial. However, when hypothalamic  
infiltration, conservative surgery followed by radiation, is now a con-  
sensus. Proton therapy offers further sparing of normal tissues expo-  
sure compared to photons and is favoured in children to reduce the  
risk of radiation-related morbidity. The objectives of the study were  
to assess the efficacy of limited surgery followed by proton therapy  
and to evaluate the feasibility of dose escalation while maintaining  
risk-adapted dose constraints to the chiasm.

**Methods:** Thirty-three patients were included (17 males), median age  
9.0 years (2.1-15.5) at diagnosis, 9.6 years (3.3-15.8) at radiation. All  
patients underwent surgery (1-5, median: 2) with measurable residue.  
Histology was adamantinomatous craniopharyngioma in 32; 1 case  
presenting aggressive characteristics was reviewed as malignant cranio-  
pharyngioma. Median interval between diagnosis and proton therapy  
was 7.2 months (2.5-73.6). Median planning target volume was 31.4  
cm<sup>3</sup> (12.7-136). Median dose 54.4 GyRBE (52-56.1). Based on dosi-  
metric parameters, five patients underwent moderate dose escalation.  
Median dose to chiasm was 52.8 GyRBE (52.4-54.7).

**Results:** At median follow-up 8 years (1-12) since radiation, 31 patients  
are alive, two patients died of metabolic or respiratory complications.  
Six patients relapsed: five locals at median 83 months (16-103) after  
proton therapy. The malignant case presented a posterior fossa metas-  
tasis. Two patients showed a second local relapse. Normal vision in at  
least one eye observed in 21/31 patients, 10/31 show restricted fields.  
All patients are on hormone replacement. Median BMI is 24,5 (18-34)  
with 15 patients overweighted and 10 obese. Twenty patients have nor-  
mal academic status, 11 patients require special schooling. One patient  
developed symptomatic arteriopathy of the polygon of Willis.

**Conclusions:** This study supports the use of proton therapy in paediatric  
craniopharyngioma and emphasises the necessity of long-term  
follow-up. Dose escalation using passive scattering delivery was  
reached in few patients only, preventing dose effect relationship  
evaluation.

EP056/#1417 | Poster Topic: AS02 Radiation Oncology - PROS

#### EFFICIENT EVALUATION OF DOSE TO BRAIN STRUCTURES IN CHILDREN TREATED WITH RADIOTHERAPY FOR BRAIN TUMOURS

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**Background and Aims:** Higher radiation doses to specific brain struc-  
tures are associated with lower cognitive scores among children  
and adolescents treated for brain tumours. Studying dose-responses  
of multiple structures requires considerable dose variation across  
patients that is also widespread across structures of interest to achieve  
suitable statistical power. Here, we report brain structure doses in  
a mixed-diagnosis cohort using spatial normalisation: the mapping of  
a patient cohort to a single reference patient to allow efficient dose  
evaluation in structures infrequently clinically contoured.

**Methods:** We included 52 patients (3-26 years) treated with photon  
radiotherapy at a single institution between 2013-2022 for: medul-  
loblastoma (19), astrocytoma (19), ependymoma (5) and germ-cell  
tumours (9).

FreeSurfer segmented the left/right hippocampus, left/right cerebral  
white matter (WM), and anterior/posterior/central corpus callosum  
(CC) in the reference scan. Individual patient CTs and dose distri-  
butions were spatially normalised to the reference using non-rigid  
registration (~2 minutes per patient). Mean structure doses were cal-  
culated from the spatially normalised dose for every patient. Median  
and inter-quartile range (IQR) of these mean doses are reported for the  
full cohort and stratified by diagnosis.

**Results:** Variation in dose was uniform across all structures with over-  
all median (IQR) of 36(24-36)Gy. Dose variability was lower for every  
group stratified by diagnosis except for astrocytoma, which showed the  
largest overall dose variation [31(19-46)Gy].

Across different structures, the mixed-diagnosis and astrocytoma  
cohort provided large and uniform variability. Patients with medul-  
loblastoma also had uniform but moderate dose variability across most  
structures. However, non-uniform variation was found for germ-cell  
tumours, with peak variation in left hippocampus [24(24-43)Gy] and  
no variation in CC anterior [24(24-24)Gy]. Uniform low variability was  
found for ependymoma.

**Conclusions:** Spatial normalisation is an efficient way to assess doses  
in structures infrequently clinically contoured in large patient cohorts.  
We observed considerable variations in dose to brain structures within  
and across diagnostic groups, which motivates dose-response analysis  
in mixed-diagnosis cohorts.

EP057/#350 | Poster Topic: AS02 Radiation Oncology - PROS

#### AN ANALYSIS OF INQUIRIES MADE ABOUT THE USE OF RADIOTHERAPY DURING THE JAPANESE NATIONWIDE CLINICAL TRIAL FOR RHABDOMYOSARCOMA

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**Background and Aims:** Rhabdomyosarcoma is a rare disease which arises in diverse sites of the body. It is subjected to a well-integrated, multidisciplinary approach consisting of chemotherapy, surgery, and radiotherapy. The treatment options vary extensively according to the area and extension of the disease, and the outcome of preceding treatment. As a result, proposing appropriate treatment alternatives for each stage of the illness, with sufficient evidence, is difficult. Although the treatment provided in a clinical trial protocol may be more favorable, inquiries about the therapy involved are inevitable. It is considered that these inquiries reflect the limitations of the protocol treatment and its descriptions.

**Methods:** Between May 1997 and February 2023, during the Japanese nationwide rhabdomyosarcoma clinical trials, the rhabdomyosarcoma radiotherapy protocol committee (RRPC) responded to questions regarding radiotherapy. Inquiries were then extracted from the recorded queries in the database. These were divided into simple questions: category of reason behind the query; and the targeted irradiation site. The proportions of each type of question were analyzed.

**Results:** RRPC accepted 73 inquiries, relating to 60 accounts, for 47% of the patients registered in the trials. These were divided into 180 questions. An analysis of the types of reasons presented for the inquiries indicated that the trade-off between efficiency and toxicity (35%) was a major motivator. This was followed by uncertainty regarding the dose (28%) and description of the target volume (28%). The sites of most concern were the extremities (28%), followed by the head and neck (23%).

**Conclusions:** Inquiries relating to the clinical trial treatment revealed that a large proportion of patients with rhabdomyosarcoma experienced uncertainty and concern regarding the use of radiotherapy in the protocol treatment. Obtaining a trade-off between efficiency and toxicity in treatment planning should, therefore, be one of the most important issues driving the standardization and optimization of radiotherapy.

EP058/#1192 | Poster Topic: AS02 Radiation Oncology - PROS

## EFFICACY & TOXICITY OF EXTERNAL BEAM RADIOTHERAPY (EBRT) FOR METASTATIC SITES (MS) PRESENT AT END INDUCTION (EI) IN PATIENTS WITH HIGH-RISK NEUROBLASTOMA (HR-NBL)

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**Background and Aims:** Radiotherapy to MS persistent at EI is included in North American treatment paradigms for HR-NBL patients. Efficacy/toxicity are not well studied.

**Methods:** Medical record review of HR-NBL patients diagnosed 2010-2020, treated with EBRT at a single center, with inclusion of MS persisting at EI. Clinical target volume (CTV) for MS was 1cm expansion from avid disease on MIBG-SPECT at EI.

**Results:** Among 99 HR-NBL patients, 35 had persistent MS on EI scans. Of these, 26 received radiation to 56 MS (8 received extended induction with resolution of MS, 1 family refused radiation). Median diagnosis age 43m (12-102m). Patients had average 2.2 MS (1-7), with 44/56 (78%) bony and 10/56 (22%) soft tissue. Radiation dose was 21.6 Gy to 54 sites (96%) and 36 Gy to 2 (4%), delivered with protons for 52 (93%), 1.8 Gy fractions. MS average CTV was 33.7cm<sup>2</sup> (2.1-128 cm<sup>2</sup>). MS were head/neck (n=12; av max lens/mean pituitary dose 5.9/4.9 Gy, respectively), pelvic (n=10; av mean bowel/bladder dose 2.9/0.9 Gy, respectively), thoracic (n=6; av mean lung/heart dose 3.7/2.9 Gy, respectively), extremity (n=25). At median follow-up 39m (14m - 145m), 7/26 pts (27%) had relapsed and 5/26 (20%) died. At first progression (median 28m from RT, range <1m - 137m), disease was present at only 2/56 radiated MS (4%). Twenty-four patients with 53 MS had follow-up of 12+ months from radiation (median follow-up 30 m from RT/ 40m from diagnosis); of these, one has hypothyroidism after neck RT. No other G2+ late toxicity has been observed related to MS radiotherapy, including clinical leg length discrepancy, arthritis, hypopituitarism, orbital asymmetry, cataract.

**Conclusions:** Relapse at MS after 21.6 Gy radiation in HR-NBL is rare (<5%, with follow-up 10 years), with 80% of patients alive. Advanced imaging and radiotherapy techniques allow this paradigm to be employed with low risk of late toxicity.



EP059/#1214 | Poster Topic: AS02 Radiation Oncology - PROS

### RESULTS OF A RETROSPECTIVE ANALYSIS OF RMS PATIENTS RECEIVING RADIOTHERAPY TREATED IN A LARGE TERTIARY CANCER CARE CENTER IN INDIA

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**Background and Aims:** Rhabdomyosarcoma is one of the most common pediatric soft tissue sarcoma. Despite of multimodality treatment approach survival is dismal. There is paucity of literature on RMS in India. Aim of this study is to analyse the disease characteristics and outcome in patients of RMS receiving Radiation Therapy at our Tertiary Cancer Centre in India.

**Methods:** A Retrospective Analysis of pediatric patients of rhabdomyosarcoma between years 2005-2021 was conducted. Out of 291 patients, radiation therapy data was available for 46 patients which was further evaluated. Overall Survival and Progression Free survival was calculated using Kaplan-Meier method.

**Results:** Out of the 46 patients, 33(72%) were male and 13(28%) female. The median age was 4.5 years (standard deviation-4.35 range-1-16 years). Most common site of presentation was head and neck (47.8%) followed by pelvic (43.5%), extremities (6.5%) and other (2.2%). The histologic subtype were Embryonal (80.4%), Alveolar (17.4%). No patient had metastatic disease on presentation. The median follow up was 31 months (Range-70 months). All the patients received Radiation Therapy with either Curative or Palliative intent. Out of the 46 patients, 32(69.6%) patients received conventional while 14(30.4%) patients received Radiation Therapy by Conformal technique. Two patients did not complete Radiation therapy. After the treatment, complete response was seen in 41.3% (84.2% in embryonal subgroup and 15.8% in alveolar subgroup), partial response in 43.5%(85%-Embryonal and 15% alveolar), 8.7%(50% in Embryonal and 25% in Alveolar) had stable disease and 6.5% patients had progression as distant metastasis (locoregionally-stable disease). The median Overall Survival was 71 months and progression free survival is 43.5 months. The median overall survival in Embryonal histology group was 72 months and in alveolar histology subgroup was 28 months. The overall survival was better in the patients showing complete response to the multimodality treatment as compared to the patients who showed partial response or had stable disease.

**Conclusions:** Outcomes in RMS remains dismal despite multimodality treatment approach. However, Radiation Therapy improves Locoregional control as well as overall survival.

EP060/#398 | Poster Topic: AS02 Radiation Oncology - PROS

### EVALUATION OF THE CTV-TO-PTV MARGINS FOR PEDIATRIC ABDOMINAL IMRT USING RIGID PERSONALIZED SHELL

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**Background and Aims:** Intensity-modulated conformational radiotherapy (IMRT) coupled with Image-guided radiation therapy (IGRT) represents a major breakthrough. But despite the technological advancements that have taken place, there are many sources of error that operate during the planning and delivery of treatment and limit accuracy. There are two types of errors that can be identified in radiotherapy; systematic and random errors. The aim of our study was to define these errors, identify them and evaluate the necessary CTV-to-PTV margins of our personalized immobilization system for pediatric abdominal cancer in the radiotherapy department of Salah Azaiez Institute.

**Methods:** This is a prospective study in the radiotherapy department of Salah Azaiez Institute involving 12 children who received adjuvant radiotherapy by IMRT using rigid personalized shell as immobilization system. We calculated the PTV using the following formula from Van Herk ( $PTV = 2.5 \times \sum + 0.7 \times d$ ).

**Results:** Our study brought together 12 patients divided into 6 patients followed for neuroblastoma and 3 for nephroblastoma and 3 for sarcoma. The mean age was 4 y.o [2-8 y.o]. The IGRT protocol adopted at the ISA was a daily kV/kV. The calculated CTV-to-PTV margins by the Van Herk formula was 0.33 mm, 0.88 mm and 0.79 mm respectively in vertical, longitudinal and lateral directions.

**Conclusions:** The 1 cm CTV-to-PTV margins arbitrarily chosen for pediatric abdominal IMRT using rigid personalized shell is sufficient. Our personalized immobilization system is reliable and reproducible. Using this shell is a solution to avoid positioning uncertainties and better carry out the treatment.

EP061/#399 | Poster Topic: AS02 Radiation Oncology - PROS

### PEDIATRIC CRANIOSPINAL IRRADIATION: TRANSITION FROM 3DCRT TO VMAT

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**Background and Aims:** Craniospinal Irradiation (CSI) is a cornerstone in the management of medulloblastoma. Three-Dimensional

Conformal Radiation Therapy (3DCRT) is the traditional technique. Recently, Volumetric Modulated Arc Therapy (VMAT) has been initiated in the radiotherapy department of Salah Azaei Institute. We aimed to report the improvement of the procedure for pediatric craniospinal irradiation in our department.

**Methods:** The simulation was performed in prone position with customized prone head rest and in supine position with thermoplastic mask and a vacuum cushion for respectively 3DCRT and VMAT. Computed Tomography images were acquired using CT scanner (Philips BigBore). For both techniques the PTV, and the OAR were delineated following the SIOP recommendations. Opposed lateral fields were used to treat the brain and depending of patient's size one or two anterior fields to treat the spine in the 3DCRT. VMAT-based treatment plans used three coplanar arcs: two arcs to cover the superior portion of the TV and two or four partial arcs avoiding arms to cover the rest of the spine.

**Results:** Complete understanding of all the steps is necessary; a continuous education and training should be planned before successfully initiate a new procedure. The VMAT position is safely reproducible; the supine position is more comfortable for children and offer better compliance to the treatment. The 3DCRT techniques uses junctions between fields resulting in inhomogeneous dose regions. VMAT-based CSI simplifies the planning and delivery process since it does not require any junction-shifts. Based in our experience, the VMAT techniques provide more homogenous target coverage while reducing the dose to multiple critical organs when compared with traditional 3DCRT.

**Conclusions:** VMAT is preferred to conventional techniques due to its simplicity and faster treatment delivery time. Although, the gain in target conformality should be balanced with the spread of low doses to distant areas that introduces concern over the potential of secondary malignancies.

EP062/#894 | Poster Topic: AS02 Radiation Oncology - PROS

#### OUTCOMES OF CHILDREN WITH UNILATERAL RETINOBLASTOMA TREATED WITH RADIOTHERAPY AS A PART OF CURATIVE INTENT COMBINED MODALITY TREATMENT PROTOCOL

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**Background and Aims:** To evaluate treatment outcomes of children diagnosed with unilateral retinoblastoma and received radiotherapy (RT) as a part of curative intent treatment protocol.

**Methods:** Retrospective study of eligible children registered at our institute from January 2013 to December 2018.

**Results:** Of the 24 cases we analyzed, gender was equally distributed. The median age of presentation was 29 months of age. Majority had orbital disease at the time of presentation (22;92%). Surgery followed by adjuvant RT was offered to 22 children (enucleation 18;82%, exenteration 4;18%). Definitive radiotherapy was offered to 2 patients with active intra-vitreous disease but with preserved vision in one and optic nerve thickening up to the apex in another. All received systemic chemotherapy. High-risk features on surgical specimen histopathology were optic nerve cut margin positivity in 6(27%), optic nerve involvement in 11(50%) and extra scleral extension in 2(9%). No child had grade III/IV acute or long term RT related toxicity. Median follow up is 42 months. At the time of the last follow-up, 16(67%) children were alive without disease and 8 (33%) had died due to disease. The 5-year local control (LC) is 100% and overall survival (OS) is 63.3%. Globe was salvaged in one patient who received definitive RT. Of children who had optic nerve cut margin positivity on histopathology, 5/6(83%) died of leptomeningeal with or without CNS parenchymal disease.

**Conclusions:** RT plays an important role in the combined modality treatment of unilateral retinoblastoma. Optic nerve cut margin positivity on surgical specimen histopathology confers poor outcomes.

EP063/#1354 | Poster Topic: AS02 Radiation Oncology - PROS

#### RADIOTHERAPY IN CHILDREN YOUNGER THAN TWO-YEARS OF AGE: A TERTIARY CARE CENTER EXPERIENCE

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**Background and Aims:** Radiotherapy (RT) in paediatrics is one of the most important aspect of the treatment. However, RT referrals are often delayed due to the perceived fear of toxicity in very young children. Here we present our initial data of RT in very young children, less than 24 months of age.

**Methods:** Radiotherapy data was reviewed to retrieve paediatric patients, who received RT over a period of 3-years from February 2020 to 2023. Patients younger than 24 months were analysed.

**Results:** A total of 217 paediatric cancer patients (non CNS) received RT during the above mentioned period. Out of this, 17 (7.83%) patients were below 24 months of the age. Commonest indication for radiotherapy in infants included rhabdomyosarcoma (n=9), Wilms tumor (n=4), Ewing sarcoma (n=2), retinoblastoma (n=1) and neuroblastoma (n=1). Median age at RT was 15 months with a male to female ratio of 1.8:1. Fourteen and two patients received RT by volumetric modulated arc technique and 3-dimensional conformal radiotherapy technique respectively. One patient received brachytherapy. Majority

of the patients required short anaesthesia for the treatment. However, few patients who initially required anaesthesia could later be managed solely by behavioural therapy as they got familiarized with the RT unit. All patients tolerated RT well without any grade 3-4 acute complications. During the follow up, one patient with bladder rhabdomyosarcoma succumbed to the disease. Remaining patients have not shown any sign or symptoms of late side effects till the last follow up and are being monitored further for late toxicity.

**Conclusions:** Radiotherapy in very young children requires a careful balance between disease control and toxicities. Several studies have shown the inferior outcome after omission of radiotherapy in very young children. Therefore, any treatment de-intensification in terms of avoidance of RT should not be done outside a clinical trial.

EP064/#1455 | Poster Topic: AS02 Radiation Oncology - PROS

### RADIOTHERAPY FOR WILMS TUMOR: LONG-TERM OUTCOMES AND THERAPEUTIC IMPLICATIONS OF POST-CHEMOTHERAPY DISEASE STAGE

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**Background and Aims:** Report the long-term outcomes and patterns of failure in patients receiving radiotherapy (RT) as part of multimodal management of Wilms tumour.

**Methods:** An audit of patients who underwent RT as part of the multimodal treatment between 2009 to 2015 was conducted.

**Results:** Seventy-nine patients, with a median age of 4 years (IQR, 2-6) were included. Majority (60.7%) were males. Of these, 64 (81%) were treated for index presentation and 15 (19%) for recurrent disease. Twenty-three (29.1%) had distant metastasis (DM) at presentation (lung: 21, liver: 2, both: 2). Treatment for patients with index disease included upfront surgery (Sx) in 17 (26.5%) and chemotherapy (CTh) followed by Sx in remaining. Post-surgical stage were stage 0 (1.3%), I (15.2%), II (20.3%) and III (57%). Median interval between Sx and starting RT was 53 (IQR: 34-81) days. Flank RT (FRT) was delivered in 50 (63%), while whole abdomen RT (WART) was used in 19 (29.6%). Liver RT and whole lung RT (WLRT) was used in 4 (6%) and 23 (35.9%) patients, respectively. Median dose for FRT/WART/Liver RT

was 10.8Gy (10.8-19.8) and WLRT was 12.6Gy (10.8-12.6) in conventional fractionation. After a median follow-up of 88 (66.6-104) months, the 10-year local regional control (LRC), disease free survival (DFS) and overall survival (OS) was 84.2±4.4%, 77±5% and 78.1±5% respectively. There were 17 relapses in 16 patients (20.2%) – 11 loco-regional recurrences (LRR, 8 tumour bed and 3 intraabdominal) and six DMs. Stage III disease after chemotherapy (9 out of 11 LRRs) was a strong predictor of local relapse (72 vs 100%, p=0.007). There were no grade III-IV toxicities attributable to RT.

**Conclusions:** LRR was the predominant pattern of failure. Increased doses of RT may be explored as a strategy to optimize outcomes in patients with persistent stage III disease after chemotherapy.

EP065/#1733 | Poster Topic: AS02 Radiation Oncology - PROS

### STEREOTACTIC BODY RADIATION THERAPY (SBRT) AND RESPIRATORY CONTROL UNDER ANESTHESIA IN PEDIATRIC PATIENTS WITH LUNG METASTASES

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**Background and Aims:** Pulmonary metastases are common in pediatric solid tumors. Stereotactic Body Radiation Therapy (SBRT) delivers highly conformal ablative doses in few fractions to a well-defined target, saving healthy nearest organs from radiation doses. SBRT is safe and efficient for lung metastases with high local control rates (>90%). However, there are few data on pediatric patients. The objective is to describe irradiation of lung metastases in two pediatric patients with SBRT guided by respiratory syncro technique under total anesthesia.

**Methods:** Two pediatric patients with pulmonary metastases of a relapsed osteosarcoma and an Ewing sarcoma were anesthetized to minimize target motion in lungs and reproduce breath-hold levels on deep inspiration achieved with synchronized non-invasive mechanical ventilation and pressure support. SBRT was planned with VMAT technique using different coplanar arcs with isocenter for each PTV. Energy used was 6MV photons with Flattening Free Filters (6FFF) to reduce dose rate, minimizing the interplay effect of moving targets. Treatment was performed using multienergetic Infinity linac (Elekta Instrument AB), with multileaf collimator of 5mm adapted for SBRT which integrates Image Guided Radiotherapy (IGRT).

**Results:** Patient 1, average dose to PTV-RIL, paraesophageal and subpleural was 54.6, 52.8 and 54.2Gy, respectively; and minimum dose was 48.6, 48.6 and 48.3Gy, respectively. Complete response was achieved and maintained. Nine months after SBRT the kid died of new-onset acute leukemia. Patient 2, average dose to PTV-right superior lobe was 53.24Gy and minimum dose was 48.19Gy. Local control is maintained

after six months of SBRT. No complications were detected during the anesthetic procedure.

**Conclusions:** An optimal dosimetry delivered with anesthetic respiratory gating obtained excellent local control without toxicity. SBRT with respiratory gating under general anesthesia is feasible and well tolerated and constitutes a novel therapy for young children with lung metastases.

EP066/#162 | Poster Topic: AS02 Radiation Oncology - PROS

### RELATIVE RISK OF CARDIAC MORTALITY AND DOSIMETRIC COMPARISON AMONG THREE-DIMENSIONAL RADIOTHERAPY, VOLUME MODULATED ARC THERAPY AND PROTON BEAM IN VERTEBRAL BODY-REDUCED-DOSE CRANIOSPINAL IRRADIATION

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**Background and Aims:** We aimed to compare dose to organs at risk (OARs), and the relative risk (RR) of cardiac mortality among three-dimensional conformal radiotherapy (3D-CRT), volume modulated arc therapy (VMAT) and pencil beam scanning proton therapy (PT) in craniospinal irradiation (CSI).

**Methods:** CSI plans of 3D-CRT, VMAT and PT were generated. To reduce dose to OARs and avoid spinal abnormality, vertebral body-reduced-dose (VBRD) CSI according to SIOP recommendation was used for VMAT and PT. We delineated 2 sets of target volumes, i.e., clinical target volume1 and planning target volume1 (CTV1, PTV1) for brain and thecal sac and CTV2, PTV2 for vertebral body. Two sets of CSI dose, i.e., 23.4 and 36 Gy were prescribed to each technique. For VMAT and PT, 23.4/18.4 Gy and 36/20 Gy for PTV1/PTV2 (CTV1/CTV2 for PT) were optimized in 13 and 20 fractions, respectively. For 3D-CRT, we prescribed 23.4 and 36 Gy, to cover only PTV1. To evaluate the relative risk (RR) of cardiac mortality compared with normal population, we incorporated the mean heart dose (MHD) with the linear model.

**Results:** In total of 8 patients, 48 treatment plans, i.e., 8 plans for each technique of each dose set, were generated. PT showed the lowest mean dose to all OARs, i.e., heart, lungs, liver, kidneys, esophagus, oral cavity, stomach, thyroids, and vertebral body. MHD of 3D-CRT, VMAT and PT were 12.15, 3.99 and 0.9 Gy for 23.4 Gy-prescription, and 18.6, 5.7, and 1.2 Gy for 36 Gy-prescription, respectively. PT showed significantly less RR of cardiac mortality compared with 3D-CRT and VMAT, 1.54, 8.92 and 3.40 for 23.4 Gy-prescription ( $p < 0.001$ ) and 1.74, 12.19, 4.40 for 36 Gy-prescription ( $p < 0.001$ ), respectively.

**Conclusions:** With VBRD-CSI, PT reduced mean dose to all OARs and significantly reduced RR of cardiac mortality compared with 3D-CRT and VMAT. The advantages of PT were manifested especially with high-dose CSI.

EP067/#1558 | Poster Topic: AS02 Radiation Oncology - PROS

### IRRADIATION OF PAEDIATRIC PATIENTS WITH IMPT USING CONTROLLED INSPIRATION - FEASIBILITY, ACUTE AND EARLY LATE TOXICITY - RESULTS FROM THE PROTON THERAPY CENTER IN PRAGUE

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**Background and Aims:** Radiotherapy to the thorax/mediastinum carries the risk of severe acute and late toxicities in long-term survivors. Proton beam radiotherapy (PBRT) with controlled breathing reduces the dose to organs at risk, minimizing adverse effects. We evaluated the feasibility, toxicity and therapeutic outcomes in pediatric patients treated at our center.

**Methods:** Between August 2018 and December 31st, 2022, 19 pediatric patients (21 courses of irradiation) underwent PBRT with pencil beam scanning and controlled inspiration. 19 courses were radical and 2 were palliative re-irradiation. All patients received initial training, followed by fixation and the planning CT.

**Results:** The age of patients ranged from 11–19 years (median 16). Median follow-up was 21.9 months (3–53 months). Six patients had soft tissue sarcomas (STS), 13 had Hodgkin lymphoma (HL). Disease status and toxicity were assessed from March 1, 2023, using the RTOG scale for acute and late toxicities. The patients with STS received 45–59.4 GyE to the chest, upper abdominal wall, diaphragm, epigastrium, or mediastinum, with a median follow-up of 13 months. There were eight courses in total with two re-irradiations. Three patients died due to metastatic disease progression, one patient is alive with disease progression, and two patients are in complete remission (CR). Patients with HL underwent irradiation to the mediastinum and other sites. Six patients received 29.8 GyE and seven patients received 19.8 GyE. All patients are currently alive (median follow-up: 29 months), with 12 patients in CR and one with marginal relapse. No acute or late toxicity above grade 2 occurred in our cohort, but follow-up duration is limited.

**Conclusions:** Pediatric patients can undergo proton radiotherapy using IMPT technique and controlled breathing with low acute toxicity. No significant late toxicity has been observed, but longer follow-up is needed. Proton radiotherapy is

appropriate for selected patients requiring mediastinal or chest wall irradiation.

EP068/#1190 | Poster Topic: AS02 Radiation Oncology - PROS

### RELEVANCE OF SPLEEN AS AN ORGAN AT RISK FOR PATIENTS WITH PEDIATRIC MEDULLOBLASTOMA TREATED WITH CRANIOSPINAL IRRADIATION

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**Background and Aims:** The SIOP-Europe statement reported the spleen as a radiosensitive organ, with higher doses increasing risk of fatal sepsis. However, there is a lack of literature regarding clinical implications of splenic doses for craniospinal irradiation (CSI), which were investigated in the current study.

**Methods:** Children (3-15 years) with medulloblastoma, treated with CSI (no dose-constraints used for spleen) followed by adjuvant chemotherapy were studied retrospectively. The spleen was segmented on radiation planning computed tomography, and dosimetric parameters were extracted. Maximum grade of hematological toxicity during radiation or adjuvant chemotherapy was noted using the CTCAE v5 criteria, along with episodes of febrile neutropenia, sepsis, or any infections. Comparison of dose parameters was done using Mann Whitney test or independent t-test.

**Results:** Details of 48 patients was available for final analysis. The mean age was 9 years, 46% received standard dose (35 Gy) CSI. The dose of spleen was significantly higher in patients treated with volumetric modulated arc therapy (VMAT) or tomotherapy (n=18) (mean Dmean 276 cGy) as compared to 3-dimensional conformal radiotherapy (n=30) (mean Dmean 181 cGy). A significant correlation was seen for acute thrombocytopenia during radiotherapy with Dmean and D100 of spleen. The dose of CSI or concurrent chemotherapy was not having a significant impact on thrombocytopenia. Incidence of  $\geq$ grade 2 thrombocytopenia was associated with a mean D100 of 110 cGy (vs. 81 cGy for others) (p=0.03). No association between spleen doses and incidence of other hematological toxicity during adjuvant chemotherapy or with episodes of sepsis, infection, or febrile neutropenia was observed.

**Conclusions:** Higher splenic doses corresponded to higher rates of acute thrombocytopenia with spontaneous recovery in most patients. In general, the spleen receives low dose with CSI, which is increased with more conformal techniques. However, without any major clinical consequences, VMAT or tomotherapy-based CSI can be safely considered.

EP069/#1665 | Poster Topic: AS02 Radiation Oncology - PROS

### IMPACT OF MULTIMODAL IMAGE REGISTRATION AND FUSION ON PLANNING TARGET VOLUME ACROSS TWO ERAS: TRENDS IN PRECISION RADIATION THERAPY

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**Background and Aims:** Modern radiation treatment planning has evolved from use of hard films (HF) to to multimodality image registration with planning CT scans for target delineation. The aim of this study was to evaluate the effect of various image registration modalities on planning target volume (PTV) in pediatric patients irradiated for sarcoma of head and neck region.

**Methods:** Head and neck sarcoma patients treated at our facility of two time periods of years 2013-15 (group-1) and 2019-21 (group-2) were reviewed for diagnostic scan image registrations with planning CT scan. Each data set was further stratified according to modality of diagnostic scan image fusion which included, CT scan, MRI scan and PET/CT scan. Demographic data and volume planning target volume (PTV) was recorded in cm<sup>3</sup>. Analysis was done to define the variation in PTV based on different fusion modalities.

**Results:** Total 52 patients were identified, 16 in group-1 and 36 in group-2. In group-1, hard films were used to define the PTV in 11 (69%) patients with mean PTV volume of 216.31cm<sup>3</sup>±163.3 cm<sup>3</sup>. Volume of PTV for HF-based and MRI fusion was 156.2cm<sup>3</sup>±49.28cm<sup>3</sup> and 338 cm<sup>3</sup>±18.34 cm<sup>3</sup> respectively and was not significant (p=0.09). In group-2, majority had MRI-based fusion (n=17;47%) followed by CT-based fusion (n=11;30%). Mean PTV was 200.19cm<sup>3</sup>±121.66cm<sup>3</sup>. Volumes of PTV in group-2 for MRI based 203.46cm<sup>3</sup>±cm<sup>3</sup>42.01 and CT based fusion 215.36cm<sup>3</sup>±48.28cm<sup>3</sup> and were significant (p=0.04). A significant difference was observed in PTV trends of both specified data sets (p=0.05).

**Conclusions:** This study shows the role of multimodal image registrations trend towards precision radiation therapy in two distinct time period. The use of multimodal image registration can provide benefit in terms of improving the accuracy and precision of radiation therapy planning along with treatment individualization. However, the outcome of tumor control and relapse patten must be co-related with these results.

EP070/#1152 | Poster Topic: AS02 Radiation Oncology - PROS

### LOCALIZED HEPATOBLASTOMA ACHIEVED COMPLETED REMISSION WITH RADIATION THERAPY ONLY IN A PATIENT WITH TRISOMY 18

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**Background and Aims:** Hepatoblastoma is the most common pediatric liver tumor. Complete surgical resection is a critical component for cure; administration of neoadjuvant chemotherapy is provided to reduce tumor size to make it amenable to resection. Very few reports exist in the literature regarding a possible association between trisomy 18 (T18) patients and hepatoblastoma. Patients with T18 present with multiple abnormalities that could make surgical resection challenging. Few cases have been reported in the literature incorporating external beam radiation therapy (EBRT) for hepatoblastoma, the role of radiation in hepatoblastoma remains to be determined. We aim to describe a case where EBRT was the only modality of treatment.

**Methods:** Case report, consent was obtained from the parents.

**Results:** 19 month old female, T18 with and severe pulmonary hypertension (PHTN) oxygen dependant and multiple other abnormalities (VSD, PDA, ASD, bicuspid aortic valve, corpus callosum agenesis, bilateral talipes, esotropia, hearing loss, seizures). She was diagnosed with a liver mass initially on a routine ultrasound, further imaging with CT and MRI also confirmed a localized right hepatic lobe mass in segment 5/6, size 3.2 x 2.6 x 2.4 cm. AFP 990 ug/L (normal <9 (ug/L)). Diagnosis was consistent with localized Hepatoblastoma. Due to PHTN, surgical resection was not option hence palliative EBRT to the mass was provided (3000 cGy was delivered in 10 daily fractions over 2 weeks). She had resolution of the mass and AFP normalized after EBRT. She has been in remission now for 45 months.

**Conclusions:** Radiation may be considered in localized hepatoblastoma when surgical resection is contraindicated. Further collaborative studies are required to confirm this finding.

EP071/#861 | Poster Topic: AS02 Radiation Oncology - PROS

#### EFFICACY OF RE-IRRADIATION FOR PEDIATRIC DIFFUSE INTRINSIC PONTINE GLIOMAS

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**Background and Aims:** To analyze the efficacy and prognosticators of pediatric diffuse intrinsic pontine glioma (DPC) treated with re-irradiation.

**Methods:** The clinical data and prognostic information of DIPG children younger than 18 years old who received re-irradiation in the Department of Oncology of Guangdong Sanju Brain Hospital from May 1, 2021, to November 1, 2022, were collected. The overall survival (OS) was calculated, and univariate analysis was performed to analyze the effect of tumor volume change and rate of change on survival.

**Results:** Fifteen patients met the inclusion criteria. The median interval between the first and second radiotherapy was 8.8 months. The median

survival after re-irradiation was 3.9 months, and the median overall survival was 16.9 months. Severe complications such as fatal radiation brain necrosis was observed after re-irradiation.

**Conclusions:** Re-irradiation is still the primary treatment for pediatric diffuse intrinsic pontine glioma, prolonging their survival.

EP072/#857 | Poster Topic: AS02 Radiation Oncology - PROS

#### APPLICATION OF SHUNT IN PEDIATRIC DIFFUSE INTRINSIC PONTINE GLIOMA COMPLICATED WITH HYDROCEPHALUS: A 10-YEAR EXPERIENCE FROM A SINGLE CENTER

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**Background and Aims:** Currently, there is no unified treatment protocol for pediatric diffuse intrinsic pontine glioma with hydrocephalus. The present study aims to explore the clinical characteristics and the best intervention modality for diffuse intrinsic pontine glioma with hydrocephalus in children.

**Methods:** The detailed data of children with diffuse intrinsic pontine glioma admitted to the Department of Pediatrics of Guangdong Sanju Brain Hospital from January 2010 to December 2021 were retrospectively analyzed. The effect of radiotherapy and shunt on the prognosis of pediatric diffuse intrinsic pontine glioma complicated with hydrocephalus was evaluated.

**Results:** In total, 165 children with DIPG aged ≤18 years were included in the analysis, of whom 9 (5.5%) had mild ventricular dilatation, 48 (35%) had hydrocephalus, and 11 (22.9%) underwent cerebrospinal fluid shunting, of whom 10 (90.9%) underwent ventriculoperitoneal shunt and 1 (9.1%) underwent endoscopic third ventriculostomy. After shunt and radiotherapy, 53 cases of hydrocephalus could be evaluated, of which 37 patients (69.8%) were significantly relieved, and 16 (30.2%) were not. 99 children had tumor progression after treatment, including 41 cases (41.4%) with hydrocephalus and 5 cases (12.2%) with ventriculoperitoneal shunt. A total of 138 children were included in the survival analysis, which revealed that hydrocephalus, mild ventricular dilatation, and no ventricular abnormality had no effect on the prognosis ( $p=0.944$ ). The treatment of hydrocephalus at the initial diagnosis did not affect the prognosis,  $p=0.405$ . The median survival of the hydrocephalus remission group post-radiotherapy was 12 months, and 8 months for the non-remission group,  $p=0.042$ . The median survival was 20 months in the shunt group and 8 months in the untreated group ( $p=0.005$ ).

**Conclusions:** Asymptomatic ventricular enlargement in pediatric DIPG does not require surgical intervention. The remission of hydrocephalus after radiotherapy is a favorable prognostic indicator. Cerebrospinal fluid shunt could improve the prognosis of children with hydrocephalus when the tumor progresses post-radiotherapy.

EP073/#1501 | Poster Topic: AS02 Radiation Oncology - PROS

### ADJUVANT RADIOTHERAPY IN PEDIATRIC ASTROBLASTOMA: A CASE REPORT AND REVIEW OF LITERATURE

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**Background and Aims:** Astroblastoma (AB) is an uncommon glial tumor. The incidence and management are unclear. We present a case of a child underwent complete surgery and radiotherapy.

**Methods:** A case report of a pediatric patient and review of literature.

**Results:** AB is a rare malignancy derived from a primitive cell, astroblast. The histopathological feature is the presence of perivascular pseudorosettes. The main localization reported is supratentorial, and the radiological characteristics are well-demarcated masses with solid and a multicystic component, giving a “bubbly” appearance. Due to the low incidence, the management can be controversial, according to the degree of differentiation.

We reported a case of a 6 years-old girl with a history of headache, nausea and strabismus, a brain MRI showed heterogeneous tumor lesion measuring 62x53 mm with vasogenic edema located in the left frontoparietal region. She underwent gross total resection (GTR) surgery, and the pathological report showed an astroblastoma with a proliferative index of 10%.

The multidisciplinary board established adjuvant chemoradiotherapy as her treatment. She did not tolerate temozolamide and only received radiation therapy to the resection cavity at a dose of 59.4 Gy (1.8 Gy/fr) with a 3D conformational technique. There were no adverse events reported during treatment, and corticoids were not necessary. After 9 months of follow up, she continuous asymptomatic and the MRI controls are negative for tumor recurrence.

**Conclusions:** AB is a rare entity with an uncertain established management. Radiotherapy adjuvant may have a role as part of the treatment. We consider it is necessary to determine factors associated with better prognosis.

EP074/#1073 | Poster Topic: AS02 Radiation Oncology - PROS

### PROTON BEAM THERAPY IN CHILDREN WITH MEDULLOBLASTOMA – PROSPECTIVE SINGLE-INSTITUTION ANALYSES OF POSTTHERAPEUTIC IMAGING CHANGES

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**Background and Aims:** Radiotherapy is a key component of treatment for medulloblastoma (MB). Proton beam therapy (PBT) plays an important role because of its potential of sparing organs at risk. We evaluated the outcome with particular regard to post therapeutic imaging changes after PBT in patients with MB.

**Methods:** Patients with MB treated between 11/2013 and 10/2017 and enrolled to a prospective in-house registry study KiProReg were eligible. Data on patient and tumour characteristics, therapy and adverse events (according to CTCAEv4/5) were evaluated. During follow-up (FU), imaging reports were screened for evidence of new lesions and changes in imaging in a standardized manner. Images were reviewed by a radiologist and graded according to Fouladi et al. *J Clin Oncol* 22, 4551-4560.

**Results:** Fifty-five patients were eligible. Median age at diagnosis was 6.1 years (range, 0.9-16.2). Eleven patients were treated for recurrent or progressive disease. Twenty-nine patients received chemotherapy (CTX) before PBT, with an intrathecal component in 21 patients. Ten patients received high-dose CTX. Craniospinal irradiation was performed in 49 (89.1%) patients and local PBT only in six patients (10.9%). Median total dose was 54.0 Gy (RBE) (range, 30.0-74.0 Gy (RBE)). Four patients received hyperfractionated irradiation. Median FU was 36 months (range, 2.7-67.1). Thirteen patients developed disease progression (7 systemic; 2 local; 4 both). Ten patients deceased. Thirteen patients were identified during standardized screening process. In six patients, full imaging was available for detailed review. Neuroradiological review revealed no transient imaging changes in 4, grade 2 in one or grade 4 in one patient, respectively. The patient with grade 2 presented brief transient diplopia and ataxia simultaneously. Imaging changes occurred 1.3 and 6.9 months after PBT and resolved during FU without any specific treatment.

**Conclusions:** Rates of symptomatic imaging changes were low after PBT in MB patients. Larger cohorts and prospective studies are desirable for further analyses.

EP075/#44 | Poster Topic: AS02 Radiation Oncology - PROS

### PAEDIATRIC RADIOTHERAPY IN ROMANIA- CURRENT PROVISION AND CHALLENGES: A SURVEY BY THE SIOP EUROPE QUARTET PROJECT

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**Background and Aims:** Significant differences in outcome and survivorship in childhood cancer still exist across Europe, with poorer results in eastern regions. We aimed to map the provision of paediatric radiotherapy in Romania, identifying the key future requirements and main challenges.

**Methods:** An online survey supported by SIOP Europe was distributed to all 33 (13 public, 20 private) radiotherapy departments operating across Romania. The questionnaire contained 22 open-ended and multiple-choice questions, exploring resources, clinical trial participation, patient referral practice, and Radiotherapy Quality Assurance (RTQA).

**Results:** Nineteen centres (58%) responded to the survey, ten of which treat children and seven having designated radiation oncologists for paediatric patients. While access to advanced photon techniques is high (16/19 with IMRT/IMAT), only six centres report availability of general anaesthesia. Participants agree that challenges include a lack of national/regional specialised paediatric radiotherapy centres, limited access to mentors or training opportunities, and availability of robust multidisciplinary tumour boards. Only one centre reports participating in paediatric radiotherapy clinical trials; likely attributable to a lack of national trial infrastructure and poor local engagement. Physicians in 16 centres refer children for proton therapy but find the long waiting time and laborious paperwork difficult. Sixteen responders considered paediatric RTQA essential; agreeing that a (inter)national RTQA program is needed and would benefit patients.

**Conclusions:** While advanced radiotherapy techniques are widely available for children in Romania, the lack of centralised and harmonised practice, scarce training opportunities, underdeveloped clinical trial infrastructure, and laborious proton referral process highlighted by the survey, describe a complex landscape with required improvements.

EP076/#1830 | Poster Topic: AS02 Radiation Oncology - PROS

### MULTIMODALITY THERAPY FOR PRIMITIVE MYXOID MESENCHYMAL TUMOR OF INFANCY (PMMTI): A CASE SERIES AND LITERATURE REVIEW

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**Background and Aims:** Primitive Myxoid Mesenchymal Tumor of Infancy (PMMTI), first described by Alaggio in 2006, has been classified as a "Sarcoma with BCOR genetic alterations" in the 2020 WHO Classifications of Soft Tissue Tumours. Due to the deleterious chemotherapeutic effect, multiple surgeries, local tumor invasiveness and recurrence, proton beam therapy (PBT) would be a beneficial treatment adjunct to reduce toxicities and improve survival.

**Methods:** The literature review (fifty-four cases) was obtained through the Internet, PubMed, Ovid, and Google Scholar. Cases were identified as PMMTI on the basis of genetic alterations (BCOR ITD and BCL6, absence of ETV6-NTRK3), immunohistochemistry, and histopathology.

**Results:** There were 26 (48%) males and 28 (52%) females. The overall median (interquartile range [IQR]) age was 5 (1,10) months; median (IQR) follow-up was 12 (4,24) months. Nine patients underwent only surgery and had no recurrences with a median (IQR) follow-up of 17 (1.4, 24) months. Eight patients had surgery alone for first recurrences at a median (IQR) of 4 (2, 6) months, and median (IQR) survival at 5 (4, 8.5). Nine patients received chemotherapy and surgery alone; their median (IQR) time to recurrences was 3 (3,8) months with a survival outcome of 32 (5, 60) months. One patient had tri-modal (surgery, chemotherapy, radiation) treatment at the time of diagnosis; she had no recurrences with a disease-free survival of 46 months. Four patients received tri-modal therapy for their tumor recurrence (median [IQR] 6.5 [2.5, 30] months after the initial diagnosis) and had a median (IQR) survival outcome of 12 (11.3, 44.5) months with no additional recurrences or major toxicities with PBT.

**Conclusions:** Treatment depends on surgery, chemotherapy, and/or radiation therapy if the tumor is unresectable or results in multiple recurrences. PBT would be a reasonable way to deliver multimodality therapy, improve local control, and further reduce normal tissue exposure.

EP077/#925 | Poster Topic: AS02 Radiation Oncology - PROS

### ROLE OF RADIOTHERAPY IN THE TREATMENT OF PREDIATRIC EWING'S SARCOMA IN A TERTIARY CANCER CENTER

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**Background and Aims:** A multimodal pattern combining systemic and local treatment is required for pediatric Ewing's sarcoma. While surgery is considered as a more preferable option for local control, we would like to investigate the value of radiotherapy based on the experience of a tertiary cancer center.

**Methods:** In this retrospective study, patients aged  $\leq 18$  diagnosed with non-metastatic Ewing's sarcoma in the Sun Yat-sen University Cancer Center were screened. Those who received both systemic chemotherapy and local treatment were considered eligible. The eligible patients were divided into groups based on treatment modality. Overall survival (OS) and locoregional relapse-free survival (LRRFS) are the two main endpoints.

**Results:** Nine hundred and twenty-three patients with Ewing's sarcoma from January 1, 1998 to July 31, 2022 were screened and 137 were eligible. The median follow-up time was 61.0 (5.4-204.2) months. The radiation dose applied in our cancer center were 40-60Gy to gross tumor volume and 30-54Gy to high-risk region. Thirteen (9.5%) patients accepted definitive radiotherapy plus chemotherapy without surgery, and 76 (55.5%) patients accepted adjuvant radiotherapy in combination to surgery and chemotherapy. Most (92.3%) patients' primary tumor sites in the definitive radiotherapy group were head and pelvis. The 5-year OS and LRRFS in the two groups were 92.3% (77.8-100.0%) and 84.6% (65.0-100.0%), 74.4% (64.4-84.4%) and 73.3% (62.9-83.7%), respectively, superior to patients receiving surgery and chemotherapy alone (58.6% [44.1-73.1%] and 56.8% [39.4-74.2%]). Moreover, applying radiotherapy after surgery could provide higher 5-year OS and LRRFS than surgery alone, even in the R0 resection subgroup (75.6% [62.5-88.7%] vs 60.9% [45.6-76.2%] and 74.5% [60.8-88.2%] vs 62.2% [44.8-79.6%]).

**Conclusions:** For the local management of pediatric Ewing's sarcoma, definitive radiotherapy might be an option that guarantees satisfactory controls for patients that are not appropriate or refuse to accept surgery. Adjuvant radiotherapy might further strengthen local control in combination to surgery, despite whether R0 resection is achieved.

EP078/#1616 | Poster Topic: AS02 Radiation Oncology - PROS

#### MANAGEMENT OF CHILDHOOD INTRACRANIAL GERM CELL TUMORS IN A LOW- AND MIDDLE-INCOME SETTING

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**Background and Aims:** Germ cell tumors (GCT) are a rare heterogeneous group of neoplasms mainly occurring in midline structures. Recent studies suggest that intracranial GCT can be managed with

surgery followed by adjuvant chemotherapy (CT) and dose-reduced radiotherapy (RT) based on the tumor response. The aim of this study is to report our local experience with intracranial GCT.

**Methods:** We reviewed the management and outcome of 5 patients treated for intracranial GCT in the Pediatric Oncology Department of Salah Azaiez Institute of Tunis, in the decade from 2013 to 2023.

**Results:** A total of 5 male patients, with a median age of 15 years were identified. Tumor location was either pineal or suprasellar. Bifocal disease was found 2 patients. No disseminated disease at diagnosis was found. Neurosurgery was limited to ventriculoperitoneal shunting in patients presented with acute intracranial hypertension. Multiagent CT was used: 4 courses of alternating Etoposide-Carboplatin/Etoposide-Ifosfamide regimen for patients with germinoma; PEI regimen (Cisplatin, Etoposide, Ifosfamide) for patients with non-germinomatous germ-cell tumors (NGGCT). RT dose and field were based on the tumor's response to CT. Complete remission after CT was obtained in only 2 patients. Localized germinoma was treated with Whole-ventricular RT with a dose of 24Gy in 12 fractions, followed by a focal boost radiation up to a total dose of 40 Gy in case of residual disease. Whereas NGGCTs were treated with focal RT with a dose of 36-40Gy in 18-20 fractions. Two patients had progressive disease with spinal dissemination discovered during RT and underwent Craniospinal irradiation (CSI) with a dose of 30Gy in 16 fractions. After a median follow up of 14 months, 2 patients remain alive and disease-free, whereas the other 3 are deceased of disease.

**Conclusions:** Our study demonstrates the feasibility of strategies combining CT and RT, under reserve of a higher rate of spinal recurrence.

EP079/#149 | Poster Topic: AS03 CCI - Childhood Cancer International

#### WHO IS THE NEW FURRY MEMBER OF THE HOME-PALLIATIVE-CARE TEAM?

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**Background and Aims:** Since March 2020 the world of health care has experienced changes in the way it provides services. This study discusses the role of an accompanying dog in home visits to children in palliative care. This study assesses the fulfillment of a series of activities carried out in an intervention assisted by animals (IAA)

**Methods:** Review of all the field notes during the period from 20 March 2020 to 15 February 2023. The observations and registered in a laptop office Excel were: • Request for consent from the caregiver • Observation of the patient's gestures (touch or caress) or fear or discomfort signals during the AAI • Transcript of comments from the child/caregiver • Quantification of the achievement obtained A Checklist is elaborated that serves as a basis for subsequent experiences.

**Results:** We reviewed 45 field notes corresponding to 8 patients followed for 3 years until the time of their death. 85% of the patients had childhood cancer. The two dogs aged 7 and 2 years, were subjected to

conditions of hygiene and biosecurity. 10% of the families had animals in their home. 99% of IAA fulfilled all the proposed activities. Signs of fear or discomfort were observed in the first minutes in 2% of the interventions. 85% of the interactions achieved between 80 and 90% the quantified objective. If this percentage was less than 80, a subsequent intervention is scheduled. The narration of the comments of the patient and his caregiver predominated to initial surprise and the desire to repeat at the end of the IAA

**Conclusions:** The situation of the pandemic brought needs not previously analyzed, in the relationship of the pediatric patient confined to his home, their family and the palliative care team. This study, with its limitations, set a precedent on pets as therapeutic assistants in palliative care domiciliary visits by the Panama national team.

EP080/#1463 | **Poster Topic: AS03 CCI - Childhood Cancer International**

### STRESS AND COPING STRATEGIES AMONG PARENTS OF CHILDREN WITH CANCER

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**Background and Aims:** Childhood cancer is still a psychological and existential challenge. Both parents and children are affected by the psychological stress associated with childhood cancer. Research on parental stress and coping strategies in pediatric oncology care in developing countries such as Tunisia is scarce. We aimed to determine the level of perceived stress, coping strategies and association between these concepts among parents of children with cancer

**Methods:** A cross sectional study was conducted in the pediatric oncology sector in a Tunisian university hospital, from April to September 2022. We included parents of children and adolescents with cancer, who were at distance of at least 02 month from diagnosis and at most 02 year s after the end of treatment. Coping strategies and perceived stress were assessed using respectively the Brief COPE Scale and perceived stress scale (PSS). Association between coping strategies and PSS score was tested using the spearman correlation test (expressed by the Rho coefficient:  $r_s$ )

**Results:** A total of 65 parents were included with mean age of 37.9 years  $\pm$  7.42. Most parents were unemployed or daily workers (64.6%). The most adopted strategies by parents were, in descending order with mean scores  $\pm$  SD: Religion (7.2  $\pm$  1.2), planning (6.8  $\pm$  1.1), acceptance (6.5  $\pm$  1.3), active coping (6.3  $\pm$  1.3), seeking instrumental support and emotional support (5.96  $\pm$  1.6), positive reinterpretation (4.9  $\pm$  1.5), denial (4.2  $\pm$  1.9), expression of feelings (4.4  $\pm$  1.0), blame (4.0  $\pm$  1.8), self-distraction (4.0  $\pm$  1.3), humor (2.6  $\pm$  0.8), behavioral Disengagement (2.6  $\pm$  1.2) and substance use (2.2  $\pm$  0.5) PSS mean score was 20.8  $\pm$  6.7. Moderate level of stress was observed in 66.2% (n=43). The sig-

nificant correlations ( $p < 0.05$ ) between the total perceived stress score and the coping strategies are as follows: Positive reinterpretation ( $r_s = -0.33$ ;  $p = 0.006$ ), acceptance ( $r_s = -0.46$ ;  $p < 10^{-3}$ ) and denial ( $r_s = 0.30$ ;  $p = 0.009$ )

**Conclusions:** Parents of children diagnosed with cancer are profoundly affected by their child's diagnosis. This study identified several sources of stress and strategies used to cope with stress by Tunisian parents of children with cancer

EP081/#1737 | **Poster Topic: AS03 CCI - Childhood Cancer International**

### DETERMINANTS OF CHILDHOOD CANCER IMPACT ON FAMILY FUNCTIONING

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**Background and Aims:** A childhood cancer (CC) is highly distressing event that can affect the psychosocial well-being of parents and family members. It constitutes one of the most disruptive experiences for parents. In Tunisia, there is not yet a published study concerning this issue, so we aimed to assess determinant factors of CC impact on Tunisian families.

**Methods:** It's a cross-sectional study conducted from April to September 2022 among parents of children diagnosed with cancer for at least 2 months and up to 2 years after treatment completion, and treated in the onco-pediatric sector of a Tunisian university hospital. We used a self-administered questionnaire. Valid Arabic versions of the Perceived Stress Scale (PSS) and the Brief cope were used to assess parents' perceived stress levels and coping strategies. Parents' self-reported functioning and family functioning were assessed using the valid Arabic version of the PedsQL TM Family Impact Scale. Multiple linear regression was used to determine associated factors to total score of PedsQL scale. The level of significance was set at  $p < 0.05$

**Results:** A total of 65 parents were recruited, with a mean age of 37.9  $\pm$  7.42 years. Participants tended to have overall moderate levels of perceived stress and family functioning with mean scores of 20.8  $\pm$  6.7 and 53.6  $\pm$  20.7 respectively. Among the 14 coping strategies, religion and planning earned the highest mean scores (7.2  $\pm$  1.2 and 6.8  $\pm$  1.1 respectively). The Mean total PedsQL score was moderate (53.6  $\pm$  20.7). Regarding CC' family impact, overall PSS score ( $\beta = -0.57$ , CI<sub>95%</sub>: [-0.61; -0.49],  $p < 0.001$ ), average socioeconomic level ( $\beta = 0.39$ , CI<sub>95%</sub>: [0.19; 0.76],  $p < 0.001$ ), and death of a parent ( $\beta = -0.19$ , CI<sub>95%</sub>: [-0.22; -1.16],  $p < 0.026$ ) were the predictors in the linear regression analysis (adjusted R<sup>2</sup> = 0.59)

**Conclusions:** CC has the potential to be traumatic for family members. Therefore, more resilience promoting and coping skills interventions must be implemented to fulfill their psychological well-being needs.

EP082/#233 | Poster Topic: AS03 CCI - Childhood Cancer  
International

### WEEKLY CONTROL AGENDA OF THE MANAGEMENT OF CHEMOTHERAPY AT HOME, AIMED AT PARENTS AND/OR ADOLESCENTS DIAGNOSED WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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**Background and Aims:** ANTECENTES: After an extensive search for information, regarding the use and existence of weekly control agenda of chemotherapy management at home, in the diagnosis of ALL. No articles were found. **OBJECTIVES:** Implement and share the weekly control agenda of chemotherapy management at home, aimed at parents and/or adolescents diagnosed with acute lymphoblastic leukemia

**Methods:** Diseño weekly agenda of treatments, for parents with children and/or oncological adolescents. The agenda will have the following sections: Data section: Patient informational data. Information section: Information on childhood cancer, detention and treatment. Treatment stages section: Explanation of chemotherapy protocol. Maintenance stage section: Weeks of treatment. Purinethol weekly calendar section, Appointments section: Importance and calendar dates. Alarm data section: Se will specify the alarm data to be identified.

**Results:** After 6 months of having implemented the weekly agenda, a quantitative survey is conducted. Which resulted in the same opinions on the part of the parents. Everyone commented that it was a great support for their daily life in the treatment of their son.

**Conclusions:** We consider that the agenda, has notworked in an incredible and positive way for our patients, it was noted that the agenda helps to take better control of the intake of chemotherapy at home, which prevents children from missing doses or forgetting the consumption of the same drug; since ignoring the medication in the long term affects recovery and with the agenda we can avoid relapses of the disease later.

EP083/#1132 | Poster Topic: AS03 CCI - Childhood Cancer  
International

### END-OF-LIFE AND BEREAVEMENT-RELATED INFORMATION AND SUPPORT NEEDS FOR FAMILIES OF CHILDHOOD CANCER PATIENTS

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**Background and Aims:** About 20% of childhood cancer patients in high-income countries do not survive their illness. In low-and-middle-income countries, 70-80% may not. The purpose of this research was to explore information needs for families of children facing end of life to use in developing content for the *Together by St. Jude*™ global online resource about childhood cancer. This effort was part of a Quality Improvement project at St. Jude Children's Research Hospital to refine existing patient education and plan future resources.

**Methods:** St. Jude Legacy Voice is an advisory committee of bereaved family members of patients treated at St. Jude. Members were invited to participate in a survey about their information preferences on topics related to facing a difficult diagnosis, palliative care, and bereavement. St. Jude health care providers (HCPs) who care for patients at the end of life were also asked to participate in a mirrored survey. Respondents had the opportunity to share comments using open-ended response fields. Two independent coders examined free-text responses and organized content by themes, which were discussed and refined to reach consensus.

**Results:** A total of 41 family caregivers and 216 HCPs completed surveys, yielding 130 provider comments and 32 family caregiver comments. Several themes emerged to describe key topics needed for bereaved parents: talking to your child about death, support for siblings, emotional support for parents, encouragement during the decision-making process, age and developmental stage appropriate information for children and teens, education about the dying process, and information about hospice.

**Conclusions:** Caregivers and HCPs described a broad range of topics to support families across illness, at end of life, and into bereavement. Our analysis uncovered a content gap in existing resources to support families whose child had died unexpectedly. These results can inform next steps in planning and delivering resources.

EP084/#287 | Poster Topic: AS03 CCI - Childhood Cancer  
International

### ASSESSMENT OF TRANSITION READINESS AMONG ADOLESCENT PATIENTS AND THEIR CAREGIVERS AT A TERTIARY REFERRAL CENTER FOR PEDIATRIC CANCER AND BLOOD DISEASES

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**Background and Aims:** Transitioning from pediatric to adult care has become vital as more adolescents with special health care needs survive into adulthood. Adolescents, their families, and healthcare providers should prepare to ensure a smooth transition. Transition readiness of adolescents must be evaluated to tailor transition programs to their needs.

**Objective:** To evaluate the readiness for the transition of adolescent patients with the following conditions: a) thalassemia, b) hemophilia, c) those who have completed anti-neoplastic therapy and childhood cancer survivors, and that of their caregivers; to describe the clinical and demographic profile of the respondents.

**Methods:** This was a cross-sectional study in the PCMC- Cancer and Hematology Division, wherein 77 adolescent-caregiver dyads answered a self-administered transition readiness questionnaire in Filipino. The questionnaire was adapted from the transition readiness assessment tools of the American Society of Hematology and Got Transition™.

**Results:** Most of the respondents were in middle adolescence (40.3%), and completed anti-neoplastic therapy and childhood cancer survivors (66.2%). Respondents with thalassemia and those who completed anti-neoplastic therapy gave a lower average rating on the importance of being able to manage their health care compared to their hemophilia counterparts. Both groups gave a low-average rating on the importance of transitioning to adult healthcare, their confidence in managing their healthcare, and in preparing for the transition. The caregivers also gave a low-average rating in the importance of and their confidence in their child to manage his/her healthcare and in preparing for the transition. Across the domains of health management skills, most adolescents were still in the beginning stages.

**Conclusions:** The Cancer and Hematology Division transition program should emphasize the develop of the adolescent's health management skills. Transition readiness assessment should be done periodically within each stage of adolescence to obtain a clearer picture of how ready an adolescent patient with special health care needs is for transition to adult care.

EP085/#1200 | Poster Topic: *AS03 CCI - Childhood Cancer International*

#### FINANCIAL SUPPORT FOR MEDICAL EXPENSES AMONG CHILDHOOD CANCER SURVIVORS BY HEARTLINK MUTUAL AID AND ITS OPERATION

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**Background and Aims:** With progress in treatment, 70–80% of children with cancer are curable. However, they face challenges of obtaining life insurance when they seek long-term self-realization as a member of society after completing treatment.

**Methods:** Study subjects were 96 who received hospitalization benefits among total of 478 enrolled in the Heart-Link Mutual Aid Plan from 2005 to 2022. The plan pays 7,000 yen/day for hospitalization due to injury or illness with an additional 5,000 yen/day for stroke, and 3,500 yen/day for hospitalization due to imminent miscarriage (up to 60 days), and 20,000 to 80,000 yen for surgical expenses. We collected information on the subjects from the debtor insurance companies. The IRB at the PI's facility approved this protocol.

**Results:** The underlying diseases of childhood cancer survivors (CCSs) who received hospitalization benefits were hematologic tumor (n=62), brain tumor (n=5), abdominal tumor (n=12), sarcoma (n=12), and others (n=5). Age at onset of primary disease ranged from 0 to 20 years (median 6), number of hospitalizations ranged from 1 to 10 (median 1), age at first admission ranged from 12 to 46 years (median 28), and 3 to 38 years after completion of treatment (median 18.5 years). The total number of hospitalizations was 198, and surgery was performed in 105 of them (53%). All insured cases were paid. Even after deducting office operating expenses from the total premium income to date, the company has been running a stable surplus, and the remainder of the proceeds support the 50th SIOP Japan as well as domestic academic conferences, and patient association activities.

**Conclusions:** The number of enrollees in the plan has reached 478, of whom 96 have received a total of 198 hospitalization benefits. There have been no cases of nonpayment, and the stable profitability of the plan is serving to alleviate the financial concerns of CCSs.

EP086/#1300 | Poster Topic: *AS03 CCI - Childhood Cancer International*

#### IMPLEMENTING SOCIAL DETERMINANTS OF HEALTH SCREENING IN AN OUTPATIENT PEDIATRIC ONCOLOGY CLINIC

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**Background and Aims:** Among children with cancer, social determinants of health (SDoH) are associated with outcome disparities. Routine screening for SDoH is critical to identify health-related social needs and to connect families with available resources in a timely manner. We implemented SDoH screening in a large pediatric oncology clinic in New York City.

**Methods:** Self-reported SDoH data were collected through the patient portal as part of the check-in process prior to appointments. Screening questions were based on those used in other areas of the hospital

and included topics such as access to transportation, food and housing security, and emergency room utilization. Demographic data including race, ethnicity, and preferred language were extracted from the electronic medical record.

**Results:** From 11/2022-3/2023, 1,160 patients were seen in the pediatric oncology clinic and thus eligible for screening. In total, 37% (n=432) pediatric oncology families responded, with 66% (n=284) responding on the day of their clinic appointment. Of those that responded, 78% (n=339) preferred English language, 38% (n=162) were Hispanic, and 18% (n=78) were non-Hispanic Black. Twelve percent (n=50) of respondents reported worrying about food or food not lasting, 12% (n=39) reported being unable to pay their housing payment on time, 7% (n=21) reported being unable to attend an appointment due to lacking transportation, and 25% (n=74) reported two or more emergency room visits in the past year.

**Conclusions:** The outpatient pediatric oncology clinic at Columbia University Medical Center serves a diverse patient population with a high prevalence of unmet social needs. With only 37% of families screened, the reported proportion of families with food, housing, and transportation insecurity likely underestimates the true number. On its own, the patient portal is insufficient to collect data from most patients, thus additional options such as paper forms must be available to optimize response rates.

EP087/#248 | Poster Topic: AS03 CCI - Childhood Cancer International

#### GIVEN THE ABOVE FINDINGS, IT CAN BE SAID THAT THE DESIGNED GRIEF THERAPY PROTOCOL IS EFFECTIVE ON REDUCING THE SYMPTOMS OF CHRONIC GRIEF

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**Background and Aims:** The present study investigated the effectiveness of grief therapy protocol based on dialectical behavior therapy (DBT) in reducing the symptoms of chronic grief in mothers who lost their child to cancer in the city of Tehran.

**Methods:** For this purpose, the research was designed as a quasi-experimental pretest-posttest on a control group. All mothers who are living in Tehran, are under support of MAHAK and lost their child due to cancer- at least 4 months should have passed since the date of their child's death-, are the statistical population. With a simple random sampling method, 30 mothers were selected based on the result of Kendall chronic sorrow instrument which shows chronic grief for them. They were randomly set apart into two groups experimental (n=15) and control (n=15).

**Results:** The grief treatment program was implemented in 10 sessions, once a week for 75 minutes. With the completion of therapeutic interventions, two experimental and control groups were evaluated

by Kendall chronic sorrow instrument as the post-test stage. After the invention, the research data were analyzed using descriptive and inferential statistical methods. The findings indicated that there was a significant difference between the experimental and control groups in reducing the symptoms of chronic grief.

**Conclusions:** Given the above findings, it can be said that the designed grief therapy protocol is effective on reducing the symptoms of chronic grief.

EP088/#424 | Poster Topic: AS03 CCI - Childhood Cancer International

#### PSYCHOSOCIAL LIVED EXPERIENCE OF PARENTS WITH CHILDREN DIAGNOSED WITH CANCER IN LUBUMBASHI

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**Background and Aims:** In the Democratic Republic of Congo, no psychological screening programs are in place to enable health care providers to identify parents at high risk of psychological morbidity so that clinical interventions can be initiated earlier and thus prevent serious cases. To determine the psychosocial problems, social acceptance and the impact of the costs of parents whose child has cancer.

**Methods:** We carried out a descriptive cross-sectional study over two-year periods (from January 3, 2018 to March 31, 2020) in the pediatric oncology unit of clinics at the University of Lubumbashi, in DR Congo.

**Results:** 129 parents of children with cancer in the pediatric oncology unit were included in our study. Most children with cancer (53%) were accompanied by their mothers who had a low level of education (53.0%). Emotional shock was the most observed reaction (68%) to the announcement of the disease (cancer). Retinoblastoma has had a significant economic impact on families without medical coverage. Only 38% received psychological support from parents. Sadness was the most common feeling (77%) of households. Support workers consider their relationship with the medical profession acceptable in 67% and difficult in 11%. The majority of parents (78%) felt that the time to provide medical care was longer than expected.

**Conclusions:** Parents of children with cancer had different feelings and reactions. This observation may be useful for the development of a health policy, in particular that of pediatric cancer in DR Congo

EP089/#431 | Poster Topic: AS03 CCI - Childhood Cancer International

### EVALUATION OF THE FINANCIAL AND ECONOMIC COST OF CHILDHOOD CANCER CARE IN LUBUMBASHI: A MIXED STUDY

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**Background and Aims:** The experience of childhood cancer imposes a considerable financial cost on a household. This financial and economic cost is often the cause of abandonment of care. The objective of this study was to determine the average total costs of childhood cancer management from diagnosis to one year of follow-up while exploring its impact on households.

**Methods:** We used a mixed study, with a micro-costing approach, to calculate the financial and economic costs of households when they support the cancer of one of their members. To analyze the data, we used descriptive statistics and descriptive qualitative methods.

**Results:** Our study covered 129 households, the average age of guardians being 36.1±9.3 years. Households traveled an average distance of 77.2±41.36 km to reach the hospital. The majority of households financed their own health care (95.9%). The tutors spent an average total cost of \$524.4±\$50, of which with a direct cost (\$378.1±\$61) representing 72.1% of the total cost and 27.9% of the indirect cost (\$146.3±\$39). Nephroblastoma had an average annual cost of \$1042 higher compared to other types of cancers followed by leukemia (\$977.3), lymphoma (\$831.7), neuroblastoma (\$803.1), and retinoblastoma (\$797.5), bone tumors (\$733.8)

**Conclusions:** The results of this study suggest the importance for the government to create a system of insurance or mutual health insurance which will make it possible to alleviate the costs and which would play an important role in alleviating the financial burden of households in patients with cancer.

EP090/#902 | Poster Topic: AS03 CCI - Childhood Cancer International

### LONG-TERM PATTERN OF PSYCHIATRIC PRESCRIPTION AMONG SWEDISH PARENTS OF CANCER-DIAGNOSED CHILDREN

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**Background and Aims:** Few studies explored the impact of a child's cancer diagnosis on psychiatric medication usage among parents. We aimed to investigate the longitudinal psychiatric prescription patterns among Swedish parents of cancer-diagnosed children.

**Methods:** Using multiple Swedish registers, we identified 1886 fathers and 1942 mothers of cancer-affected children who were diagnosed at age of 0-14 years from 1st, Jul 2007 to 31st, Dec 2014 in Sweden. Random 5 individuals were matched for each parent (8615 fathers and 8857 mothers) conditionally. We calculated annual average cumulative DDDs for any psychiatric prescription or for a specific main type among parents of children with cancer. Regression models were built within an interrupted time series framework to explore the impact pattern of a child's cancer diagnosis on the psychiatric dosage changes over time.

**Results:** The number of DDDs dispensed for psychiatric prescription among parents with cancer-affected children was higher than the matched comparisons after the child's cancer diagnosis. Mothers were more likely than fathers to be prescribed psychiatric medication. A slope change impact pattern was found for mothers of children with cancer while a level change impact pattern was found for fathers. Compared with the matched parents, 11.0% of the number of DDDs dispensed for any psychiatric medication among fathers with a cancer-affected child might be attributable to the child's cancer diagnosis around one year after the index date, while the attributable proportion was 22.7% among mothers during the same period.

**Conclusions:** Mothers were affected in a long-term pattern with an increase in psychiatric medication usage over time, while fathers were affected immediately after the child's cancer diagnosis and the adverse impact was constant over time. Psychiatric support and needs of prevention are highly required for both mothers and fathers of children with cancer.

EP091/#584 | Poster Topic: AS03 CCI - Childhood Cancer International

### AN EXPLORATION OF THE PSYCHOSOCIAL ISSUES AND SUPPORT NEEDED BY PARENTS AND CARERS OF CHILDREN DIAGNOSED WITH CANCER: THE CASE OF KIDZCAN ZIMBABWE

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**Background and Aims:** This study focused on exploring psychosocial issues and support needed by carers of children diagnosed with Cancer. KidzCan was used as the case study. The objectives of the study were to explore psychosocial issues of carers of children diagnosed with cancer, to assess the needs of carers of children diagnosed with cancer and to establish support services for carers of children diagnosed with

cancer. A qualitative approach was used during the study where in-depth interview schedules and key informant interview guides were used as data collection tools. There were about twenty-two (22) participants to the study.

**Methods: qualitative research, indepth interviews, key informants**

**Results:** The findings of the research were that there are psychological issues affecting carers of children suffering from cancer, there is an array of needs for carers and there are not enough support services available for carers of children suffering from cancer. The study concludes that carers of children with cancer have psychosocial issues that are often neglected as focus is mainly directed towards curative interventions. The study also found out that carers of paediatric cancers have needs that are overlooked. The researcher further looked at available support services for carers, hence the need for integrating palliative care in the healthcare sector at national level. Also the researcher found out that a holistic approach to chronic illnesses ensures quality of life for both children suffering from cancer and their carers.

**Conclusions:** The study recommends training of Psychotherapists in the field of oncology and development of attitudes of Nurses towards emotional, psychosocial as well as behavioural needs of carers of children diagnosed with cancer. The oncology centres should have formal support groups to help the carers of children diagnosed with cancer for psychosocial issues and should also offer professional psychotherapy to carers to further help them with the psychological issues.

EP092/#314 | Poster Topic: AS03 CCI - Childhood Cancer  
*International*

### THE CLUB OF JOY DOCTOR HEART

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**Background and Aims:** BACKGROUND: The COVID Pandemic led to the creation of virtual platforms for access to health, aimed at the family children's cancer group.

**Methods:** MATERIAL AND METHODS: Created conferences given by zoom and live, and free educational workshops led by Doctor Heart and the moms and Whatassp group; the patients of the Rebagliati Hospital and 5 clinics where I work and volunteers.

**Results:** RESULTS: Experience of 25 as a pediatric oncologist, I have created the non-profit Association for the Fight against Cancer Doctor Heart, where the main axis is face-to-face training since 2010 at the national level and by virtually the Club of Joy is created for the period 2020-2022. 1. Video conferences: Prevention Early diagnosis of childhood cancer, Management of Anemia, Healthy foods, Vaccines, Adenopathies when suspecting cancer, Adolescent Psychology. 2. Via Zoom: the mothers and the patients were the teachers: Organic Cooking Workshops. Mini chef in pastry shop. Certified makeup. On-site painting. Pet breeding. Birthday celebration. 3. Weekly Doctor Heart video stories. 4. Parent volunteers delivered gifts to hospitalized chil-

dren at each celebration. 5. The WhatsApp group encouraged the endeavors of the parents of cancer children and we all contributed to buying and disseminating what they produced. They formed prayer chains for the mothers and biblical stories to give hope, encouragement and strength to the fathers who accompany their children in the fight. Guidance for parents: access to quality care virtually and/or in person during the COVID pandemic to prevent abandonment of treatment.

**Conclusions:** CONCLUSIONS: Teamwork of health professionals, volunteers and, above all, parents of children with cancer, we managed to form a community of support and empowerment in child health and a sample that together we can do great things, creating a Brotherhood as a pillar of progress of a nation.

EP093/#1441 | Poster Topic: AS03 CCI - Childhood Cancer  
*International*

### COLLABORATIVE WORKING OF NON- PROFIT INSTITUTIONS TO ACHIEVE UNRELATED DONORS STEM CELL TRANSPLANTATION IN LATINOAMERICAN COUNTRY

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**Background and Aims:** Stem cell transplantation (SCT) is a therapeutic options for malignant and non malignant diseases. Allogeneic transplantation can be affected by several patient and donor factors: Donor factors associated with morbi mortality are: matched/ source (bone or Peripheral blood)/age/ gender Haploidentical SCT or matched unrelated donor (URD) are options in this country. Haplo is first option in order to go ready and no more direct cost asociated but viral infections, postransplant relapsed and mortality are more frequent than URD. URD is expensive and delay around 3-6 months. A collaborative working group of non profit intitutions in Mexico: Casa de la Amistad (CDLA) Pre transplant evaluation with minimal Residual disease by Flow cytometry or RT- PCR in some cases. HLA typing Teleton Childrent's Hospital: Hospitalization and conditioning regimen Be the Match: 50% for direct cost for SCT source an HLA typing Aqui Nadie Se Rinde (ANSer) 50% direct cost for SCT source

**Methods:** Cohort study to evaluate results of URD as source for SCT in a collaborative working with non profit institutions in Mexico Pre

transplant evaluation: MRD by FC or PCR to evaluate remission, HLA typing and URD searching was done. URD matched or mismatched available was mandatory. Time between searching and source reception was evaluated too. Overall survival relapse rate and infections was obtained

**Results:** Thirteen patients completed Pre and posttransplant follow up. All patients in remission: 10/13 ALL 3/13 AML. 90% male, 10% female. 6.7 years old (2-10). 3 patient were transplanted after relapsed a first Haplo SCT (6 months between relapsed and second URD transplant) 1 year Overall survival 0.8 Relapsed rate 0.1 mortality due to infections 0.1

**Conclusions:** Non profit Institution working and collaborative is feasible in LMIC Overall survival is 80% excellent comparing 50% for ALL overall survival in México

EP094/#956 | Poster Topic: AS03 CCI - Childhood Cancer

*International*

#### UNMET NEEDS OF FAMILIES WITH NEUROFIBROMATOSIS TYPE 1 IN CANADA: PATIENT VOICE BASED ANALYSIS

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**Background and Aims:** Neurofibromatosis type 1 (NF1) is a rare genetic disorder having multiple manifestations including tumours. Knowledge of the experience of NF1 paediatric patients and their caregivers remains limited. The aim of this research was to better understand the NF1 patient experience in Canada based on first-hand testimony extracted from "Big Data". The research scope included barriers to treatment, unmet needs of patients and caregivers, and quality of life (QoL) issues.

**Methods:** This social listening research involved multilingual artificial intelligence-based analysis of Patient Voice in Canada obtained through anonymised stories (3,035 messages, 835 patients and caregivers) from domestic and international social media (2017-2022). Comparative cross-country analysis was included.

**Results:** The top identified barriers to diagnosis and treatment included: insurance policy issues (23.2% of all cases; e.g. when removing fibromas for aesthetic reasons); lack of NF1 specialists (19.6%); lack of information (18.7%), especially for French-speaking Canadians; poor awareness among physicians (12.5%); and issues with transition of care into adulthood (8%). There was also a general lack of awareness of treatment options. Top concerns of patients/caregivers were: the fear of existing symptoms worsening and new ones appearing (18.6%); tumour growth (14%); fear of surgery (14%); and inadequate healthcare support (11.6%). Pain (12.3%), lack of support (9.8%) and issues with physical appearance (8.4%) were highlighted as having the biggest impact on patients' QoL. Many QoL issues are similar in chil-

dren and adults (e.g. lack of support), whereas some are related to children specifically. They vary greatly country-wise: e.g. bullying at school reported by Canadian caregivers is also common for Mexico but less frequent in Korea.

**Conclusions:** This analysis demonstrates the wide range of unmet needs and burden experienced by patient with NF1 and their caregivers in Canada. These insights may help address gaps, improve advocacy policy, and raise awareness of NF1.

EP095/#1050 | Poster Topic: AS03 CCI - Childhood Cancer

*International*

#### DEVELOPMENT OF TAILORED SUPPORT MATERIALS FOR THE PARENTS/CAREGIVERS OF CHILDREN WITH CANCER AT THE UGANDA CANCER INSTITUTE

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**Background and Aims:** The Uganda Cancer Institute (UCI) is the national referral centre for paediatric cancers in Uganda, receiving 600 new children annually. Education of parents about their child's illness can contribute to an improved experience of and engagement with treatment, but in the context of significant financial and human resource constraints, time with clinicians can be limited. This international collaborative project aimed to address this need by co-producing tailored information resources for families undergoing treatment at UCI.

**Methods:** UCI paediatric oncologists and specialist nurses identified unmet information needs among families receiving treatment that may contribute to treatment abandonment. After discussion with the UCI parent group, a team of consultants, specialist nurses and medical elective students from the longstanding UCI-Cambridge partnership worked both on site and remotely to develop a booklet series providing information about cancer diagnosis, treatment and local support services. Input was also sought from third sector experts including the Uganda Child Cancer Foundation (UCCF) and managers of children's cancer hostels in Kampala.

**Results:** Drafts of three booklets entitled "What is Cancer?", "Treatments for Cancer" and "Living with Childhood Cancer" were produced, and copies of the first booklet designed, illustrated and printed for distribution to parents at UCI. Further plans have been established to translate the series into other regional languages and distribute them at satellite centres.

**Conclusions:** This project demonstrates the feasibility of developing parent support materials in a resource-constrained context by harnessing medical elective students as part of a vibrant international partnership. This could provide a model to address similar unmet



needs at other centres. It also builds capacity for future collaboration to further support families at UCI with completing cancer treatment.

**Acknowledgements** With thanks to all members of the UCI-Cambridge Children's Cancer Partnership, the UCI parent group, the UCCF, and the Makerere medical illustrations team.

EP096/#1639 | Poster Topic: AS03 CCI - Childhood Cancer  
*International*

### DEPRESSION AND ANXIETY IN PARENTS OF CHILDREN WITH CANCER

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**Background and Aims:** Mental health in parents of children with cancer diagnosis has shown different disorders. Indeed, the diagnosis of pediatric cancer is a calamity to the caregivers. Thus, we aimed to explore the degree of depression and anxiety within parents of children with cancer.

**Methods:** The Hospital Anxiety and Depression (HAD) scale was the instrument used to screen for anxiety and depressive disorders. This is a questionnaire composed of 2 sub-scales rated from 0 to 21 (maximum total score of 42). Results interpretation for each scale is either: no symptoms, doubtful symptomatology, or certain symptomatology. The study was conducted over a period of 3 months between October 2022 and December 2022 at the Pediatric Oncology Unit of Salah Azaiez Institute.

**Results:** The questionnaire was conducted on 35 parents. The majority of the parents (n=30) were diagnosed with certain symptomatology of anxiety. Only 2 parents did not present any symptoms of anxiety and 3 of them had doubtful symptomatology. Whereas 21 out of the 35 parents presented with certain symptomatology of depression, 10 of them had doubtful symptoms and only 4 had no symptoms of depression at all. All the parents in this survey were asked if they sought psychological support and none of them did. The majority of them (85.7%) categorically refuse psychological assistance mainly because of stigma, triviality, and lack of means. There was no significant correlation between the stage of the disease and the anxiety and depression (p=0.38).

**Conclusions:** The levels of anxiety and depression within parents whose children are diagnosed with cancer are unreasonably excessive with a higher level of anxiety. The psychological disorders within these families are being neglected, therefore it is essential to educate the parents and raise awareness on the importance of their mental health along with the process of treatment of their children.

EP097/#1151 | Poster Topic: AS03 CCI - Childhood Cancer  
*International*

### IMPACT OF PEDIATRIC CANCER ON THE COUPLE'S RELATIONSHIP

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**Background and Aims:** Cancer has a significant impact on marriages and other long-term relationships. Following a cancer diagnosis within a child, the couple might experience change in their relation. The aim of this study is to assess the impact of pediatric cancer on the couple's relationship.

**Methods:** A cross-sectional, questionnaire-based survey was undertaken among parents who had a child diagnosed with cancer. The study was conducted over a period of 3 months between October 2022 and December 2022 at the Pediatric Oncology Unit of Salah Azaiez Institute. Seven items were analyzed: Intimate relationship, conflict, quality of support by the partner, time and activities, sexuality, satisfaction of the relationship, and general impact of the disease on the relationship. The parents were told to answer either positive change, negative change, or no change at all.

**Results:** 35 parents were included in our study. Children's ages ranged between 4-17 years old. Most parents experienced negative change in their intimate relationship (n=15). Only 3 couples had positive change. Seventeen couples didn't notice a change. Parental conflicts were found in 14 couples. Sexuality have been reported to worsen for almost half of the couples surveyed (n=17). Positive change in the quality of support by the other partner was found in 26 couples. Results were diverse on the time and activities: 12 couples had negative change, 11 didn't experience any change and 12 had positive change. Positive change was found slightly predominant in the general impact of the disease and the satisfaction of the relationship (42.9% and 40%, respectively).

**Conclusions:** After diagnosis of cancer within a child, the majority of the couples find trouble in their affinity, either in their intimate relationship or in their sexuality. They are also more likely to experience conflicts. However, the quality of support of one's partner is mainly positive.

EP098/#1154 | Poster Topic: AS04 Nursing/AS04.a Education

### NURSING POLICY IMPLEMENTATION EVALUATION USING FIDELITY AND ADOPTION OF A STRUCTURED EDUCATION PROGRAM

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**Background and Aims:** Implementation fidelity matters when attempting to improve policy and investment towards improving nursing outcomes. Adoption is important to meet the goal, make interventions culturally-, and contextually-relevant. This study aims to measure fidelity and adoption of a standard operating procedure (SOP) for basic health education a year after its introduction.

**Methods:** Although fidelity is measured optimally using five dimensions, this study evaluated the dimension of adherence using self-report, and adoption using observations during health education sessions.

**Results:** Thirteen (100%) participants who completed the Basic Health Education training through flexible learning initially reported agreement on the SOP for health education of parents of children with cancer for identified high-value topics. They described it as clear, simple, concise yet succinct, systematic, easy to follow and understand. Only 6 (46.15%) of the initial sample are still in the same institution a year after training - highlighting challenges of high turnover rate of health human resources in LMICs. All those who remained (100%) reported that they implement the SOP but make changes depending on time and staffing which implies that adherence of the intervention fall short of ideal. Since the SOP is simple, adoption is high among those who were observed in the units but challenges were seen to arise from the amount of time spent on health education on high-value topics, and some language had to be changed for ease of participant understanding.

**Conclusions:** Evaluation of fidelity and adoption of policies, even SOPs, should be done with staff nurses, administrators, and stakeholders to inform decisions on how to allocate logistics, including materials and health human resources. Implementing tested interventions (ie. staff training) expecting high degree of fidelity and adoption comes with challenges but evaluation to include measuring moderators will make implementation more evidence-informed, responsive, culturally-, and contextually-relevant and will give more value to eventually affect nursing outcomes.

EP099/#867 | Poster Topic: AS04 Nursing/AS04.a Education

#### DEVELOPING A THERAPEUTIC EDUCATION PROGRAM FOR PATIENTS IN ONCOLOGY AND HEMATOLOGY DEPARTMENTS

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**Background and Aims:** Patient Therapeutic Education (ETP) aims at helping patients to have a better control on their life concerning their chronic disease. It is an ongoing process completely fitting into the

patient's welfare. So far, this aspect of care wasn't developed in a formal way within the Hematology and Oncology Institute. As we are very concerned with improving the patient's welfare, we have conceived and spread a project.

**Methods:** In 2021, thanks to private financing, we had managed to get a pluridisciplinary group training during which we built our paediatric ETP program. All the team had a 42 hours training necessary to successfully carry the ETP sessions. Along training, we have conceived our ETP program split in two parts: One for the kids suffering from cancer and another one for patients getting bone marrow transplant. We created ETP meetings fitting our paediatric population, using games and the active participation of our patients. Most of the necessary tools for our meetings had been created by the pluridisciplinary team.

**Results:** Our ETP program started in June 2022, with the subprogram for kids suffering from cancer. So far, 16 children have joined the ETP program and their satisfaction is expressed on different levels. During the end of program interviews, the kids emphasized that it was good for them to share their experience with their peers, to meet the pluridisciplinary team in another way and finally to get skills about their pathology. So far, our evaluation only relies on the gained knowledge during the meetings and on the way we feel the program useful.

**Conclusions:** Our program seems to help improving the kids' health and their life quality. However, these data remain still subjective and must be reinforced by a quantifiable advantages test.

EP100/#464 | Poster Topic: AS04 Nursing/AS04.a Education

#### IMPROVING COMPLIANCE IN CHILDREN WITH CANCER RECEIVING RADIATION THERAPY IN UGANDA

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**Background and Aims:** Radiation therapy is a key modality used to treat different types of cancer in Uganda and appropriate timing of radiation therapy is crucial to improve survival outcomes. Radiation therapy treatment must be explained to patients and caregivers so that they fully understand the importance of the treatment and schedule. At Mulago National Referral Hospital, children with cancer receive radiation therapy services from another facility. With no dedicated person to coordinate radiation therapy services, there were gaps in receiving radiation therapy as patients missed appointments and failed to return for treatment. This led to the development of a nurse-led radiation

therapy committee with the aim to improve compliance among children with cancer receiving radiation therapy.

**Methods:** The radiation therapy committee, led by a nurse, developed a follow-up system for all patients receiving radiation therapy. Different approaches were used to improve treatment compliance including training nurses, holding education sessions with caregivers, scheduling patients, and sending reminders. Teaching methods included one-on-one sessions with caregivers and patients to address the importance of radiation therapy, side effects and management. Nurse led education sessions addressed concerns of patients and caregivers related to radiation therapy.

**Results:** In six months, ninety (90) patients have been educated about the importance of radiation therapy with close follow-up of appointments. Over two-thirds of the patients (60) have completed radiotherapy on time, and the remaining 30 are receiving treatment as scheduled. Patients and caregivers understand the importance of radiation therapy as part of cancer treatment.

**Conclusions:** With implementation of the radiation therapy committee led by nurses, there is increased awareness, compliance, commitment, and overall positivity in attitude towards radiation therapy. In facilities where radiation services are offsite, education and training improve compliance and timely completion of radiation therapy in children with cancer.

EP101/#501 | Poster Topic: AS04 Nursing/AS04.a Education

#### ROLE OF AUDIO VISUAL AIDS TO IMPROVE NUTRITION COUNSELING AND EDUCATION AMONGST CAREGIVERS OF PAEDIATRIC ONCOLOGY PATIENTS IN INDIA

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**Background and Aims:** Paediatric oncology patients from the lower socioeconomic group are at a higher risk of malnourishment, which can result in poor treatment outcomes. Caregivers of these children are integral to preventing and addressing malnutrition. This study highlights the role of audio-visual aids, that Cuddles Foundation (CF) utilises to enhance the caregiver's knowledge on health and nutrition.

**Methods:** CF collaborates with government hospitals and provides nutrition assistance and counseling to children and their caregivers, through the services of specialised nutritionists placed in the pediatric oncology departments. Nutritionists supplement their counselling by incorporating short 2-3 minute videos, which are available in 7 different languages to accommodate caregivers across India. The videos were based on the most frequently asked questions to the nutritionists by the caregivers. The topics addressed in the videos included importance of nutrition and protein, hygiene, ideas for making meals more calorie-dense, and managing various side effects during cancer treatment. Additionally, the caregivers are given access to the videos,

allowing them to view them at their convenience. To get a better understanding of the impact of the videos, CF administered a structured questionnaire to 79 caregivers between March and May 2022. Questions were designed to elicit data on their response after viewing the videos.

**Results:** The results indicated that 100% of caregivers found the videos helpful. They all agreed that they needed to make changes to their child's current food habits and felt that the videos would help them properly manage the treatment side effects. The majority of caregivers (98.7%) also opined that they learnt something new from the videos.

**Conclusions:** The study demonstrates that the use of audio-visual aids in the caregiver's preferred language to supplement the nutrition counselling is beneficial in enhancing caregiver's knowledge and also improves their confidence to better manage their child's nutritional status during cancer treatment.

EP102/#1632 | Poster Topic: AS04 Nursing/AS04.a Education

#### PEDIATRIC ONCOLOGY LITERACY: DEMAND FOR EDUCATIONAL BOOK

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**Background and Aims:** Talking about cancer with children and adolescents is still a stigma and there is a **lack of materials with adequate language** which facilitate this **communication**. The Beaba Guide is a book with humanized, honest and objective language, containing the meaning of 165 words present in the treatment routine, distributed free of charge to patients. It's an exclusive material, **co-created** since 2014 with patients, families, health professionals and Technology, Communication and Information professionals. This study evaluates the demand of health institutions for **improvements in communication with children and adolescents** undergoing cancer treatment and assesses the need for instruments that facilitate this communication over the years.

**Methods:** Data collection of the Beaba Institute on the distribution of guides of the 1st, 2nd and 3rd editions, in addition to the numbers of institutions which **requested this material between 2015 and 2023**. With these data, a chronological comparison was performed to verify whether the search for the material increased or decreased.

**Results:** Between 2015 and 2023, **12,500 books** were distributed to **201 institutions**. Since its inception until now, the books have been present in **17 international institutions in 14 countries**. During this period, there was an increase of **144% in the donation and 290% in the demand of the institutions**. In addition to hospitals, the material was also requested and sent to support homes and libraries.

**Conclusions:** The search for the material has grown significantly in the last 8 years, with demand from other countries, suggesting that its **content is universal**. The increase in the demand shows the search for

improvements in communication, which can serve as a support tool for health professionals. There is a shortage of specialized materials to assist family members and professionals in communicating with children and adolescents, making it necessary, in the next edition, to invest in validation in other languages.

EP103/#834 | Poster Topic: AS04 Nursing/AS04.a Education

#### DEVELOPMENT OF A DISCHARGE TEACHING TOOL FOR CHILDREN NEWLY DIAGNOSED WITH CANCER IN LMIC

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**Background and Aims:** Appropriate pre-discharge education for families of children with cancer lays the foundation for improving continuing care at home that can influence patient outcomes in low-income countries. Studies document that improved patient education through clarity and consistency of discharge instructions can contribute to improved treatment adherence. Conversely, poor adherence can lead to adverse events and potentially avoidable outpatient or emergency department visits. In Lilongwe, Malawi, discharge information given to parents before their child's initial hospital discharge lacked coordination and consistency. A discharge-planning tool was developed to deliver concise and consistent information to parents of children newly diagnosed with cancer

**Methods:** A nurse led team developed a structured and concise discharge teaching tool with all pertinent information necessary to ensure a safe departure from the hospital and successful follow-up. This information, based on published evidence, included what cancer is, causes, types, signs and symptoms, treatment, side effects of treatment and danger signs. The initial draft was circulated to members of the multidisciplinary team who made changes to ensure information was comprehensive.

**Results:** All nurses were trained on the discharge tool before implementation. Before discharge, parents discussed with a nurse the key areas found in the tool to teach them how to recognize problems early when at home. Instructions for care at home, including medications, diet, therapy, warning signs and symptoms along with follow-up appointments were explained in detail to parents upon discharge. A phone number to call for questions and emergencies is given to all parents.

**Conclusions:** A structured, systematic, and coordinated system of hospital discharge is required to facilitate the discharge process for newly diagnosed children with cancer. This process ensures a smooth patient transition from the hospital to the community and will improve patient health outcomes. The effectiveness of the discharge tool will be assessed to measure the impact of this intervention.

EP104/#172 | Poster Topic: AS04 Nursing/AS04.a Education

#### STANDARDIZING GLOBAL NURSING EDUCATION ON ACUTE LYMPHOBLASTIC LEUKEMIA AND PEGYLATED ASPARAGINASE THERAPY THROUGH A VIRTUAL NURSING COURSE

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**Background and Aims:** Due to variability in nursing education globally, standardized global education acute lymphoblastic leukemia (ALL) management is needed to improve healthcare provider confidence in diagnosing, treating and managing toxicities associated with ALL therapy. This project's purpose was to educate oncology nurses globally on therapeutic management of patients with ALL to improve nursing clinical knowledge, competence, and treatment of ALL and adverse events associated with pegylated asparaginase.

**Methods:** Servier Pharmaceuticals sponsored this project with content presented by three nursing experts in pediatric oncology and asparaginase therapy during a three-hour, virtual global oncology nursing event. Curriculum included a background of ALL, diagnosis and prognostic factors, potential treatment regimens, asparaginase mechanism of action, and identifying and managing pegylated asparaginase adverse effects. Course materials were provided to attendees upon completion to disseminate within their respective healthcare institutions. Pre and post course evaluations were utilized to evaluate course effectiveness.

**Results:** One hundred percent of post-course evaluation respondents agreed course content was informative and helpful, 85.7% agreed course learning objectives were met, 100% agreed course presenters were knowledgeable about subject content, 85.7% agreed information presented was applicable to their nursing practice, 64.3% agreed information presented would be used to create a practice change at their facility, and 85.7% agreed they would recommend the course to colleagues interested in learning about ALL and asparaginase. A 27.3% increase was seen among respondents feeling very knowledgeable with the diagnosis and treatment of ALL and zero reported feeling not very knowledgeable after course completion. A 52.9% increase was seen among respondents reporting feeling very comfortable with identifying and managing adverse events associated with pegylated asparaginase therapies after course completion.

**Conclusions:** Improvement in nursing knowledge and comfort with the course subject matter was seen among respondents, which supports the need for continued standardized global nursing education on ALL and asparaginase therapy.

EP105/#1796 | Poster Topic: AS04 Nursing/AS04.a Education

#### DESIGNING A PLAN FOR DEVELOPING THE ONCOLOGY ADVANCED PRACTICE NURSE ROLE IN KENYA

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**Background and Aims:** The International Council of Nurses advocates for investment in skilled nurses to address global health challenges and patients' needs. In Kenya, the Master of Science in Oncology Nursing and higher national diploma, are accredited by the nursing council for oncology nursing education. An APN in oncology collaborates within a multidisciplinary model in various practice settings in planning, provision, and evaluation of care to patients with cancer and their families. We are reporting the design and development of the APN role in Kenya. **Methods:** The nursing council of Kenya (NCK), in collaboration with local universities, held a series of meetings in 2021 to plan the APN role development, building on other African countries experience. The team included representatives from local universities, the NCK and 3 nurses who had received APN training abroad. To define the terminology and experiences of implementing the APN role in Africa, we conducted a scoping review, on EBSCO host, PubMed and Google scholar databases.

**Results:** The literature review yielded 11 studies, reflecting that twelve countries in Sub-Saharan Africa have a documented plan for introducing the APN role. Among them, 4 countries have successfully implemented and regulated the role. The remaining 8 countries cited implementation challenges such as lack of local ownership and complicated, legislative processes. These findings informed the design of the curriculum, the legal licensure and scope of practice with various specialties. Particularly for pediatric oncology, a curriculum and legislation have been developed and processed for approval.

**Conclusions:** There is growing evidence that highly trained nurses contribute significantly to better health outcomes. Once implemented, the APN role can enhance effective collaboration within the multidisciplinary team while aligning with the country's regulation and patients' needs.

EP106/#657 | Poster Topic: AS04 Nursing/AS04.a Education

## TEACHING PEDIATRIC WOUND ASSESSMENT AND MANAGEMENT TO ONCOLOGY NURSES IN SUBSAHARAN AFRICA

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**Background and Aims:** Wound care represents a major health burden in Africa; this burden is on the rise with increased pediatric cancer cases, the primary source of interventions is traditional medicine in rural communities and hospitals in urban settings. Nurses in Sub-Saharan Africa are involved in wound care but have minimal knowledge of proper assessment, documentation, and management of different types of wounds.

**Methods:** The online course was developed by nurses from Sub-Saharan Africa: Uganda, Botswana and Malawi, and wound care experts at Texas Children's Hospital. This group formed the faculty for the course. A needs assessment to determine the essential elements to be included in the course was completed with key stakeholders from the three countries. A draft outline of the content was formed, and faculty met to organize the course into four modules: skin anatomy and physiology, wound assessment, wound management, and special wound considerations. Simulated videos were created to demonstrate wound assessment, irrigation, and cleaning along with dressing changes. Faculty developed a wound assessment tool to document the wound and how it is cared for. Each module presents the content through short video lectures; participants must pass a quiz to move to the next module. Upon completion of the course, a formal evaluation is completed, and a course certificate is sent to the participant

**Results:** The course was launched online as a free, open course to healthcare providers throughout Sub-Saharan Africa. Since launching the course in December 2022, 44 individuals from 7 countries throughout sub-Saharan Africa have enrolled. Seventeen participants have completed the course and received a certificate.

**Conclusions:** This online course is the first of its kind focused on teaching healthcare providers on proper wound care in children and has the potential to significantly improve their care.

EP107/#664 | Poster Topic: AS04 Nursing/AS04.a Education

## KEEPING UP-TO-DATE WITH IMMUNOTHERAPY TO EXPERIENCED NURSES

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**Background and Aims:** Nurses in Denmark must be certified to administer medical cancer treatment. The certification takes place at Copenhagen University of Applied Sciences after one year of employment. The purpose of the course is for nurses to acquire competences to observe and react to general and specific side effects of medical cancer treatment. Immunotherapy has gained traction in recent years in the treatment of childhood cancer. Though many of the department's experienced nurses administer immunotherapy, they have not had the formal education, as their certification was obtained prior to the introduction of immunotherapy. There is at present no re-certification of

this course, leaving experienced nurses at a disadvantaged learning situation.

**Methods:** Nurses employed for more than four years participated in five sessions of two hours as their certification was outdated in relation to the introduction of immunotherapy as part of the teaching at KP. We tailored the content of the training for nurses working with children and adolescents. We evaluated the content and form on a 5-point scale from 1 (very bad) to 5 (very good).

**Results:** We identified 17 nurses of which 14 participated. Of these, four had received a course in medical cancer treatment more than 10 years ago, 7 had received the course 4-6 years ago and 3 did not answer. Overall, the professional content of the teaching was evaluated as very good or good. The professional level of the teaching was assessed from 3 to 5 and 8 of the participants would definitely recommend others to take the course, while 5 would recommend it.

**Conclusions:** Learning at work is no guarantee for knowledge being up to date. When new forms of treatment are introduced to clinical practice, it is essential that experienced personnel are formally introduced to new side effects and precautions to ensure patient safety.

EP108/#675 | Poster Topic: AS04 Nursing/AS04.a Education

#### END-OF-LIFE-CARE: DELIVERING THE "RIGHT" CARE

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**Background and Aims:** Increasingly, end-of-life care takes place in the child's or adolescents' home. This involves interprofessional palliative care teams coordinating the best possible end-of-life care. As desirable as this is, healthcare professionals' competencies in handling end-of-life care in hospitals are lost. This leaves nurses feeling insecure in handling both practicalities relating to dying and parents' psychosocial needs with increased risk of work-related burnout and stress. We designed an education day relating to learning objectives from the interprofessional education program concerning paediatric palliative care, i.e., alleviating physical, psychological, and spiritual issues and identifying ethical dilemmas.

**Methods:** All 54 nurses and the department's pedagogue participated in one of six education days. Mean years of paediatric experience was 21 years (1 month - 44 years). It consisted of a lecture on physical symptom treatment, parents' perspectives, theory on grief and communication, visiting the chapel, reflection with a priest, and skills training relating to the deceased, including rituals and rites. The participants completed a qualitative evaluation of six incomplete sentences which was analysed with direct content analysis.

**Results:** Despite being a group of experienced nurses, all indicated that they lacked knowledge and skills relating to paediatric end-of-life care. Receiving knowledge on these issues released mental excess to better

manage parents' and sibling's feelings of grief. Being presented with the different professionals' perspectives gave the nurses a security in being part of a bigger team surrounding the families. Ultimately, the nurses reported that they felt more comfortable in delivering the "right" care.

**Conclusions:** Hospital nurses' competencies in end-of-life care need to be continuously trained for optimal patient care, especially in areas prone to work-related burnout and stress. Healthcare professionals need to be trained to be able to support parents and siblings in the worst possible situation.

EP109/#805 | Poster Topic: AS04 Nursing/AS04.a Education

#### KNOWLEDGE RETENTION AMONG CLINICAL HEALTHCARE WORKERS FOLLOWING TRAINING ON PAEDIATRIC CANCERS AT THE GREATER ACCRA REGIONAL HOSPITAL, GHANA

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**Background and Aims:** Despite a rising number of reported childhood cancers in Ghana, trained expertise to recognise and manage these children is still inadequate. To assess improved knowledge in early detection and care of children and adolescents with cancers among healthcare workers following training that utilised resources from the Foundation Course developed by the SIOP Africa Nursing Network.

**Methods:** A cross-sectional study was conducted among participants. Two groups (A and B) were trained over a period of five days each. Pre-test and post-tests were conducted using self-administered structured questionnaire and test repeated eight months later. Knowledge level was categorised as poor (score  $\leq 21$ ), good (score  $22 \leq 31$ ) and very good (score  $32 \leq 41$ ). Data was analysed using Stata 15. Descriptive and bivariate analyses were performed. Paired t-test was also performed to determine the difference in the mean scores of trainees.

**Results:** Thirty-two healthcare workers participated. Group A was made up of 18 (56.3%). The mean age of participants was 34 years  $\pm 6$  years. Majority [26 (81.3%)] were nurses. Out of a total score of 41, the mean pre-test score for group A was  $25 \pm 8.4$  while group B scored  $24.2 \pm 11$ . Two sample t-test with equal variance was performed to determine any difference in the mean pre-test scores of both groups. Although there was no statistically significant difference in scores between both groups, this difference was present by paired t-test in the mean pre-test and post-test scores [ $t = -3.96$ ,  $df = 24$ ,  $p = 0.0006$ ]. At eight months post training, paired t-test between post-test score and current score showed that mean post-test score was  $28.5 \pm 8.9$  while the mean current score was  $33.6 \pm 2.6$  and the difference was statistically significant [ $t = -2.6$ ,  $df = 25$ ,  $p = 0.0136$ ].

**Conclusions:** There has been improved knowledge outcomes among healthcare workers more than half a year post training.

EP110/#776 | Poster Topic: AS04 Nursing/AS04.b Research

### SYSTEMATIC REVIEW AND EVIDENCE MAPPING OF RESEARCH ON TRADITIONAL AND COMPLEMENTARY MEDICINE IN PEDIATRIC ONCOLOGY GLOBALLY

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**Background and Aims:** Traditional and complementary medicine (T&CM) is commonly used in pediatric oncology. We systematically reviewed recently published studies on T&CM use in pediatric oncology and aimed to create an evidence mapping to identify gaps based on geographical location and quality of evidence.

**Methods:** The search strategy was implemented in major electronic databases (MEDLINE, Embase, PsycINFO, Cochrane, AMED, and CINAHL). Primary studies published in any language about the use of T&CM in pediatric oncology between 2016 and 2022 were included. Two reviewers independently screened titles, abstracts, and full texts. Cochrane risk of bias and the T&CM in pediatric oncology-specific quality assessment tools were used to assess quality of evidence. We used the World Health Organization (WHO) geographic locations and the quality of evidence to provide current evidence mapping of T&CM research globally.

**Results:** Initially, 1900 studies were identified; after removing duplicates and reviewing eligibility (title/abstract and full text), 119 studies from 40 countries were included. Studies were grouped according to WHO regions: Americas (n=45), European (n=43), Western Pacific (n=12), South-east Asia (n=7), Eastern Mediterranean (n=7), African (n=4), and multiple regions (n=1). Articles were published in English (n=113), French (n=3), Spanish (n=2), and German (n=1). Two-thirds of the studies were non-interventional (n=78), and only 41 interventional studies, mainly from the Americas and European regions. Risk of bias concerns were captured in all studies.

**Conclusions:** While there is a shortage of research from most WHO regions, our findings indicate growing research efforts about T&CM use from all regions. Filling the regional gap in research about T&CM is crucial since each region may have unique T&CM use according to cultural background, natural environment, and socio-economic status. Contrary to prior systematic reviews, our study showed robust study designs in 34% of included studies. This is viewed as a promising advancement, despite the risk of bias concerns.

EP111/#1130 | Poster Topic: AS04 Nursing/AS04.b Research

### IMPROVING THERAPEUTIC COMMUNICATION BETWEEN NURSES AND PARENTS AT THE PAEDIATRIC ONCOLOGY UNIT, KATH, GHANA

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**Background and Aims:** Therapeutic communication is an indispensable component in the provision of healthcare to patients, especially children with cancer. All communication is behavior and all behavior affects communication, hence it is entirely necessary for both parents and nurses to communicate therapeutically among themselves to promote quality care and outcomes for children with cancer. We therefore set out to identify the gaps in therapeutic communication between nurses and parents at the paediatric oncology unit at Komfo Anokye Teaching Hospital (KATH).

**Methods:** A cross-sectional survey was employed with nurses and parents at the paediatric oncology unit, Komfo Anokye Teaching Hospital. Participants came from diverse ethnic groups and geographical distribution in Ghana. Ten (10) nurses and 10 parents were interviewed using convenient sampling to collect data after seeking their consent. Data was analyzed using SPSS version 12. Confidentiality was ensured by de-identifying the data

**Results:** About 50% of respondents were males and the other 50% females. Parent - related characteristics that were identified in improving therapeutic communication included culture, parent nurse relationship, anxiety and stereotype mindset. Nurse - related characteristics on the other hand identified in improving therapeutic communication were emotional intelligence, time management, good nurse-parent relationship and also appropriate nonverbal gestures. The overall frequencies for both nurse-related and parent-related characteristics were as follows: Culture 5%, nurse-patient relationship 30%, anxiety 10% and stereotype mindset 5%, emotional intelligence 25%, time management 15%, good nurse-parent relationship 5% and appropriate nonverbal gestures 5%.

**Conclusions:** Therapeutic communication is an indispensable component that improves the sensitivities and feelings of parents and nurses and the meaning of those feelings. Nurse-patient relationship and emotional intelligence needs to be improved for good therapeutic communication.

EP112/#1047 | Poster Topic: AS04 Nursing/AS04.b Research

### PROBLEMS WITH HEALTH AND FUNCTIONING IN EVERYDAY LIFE FOR CHILDREN WHO COMPLETED BRAIN TUMOR TREATMENT - A LONGITUDINAL PERSPECTIVE

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**Background and Aims:** Late effects after ending brain tumor treatment can heavily impact the child's life for many years. Research reveal that healthcare, habilitation and school often retain focus on the child's bodily problems after ending braintumor treatment, while problems related to the child's functioning in everyday life receive less attention eventhough it is known that participation in everyday activities is related to wellbeing. The aim with this study was to describe how problems with participation in everyday life tended to co-occur with problems related to body function, activity, and environment over time after ending brain tumor treatment.

**Methods:** Seven children were enrolled. Data i.e problems describing the perceived discrepancy between the child's current and ideal state of functioning were collected (mean 5,1 years, range 2,7-10,4 years) from healthcare and school records starting one year after treatment completion. Codes within the International Classification of Functioning, Disability, and Health (ICF) were used to code the identified problems. These were then analyzed in six-month blocks (T1-T8) using descriptive statistics describing problems related to participation, body function, activity, and environment.

**Results:** The highest proportion of problems related to activity and participation were found at the first time point (T1). These problems fluctuated more than problems related to body function which dominated. However, for two participants problems related to activity and participation increased at T3 and for three participants at T7. Five children displayed a decrease in problems related to body function while two children had an increase at T8. Problems related to the environment fluctuated differently for everyone but seemed to increase at T2.

**Conclusions:** In the follow up care, it is important to focus both on the child's health but also function in everyday life. The care needs to be individualized since the pattern of problems seems to vary over time for each individual.

EP113/#465 | Poster Topic: AS04 Nursing/AS04.b Research

#### THE FEASIBILITY OF THE CHILDREN INTERNATIONAL MUCOSITIS EVALUATION SCALE AND WORLD HEALTH ORGANIZATION SCALE (CHIMES/WHO) ACCORDING TO CHILDREN, PARENTS AND NURSES

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**Background and Aims:** A complication of cancer treatments is oral mucositis, an irritating and painful side effect in up to 20-100% of children receiving chemo and/or radiotherapy. To assess mucositis in

children, the CHIMES, combined with the WHO oral grading scale, needs to be implemented. The CHIMES is a self and parent proxy reporting measurement tool for evaluating oral mucositis. This study aimed to evaluate the feasibility to implement the CHIMES/WHO in practice and assess mucositis in children receiving chemotherapy and/or radiotherapy according to children, parents & nurses.

**Methods:** A feasibility study was performed in 2022. Feasibility was measured by statements of understandability, acceptability, adoption, practicality and integration. Responses of structured interviews with children and parents and questionnaires of nurses were rated on a Likert scale. Open ended questions were thematic analyzed.

**Results:** In total 20 children and/or parents and 25 nurses participated. Overall CHIMES/WHO was found, easy to understand, easy to use and easy to score. The majority of the statements was rated positive by more than 70% of the children, parents and nurses. Additional comments concerned usefulness of the information for interventions, burden and meaningfulness of the tool, were given by children and parents. Some nurses (32%) were unsure whether the tool could easily be integrated their daily work. Two themes were identified. The first: "being in control". CHIMES gives awareness and helps child, parent or nurse decide if a mouth hygienist or a pain consultant is needed. The second: "use of CHIMES/WHO in daily practice".

**Conclusions:** CHIMES is feasible in terms of understandability, acceptability, adoption, practicality and integration for the implementation and assessment of oral mucositis in children receiving chemo or radiotherapy. Implementation, guidelines how to use the CHIMES in practice, and monitoring of the implementation is necessary for (daily) practical use in terms of meaningfulness and burden and being in control.

EP114/#1416 | Poster Topic: AS04 Nursing/AS04.b Research

#### BARRIERS TO IMPLEMENTING A SYMPTOM SCREENING 'TOOL' INTO CLINICAL PRACTICE- LESSONS LEARNED FROM THE UK SSPEDI STUDY

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**Background and Aims:** Cancer and its treatment causes a range of symptoms and problems for children and young people. In the UK, use of symptom screening tools is not routine. Finding ways for symptom management systems to be integrated into clinical workflow is essential. SSPedi is a symptom screening tool. Our aim was to introduce



SSPedi and learn from those using it what works well, what works less well, and what information was needed, to understand its uptake and impact.

**Methods:** We undertook a process evaluation at two case study sites in the UK. A sequential programme of work was planned, starting with Key Informant Interviews, researcher and professional co-production in Phase 1. This was to ensure that plans for using SSPedi in clinical practice reflected the realities of settings. In phase 2, children with cancer aged 8 to 18 years and their parent proxies were recruited to use SSPedi for 5 consecutive days. In phase 3 participants were interviewed about their experiences and in phase 4 we plan to build on what we have learned for a future study.

**Results:** There were significant barriers to implementing SSPedi into clinical practice. The majority of these were regulatory, workforce and technological. While gaining ethical approval was swift, receiving the necessary local approvals took considerably more time than previously foreseen. Unfortunately, the UK SSPedi study also coincided with a time of low staff morale, significant workforce capacity issues and wide-spread NHS strikes. Poor recruitment of staff for Key Informant Interviews at one site led to a decision to close the study in that setting. Technology, workforce, and infrastructure problems also affected data collection in phase 2.

**Conclusions:** There were significant barriers to implementing SSPedi into clinical settings. The use of a process evaluation allowed these to be identified prior to a more expensive trial.

EP115/#1070 | Poster Topic: AS04 Nursing/AS04.b Research

#### CHARACTERISTICS OF PEDIATRIC PATIENTS PRESENTING WITH FEBRILE NEUTROPENIA IN SOUTHWESTERN UGANDA

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**Background and Aims:** Neutropenic fever is a leading cause of morbidity and mortality among pediatric cancer patients worldwide. However, there are few published studies characterizing the affected patient population and their disease management in Sub-Saharan Africa. We sought to describe the pediatric oncology patients affected with neutropenic sepsis and their outcomes at a referral hospital in Southwestern Uganda.

**Methods:** The Mbarara Regional Referral Hospital (MRRH) Department of Pediatric Oncology registry was reviewed to identify all patients presenting with neutropenia (ANC < 500 cells/mm<sup>3</sup>) and fevers (3 temperature measurements >37.5 C) between January 2022 and December 2022. Data was analyzed using STATA 14.2.

**Results:** A total of 146 pediatric cancer patients were initiated on chemotherapy between January and December 2022 at MRRH and

41.7% (n=61) of them were admitted with neutropenic fevers with a mean ANC of 283 cells/mm<sup>3</sup> (SD: 203). The mean patient age was 9.6 years (SD: 4.8) and 57.3% (n=35/61) were male. A total of 14 cancer types were treated, and most common types were acute lymphoblastic leukemia (ALL) (n=13/61, 21.3%), Wilms tumor (n=12/61, 19.7%) and osteosarcoma (n=7/61, 11.5%). The most common chemotherapy regimen was ifosfamide/doxorubicin (n=9/61, 14.7%). The majority of patients were prescribed either ceftriaxone (n=25/61, 41%) or piperacillin/tazobactam (n=24/61, 39.3%) for treatment and the mean duration of treatment was 8 days (SD: 5.3). More than half of all patient remained in remission (n=34/61, 55.7%), while mortality rate was 24.6% (n=15/61).

**Conclusions:** Chemotherapy-induced febrile neutropenia is a common complication of management of childhood cancers in Southwestern Uganda. This leads to chemotherapy dose reduction, deferred and delayed chemotherapy appointments and treatment suspension for many pediatric cancer patients. This eventually affects patient treatment outcomes and results in higher mortality rates. Standardized protocols for diagnosis and treatment of neutropenic sepsis among the pediatric oncology population is necessary in Uganda.

EP116/#1419 | Poster Topic: AS04 Nursing/AS04.b Research

#### TRADITIONAL AND COMPLEMENTARY MEDICINE USE IN PEDIATRIC ONCOLOGY IN TUNISIA

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**Background and Aims:** The use of Traditional and Complementary Medicine (T&CM) is common in pediatric oncology. Due to the lack of prior research on the use of T&CM in pediatric oncology in Tunisia, our objective was to evaluate its use in a single cancer center located in Sousse, Tunisia.

**Methods:** A convenience sample of 32 parents of children with cancer completed the survey at the medical oncology department of Farhat Hached university Hospital. We adopted a short proxy-report T&CM questionnaire that have evidence of initial validation.

**Results:** The median age of children was 7 years (range=1-16). The majority were on cancer treatment (93%) with male predominance (62%). The sarcoma, nephroblastoma, and nasopharyngeal carcinoma diagnoses accounted for 29%, 22.6%, and 16%, respectively. About 12% of parents were illiterate and 94% married. All parents used T&CM for their children including 60% during chemotherapy, 15% during radiation, and 62% during other treatments. Parents deciding using

T&CM in 81% of the sample and 12% of children made decision. The types of T&CM utilized included nutritional, psychological, and physical approaches, with respective usage rates of 53%, 40%, and 50%. Only 21% of the parents disclose the use of T&CM to the child's healthcare providers (HCPs). The use of T&CM was helpful in 66.7% and 53% patient felt better. Prayer was the predominant method for psychological approaches (94%), while the predominant method for nutritional approaches was the use of herbs (83%). Approximately, 40% of the parents plan to use the T&CM in the future.

**Conclusions:** T&CM is frequently used by children with cancer in Tunisia. However, most parents do not discuss the use of T&CM with the treating HCPs. Thus, initiating routine clinical dialogue about T&CM by HCPs is crucial to help parents make informed decision of using T&CM and avoid any potential risk of interaction with conventional treatments.

EP117/#283 | Poster Topic: AS04 Nursing/AS04.b Research

### CLINICIAN PERSPECTIVES ON IMPAIRED NUTRITION AMONG CHILDREN UNDERGOING CANCER CHEMOTHERAPY IN THAILAND

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**Background and Aims:** Prior studies examining the impact of gastrointestinal tract symptoms on eating habits and nutritional status among children with cancer have been conducted primarily in Western countries, leaving a knowledge gap about children in Thailand. Guided by a tentative logic model of problem, this study examines these issues from perspectives of Thai clinicians and identifies factors that influence children's nutritional status during active treatment with chemotherapy.

**Methods:** Pediatric oncology clinicians and staff employed at the tertiary hospital in Bangkok were study eligible. Data were collected through semi-structured interviews with participants about (a) children's symptoms, eating behaviors, and nutritional status, (b) clinicians' cognitions and behaviors influencing children's nutritional status, and (c) influential factors in the physical environment. Each clinician identified another clinician or staff member who could provide additional perspectives. Interviews were conducted in Thai and analyzed using directed content analysis guided by the tentative logic model.

**Results:** Participants (N=22) enrolled in the study, ten registered nurses, six licensed practical nurses, four physicians, one child life specialist, and one nutrition service staff member. Most participants were female (95.4%), with an average age of 37.77 years (SD=7.69, 25-55) and 15.55 years of experience (SD=7.35, 3-30) caring for with Thai children with cancer. Identified influential characteristics of the children

included cancer, treatment exposures, and psychological and physical symptoms. Participants attributed changes in children's weight and eating to symptoms. Influential clinician characteristics included current practices that affected children's symptoms and food intake such as lack of knowledge, lack of time, lack of agreement about allowable foods, and care goals focused on treatment cure. Hospital level factors included hospital odors and repetitive food offerings.

**Conclusions:** Multi-level interventions that target children's symptoms, clinician's knowledge and role norms, unpleasant features of the hospital environment are needed to optimize eating and thus nutritional status of Thai children undergoing chemotherapy.

EP118/#1331 | Poster Topic: AS04 Nursing/AS04.b Research

### TABOO WORDS IN PEDIATRIC ONCOLOGY: COMMUNICATION EXPERIENCES OF NURSES AND PHYSICIANS WITH DYING CHILDREN AND THEIR FAMILIES

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**Background and Aims:** Effective communication positively influences the rate of patient recovery, pain control, adherence to treatment regimens, psychological functioning, and quality of life. Despite the numerous benefits of effective communication between patients, families and health workers, they still have substantial barriers and communication challenges within their practice. This study explored healthcare professionals' experiences in direct communication with dying children and their families in pediatric oncology settings.

**Methods:** Twenty-nine pediatric oncologists and nurses participated in semi-structured interviews. The phenomenological approach was used. Data were analyzed line-by-line with codes and categories developed inductively from participants' narratives. The MAXQDA software was used to facilitate data management.

**Results:** Physicians and nurses mentioned serious communication barriers, although children and their families are generally aware of their prognosis. Not feeling competent in communicating with dying children and their families, limited use of the words death and cancer, workload and cultural perceptions made it difficult to communicate. For this reason, they stated that they avoid seeing children and families at the end of life, that there are situations that everyone knows but cannot talk about, and that they are afraid of breaking the hopes of the child and family. However, acting as a multidisciplinary team eased the communication constraints of healthcare professionals.

**Conclusions:** Communication with dying children and their families is essential. However, multiple barriers remain for healthcare providers to do so. Children and their families are often aware that the situation is not going well, but there is closed communication. The circumstance

places an additional burden on both the child and their family during the end-of-life, which is already a challenging experience to handle. Healthcare professionals need urgent training in open communication with the dying children and their families.

EP119/#213 | Poster Topic: AS04 Nursing/AS04.b Research

### HOME MEDICATIONS PRESCRIBED FOR NEWLY DIAGNOSED PEDIATRIC ONCOLOGY PATIENTS

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**Background and Aims:** Upon initial hospital discharge, parents of children newly diagnosed with cancer require specialized education to provide safe care for their child at home, including proper management of home medications. However, there is a paucity of literature regarding the number and types of home medications prescribed to newly diagnosed pediatric oncology patients. We aimed to describe medications prescribed at discharge and identify factors associated with larger quantities of discharge medications in newly diagnosed pediatric oncology patients, to inform patient/family education curricula.

**Methods:** We performed a secondary analysis of data from a study evaluating a structured discharge teaching intervention for parents of newly diagnosed pediatric oncology patients treated at a tertiary children's hospital. We inventoried and categorized all prescribed discharge medications and used logistic regression to identify clinical and sociodemographic factors significantly ( $P < 0.05$ ) associated with being prescribed  $>$  the median number of discharge medications.

**Results:** The cohort consisted of 102 newly diagnosed pediatric oncology patients: 60.8% male, 65.7% non-Hispanic White, 67.6% leukemia/lymphoma; median (range) age at diagnosis: 7.2 (0.4-17.7) years, number of discharge medications: 8 (2-14). The proportion of patients prescribed  $\geq 1$  medication in each pharmacologic class was: Antimicrobials, 93.1%; antiemetics, 90.2%; mouth care, 85.3%; pain, 80.4%; stool softeners/laxatives, 75.5%; gastrointestinal protectants, 55.9%; steroids, 51.0%; other, 68.6%. In a multivariable model that controlled for patient sex, race/ethnicity, and pre-diagnosis medication use, factors associated with  $\geq 9$  discharge medications included a diagnosis of leukemia/lymphoma (Odds Ratio [OR]=3.1, 95% Confidence Interval [CI]=1.1-8.8;  $P=0.037$ ) and older age (OR=1.2/year, 95% CI=1.1-1.3;  $P < 0.001$ ).

**Conclusions:** Our findings suggest that most parents of newly diagnosed pediatric oncology patients must manage a substantial number

of home medications, including many for symptom management. These findings can be used to tailor patient/family education curricula, placing particular emphasis on home medication teaching for parents of older children and those with leukemia/lymphoma.

EP120/#1066 | Poster Topic: AS04 Nursing/AS04.b Research

### PARENT'S/CAREGIVER'S PERSPECTIVES ON THE REASONS AND STRATEGIES FOR MINIMIZING CHILDHOOD CANCER TREATMENT ABANDONMENT AT MUHIMBILI NATIONAL HOSPITAL, TANZANIA

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**Background and Aims:** Approximately 1 - 2% of all cancers occur in children under 15 years old. The annual global incidence of childhood cancer is estimated to be 400,000 children, with approximately 1,000 children diagnosed with cancer daily. Abandonment of treatment in low- and middle-income countries is an important cause of treatment failure in the process of cancer care and a significant problem in sub-Saharan Africa. Abandonment contributes to overall low cancer survival rates of less than 20% and reported as related to 25% of deaths amongst children with cancer in the Northern Zone of Tanzania. **Aim:** This study explored reasons for treatment abandonment among parents/caregivers of children with cancer in Tanzania and to document their perspective on strategies to minimize abandonment.

**Methods:** A phenomenological qualitative research design was used and purposive sampling technique to recruit participants was employed. An in-depth interview guide was used for data collection. Interviews were recorded, transcribed, coded, and analyzed using a thematic approach.

**Results:** Parents/caregivers' knowledge about their child's cancer; influences on treatment abandonment; and parent/caregiver suggestions for support to avoid treatment abandonment were the three themes that were identified. Poor parental understanding of childhood cancer, marital challenges, myths and beliefs, long-time stay in the hospital, lack of family and community support, use of alternative medicine, and both positive and poor treatment response were found to influence cancer treatment abandonment. Parents/caregivers perceived that; community awareness activities, health care worker capacity building at district levels, formation of parent/caregiver network and provision of diagnostic services at all levels of hospitals will help to reduce abandonment.

**Conclusions:** Study findings implied that parents'/caregivers' understanding about childhood cancer and treatment modalities were found to have an impact on their decision to adhere to their child's treatment or abandon the treatment

EP121/#108 | Poster Topic: AS04 Nursing/AS04.b Research

### EVALUATION OF THE CONTENT VALIDITY AND READING LEVEL OF INSTRUMENTS TO MEASURE SYMPTOM SELF-MANAGEMENT BEHAVIORS IN SCHOOL-AGE CHILDREN WITH CANCER AND THEIR PARENTS

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**Background and Aims:** Self-management of children's cancer-related symptoms is a shared process, requiring engagement of children and their parents. Instruments to measure symptom self-management behaviors of children and their parents are lacking. We describe evaluation of the content validity and reading levels of child and parent versions of the Symptom Self-Management Behaviors Tool (SSMBT).

**Methods:** The project was guided by the Individual and Family Self-Management Theory. Items were derived from the authors' prior work addressing symptom self-management strategies reported by children and adolescents with cancer. Ten English-speaking children with cancer 6-12 years of age (median 11 years; 6 boys) completed cognitive interviews in which they related their understanding of each proposed item, its perceived importance, and rationale for its importance. Eleven parents (median 40 years; 10 mothers) completed a content review survey in which they rated the perceived clarity and importance of proposed items followed by a brief interview. Responses were iteratively reviewed after 3 dyads to determine items deemed confusing or unimportant and to refine or delete items. Reading levels of the completed tools were evaluated using Readability Studio.

**Results:** Initial drafts of the child and parent versions of the SSMBT included 7 and 12 items, respectively. After three cycles, two items were dropped from the child instrument due to difficulties in comprehension. Children expressed a preference for phrasing that referenced "not feeling good" rather than "symptoms." The reading level of the 5-item child SSMBT was 3rd grade (range 2<sup>nd</sup>-4<sup>th</sup>). All items on the parent version were retained; however, 4 items were rephrased in response to feedback. The reading level of the 12-item parent SSMBT was 8<sup>th</sup> grade (range 6<sup>th</sup>-11<sup>th</sup>).

**Conclusions:** The final child and parent versions of the SSMBT are presently undergoing evaluation for internal consistency reliability and construct validity prior to implementation in future studies.

EP122/#536 | Poster Topic: AS04 Nursing/AS04.b Research

### UNDERSTANDING HOW CHILDREN WITH RETINOBLASTOMA PERCEIVE THEIR AFFECTED EYES AND VISION: A QUALITATIVE STUDY OF PARENTS' PERSPECTIVES

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**Background and Aims:** Retinoblastoma affects children's eyes and vision during infancy. To support them, it is essential to understand how children perceive their affected eyes and vision. This study aimed to clarify how parents understand their children's realization process.

**Methods:** Individual semi-structured interviews were conducted under a qualitative descriptive design. Participants were 11 mothers of 3- to 7-year-old children with retinoblastoma. This study was approved by the research ethics committee of the author's institution.

**Results:** The median age of the mothers was 42 years (29-45 years). The children's median age was six years (4-7 years) at the survey and two months (1-24 months) at diagnosis. Eleven categories were generated from 26 subcategories. Parents observed that their child became "aware of the existence of both their eyes as parts of their body and responding when they were spoken to" from around one year old. As visual obscuration occurred in their early childhood, children seemingly "failed to feel uncomfortable with the impaired vision" or "failed to perceive visual change after eye enucleation." Children's perceptions and reactions changed through events in nursery school and kindergarten. They "perceived and expressed their poor visibility or visual difference between left and right eyes" and expressed it as "I can't see." This gradually became "dealing with their poor visibility by themselves." They "recalled the visual memories of what was seen when they could see." Some "became aware of differences in visual sensation and appearance between them and other children" based on their friends' suggestions, while others "had questions about their 'sick' eyes and envied others who can see."

**Conclusions:** When children with retinoblastoma enquired about their parents' visual acuity or why their vision was impaired, the parents had to confront the realities of their children's disease and visual impairment. This suggests the need for parental support in explaining the disease and impairments to their children.

EP123/#540 | Poster Topic: AS04 Nursing/AS04.b Research

### SUPPORTING CHILDREN WITH RETINOBLASTOMA: PARENTAL APPROACH TO PROMOTE UNDERSTANDING OF AFFECTED EYES AND VISIBILITY, AND ITS IMPACT ON PARENTAL PSYCHOLOGY

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**Background and Aims:** It is important for children with retinoblastoma to fully understand their motor and visual functions to build a positive self-image. This study investigated how parents help their children understand their affected eyes and visibility focusing on the parents' psychological state.

**Methods:** A qualitative descriptive analysis of data taken through semi-structured interviews with 11 mothers of 3- to 7-year-old children with retinoblastoma. This study was approved by the research ethics committee of the author's institution.

**Results:** The median age of the mothers was 42 years (29–45 years). The children's median age was six years (4–7 years) at the survey and two months (1–24 months) at diagnosis. Thirteen categories were generated from 27 subcategories. Parents "explained the difference between the left and right eyes and how to improve their sight," such as looking to the side of an artificial eye. As the child's sphere of activities expands with development, the parents "help their children understand the importance of preventing accidents caused by falling or narrowed vision" and "encouraged them to know the traffic rules and compensate for their impaired vision." The parents made their children aware of their surroundings, encouraging them to "protect the remaining eyeball and vision." Some parents "encouraged their children to memorize images for as long as vision lasts." In addition, parents "encouraged their children to realize what they can without thinking of visual impairment as a weakness" or "to positively see the appearance of wearing an artificial eye, and to take actions against various things." They taught their children "to get support for the impossible." Parents felt "difficulties of explaining and helping children to understand their visual sensation, facing to children's awareness."

**Conclusions:** Parents often struggle to balance helping their children develop a positive self-image while acknowledging the lifelong consequences of visual impairment. It is necessary to provide parents with explanations and psychological support.

EP124/#1090 | Poster Topic: AS04 Nursing/AS04.b Research

## THE LIVED EXPERIENCE OF ADOLESCENTS WITH CANCER. A QUALITATIVE PILOT STUDY AT THE UGANDA CANCER INSTITUTE

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**Background and Aims:** To receive a diagnosis of cancer must be absolutely devastating especially when you are in a developmental stage where you are already battling with issues such as self-esteem,

body image, independence, and career choices. A diagnosis of cancer disrupts almost every aspect of life continues to affect the child, potentially their whole family and, throughout adulthood. Cancer is one of the leading causes of death among children and adolescents worldwide. Of the 400,000 children diagnosed annually with cancer, a significant number of them are adolescents. And live in low- and middle-income countries where treatment outcomes are less than 20%. Due to this high acuity of terminal illness, adolescents are often faced with daily suffering, pain and death. **Objective** Describe the lived experience of adolescents with cancer receiving care cancer at the Uganda Cancer Institute.

**Methods:** A qualitative pilot study was conducted by in-depth, unstructured individual interviews with open-ended questions to evaluate the lived experiences of five adolescents with a histological diagnosis of cancer, receiving care at the Uganda Cancer Institute. Interviews were conducted over two months by a single interviewer, in English or Luganda, at UCI. Interviews (60-90 minutes) were transcribed and analyzed using content analysis.

**Results:** The adolescents' lived experiences were categorized into five main themes: fear, repressed feelings, feelings of anger, suffering, and the need to be supported.

**Conclusions:** Findings from the pilot study confirmed that adolescents diagnosed with cancer face traumatic experiences and would benefit from support. Programs and services need to be tailor made for adolescents and given options for both physical and psychological support. Adolescents are not young children, neither are they adults. They have a strong understanding of their illness and as such need to be considered and involved in decision making pertaining their lives.

EP125/#962 | Poster Topic: AS04 Nursing/AS04.b Research

## MOST RELEVANT ACUTE TOXICITY SYMPTOMS IN RELATION TO THE TREATMENT WITH PROTON BEAM THERAPY IN CHILDREN WITH BRAIN TUMORS – A HEALTH CARE PROFESSIONALS PERSPECTIVE

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**Background and Aims:** Proton Beam Therapy (PBT), is a relative new radiation technique and if available, used for most children receiving curative radiotherapy for brain tumors. This treatment is associated with both acute and late toxicity. To gain more insight into the acute toxicity, it is important to register toxicity systematically and prospectively. The aim of this study is to gain more insight into the most relevant symptoms of acute toxicity in order to develop a list for

adequate symptom registration. With this knowledge, the quality of care can be improved, because more appropriate interventions can be used to prevent or limit this toxicity.

**Methods:** Based on literature review and expert consultation a list of twenty-five symptoms was developed. In a Delphi study, consisting of two survey rounds, these symptoms were queried among a fixed group of thirty-six experts comprising of pediatric oncologists, neurologists, radiation oncologists and nurse practitioners, all involved in pediatric oncology. All relevant symptoms were rated for prevalence, severity and clinical relevance using a five point Likert scale.

**Results:** In the first round twenty-one participants took part in the study, of which seventeen participants submitted the questionnaire complete, and were included in the data analysis. Round two consisted of fifteen participants. The following seven symptoms were rated as most relevant to register: nausea/vomiting, headache, distress, fatigue, pain/discomfort, malnutrition and seizures.

**Conclusions:** Two Delphi rounds resulted in prioritizing seven symptoms of acute toxicity of PBT in children with a brain tumor. This is the first step in the development of a systematic registration tool of acute toxicity. To gain more insight into the degree and severity of acute toxicity, a registration system including these symptoms expressed in terminology of the Pediatric Common Terminology Criteria Adverse Events, will be developed. Further research should include the patient's opinion.

EP126/#366 | Poster Topic: AS04 Nursing/AS04.b Research

### THE USE OF CHILDREN AS LANGUAGE MEDIATORS IN NORDIC PAEDIATRIC ONCOLOGY CARE

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**Background and Aims:** Background Language barriers constitute major challenges in paediatric healthcare, threatens quality of care and patient-safety, and diminishes children's/guardians' possibilities to participate in care. Misunderstandings due to language barriers between healthcare professionals and patients/guardians can, at worst, result in life-threatening consequences. An insufficient use of interpreters together with the use of children (e.g. siblings or the patient) as language mediators have been found in Swedish paediatric oncology. **Aim** To assess to what extent children are used as language mediators, when their guardians have low proficiency in the majority language, among registered nurses (RNs) and medical doctors (MDs) in Nordic paediatric oncology care.

**Methods:** A survey using the Communication over Language Barriers questionnaire (CoLB-q©) has been performed among RNs and MDs at all Nordic paediatric oncology centres. The survey is assessing, on a Likert scale (never/seldom/sometimes/often), to what extent children are used as language mediators, when their guardians have low

proficiency in the majority language. Data was analysed using descriptive statistics.

**Results:** At 20 centres in Sweden (n=202), Finland (n=97), Denmark (n=77), Iceland (n=22), and Norway (n=70) a total of 468 participants answered CoLB-q©. RNs reported, more often than MDs, that they sometimes/often used children as language mediators. This was most common among RNs in Finland (71%) and Sweden (59%); comparing to MDs in Finland (38%) and in Sweden (33%). The lowest reported use of children as language mediators among RNs were in Norway (30%) and among MDs in Denmark (0%).

**Conclusions:** In all the Nordic countries, children were used as language mediators to a relatively high extent. This could pose risks of wrong translations and in relation to the burden and responsibility the child is exposed to. It is of importance to further investigate reasons, among RNs and MDs in Nordic paediatric oncology care, for not using professional interpreters to secure patient-safe communication.

EP127/#97 | Poster Topic: AS04 Nursing/AS04.b Research

### THE IMPACT OF PAEDIATRIC CANCER ON CAREGIVERS: MULTI-CENTRE CROSS-SECTIONAL STUDY

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**Background and Aims:** A Diagnosis and treatment of childhood cancer can be stressful for family caregivers, who manifest with signs of anxiety, depressive symptoms, and poor quality of life. The associated factors that impact anxiety, depressive symptoms, and health-related quality of life have been found to impact these outcomes differently across cultures. This study aimed to estimate the prevalence and identify determinants of anxiety, depressive symptoms, and health-related quality of life in caregivers of children with cancer in Malawi.

**Methods:** A cross-sectional study recruited 167 caregivers of children with cancer between September and December 2022. Participants completed the Generalized Anxiety Disorder-7, Patient Health Questionnaire-9, and 12-item short-form health survey. Multivariate analysis was performed to identify the predictors of anxiety, depressive symptoms, and health-related quality of life.

**Results:** Anxiety and depressive symptoms accounted for 62.9% and 60.4% of caregivers of children with cancer, respectively, whereas 17.5% and 10.2% reported very high anxiety and depressive symptoms scores. Caregivers reported poor health-related quality of life, especially on the mental health component (Mean= 39.33, SD=6.35). Caregivers from Muslim (B= 7.800,  $p < .001$ ) and Pentecostal (B= 3.067,  $p = .023$ ) denominations were more likely to be anxious, whereas unemployed caregivers were more likely to experience a lower level

of anxiety ( $B = -4.080, p = .016$ ). Moreover, caregivers of children from Muslim ( $B = 7.140, p = .002$ ), catholic ( $B = 3.702, p = .033$ ), and Pentecostal ( $B = 3.450, p = .034$ ) denominations were more likely to be depressed. Regarding the health-related quality of life, female caregivers ( $B = 3.962, p = .031$ ) and older caregivers ( $B = 3.415, p = .020$ ) were more likely to report better physical health.

**Conclusions:** The current study demonstrates high anxiety levels, depressive symptoms, and poor health-related quality of life among caregivers of children with cancer in Malawi. It is vital to include psychological interventions when caring for caregivers of children with cancer.

EP128/#1512 | Poster Topic: AS04 Nursing/AS04.b Research

### WILL MY CHILD SURVIVE? VOICES OF PARENTS TO ONE SEVERELY ILL CHILD AND ONE HEALTHY SIBLING AS STEM CELL DONOR

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**Background and Aims:** When the potential stem cell donor to an ill child is a healthy sibling below the age of 18 years, Swedish parents have the legal right and obligation to decide on behalf of the donor. However, parents have conflicting loyalty with one severely ill child and one healthy child. This study aimed to explore parents' experiences during the donation and transplantation process.

**Methods:** Individual interviews were performed with 18 parents of 13 earlier interviewed minor donors, after successful paediatric stem cell transplantations. The interviews were analyzed using qualitative content analysis.

**Results:** *Living with the unbearable threat of losing a child* was the main category in this study. The parents were *Focusing on the best for the ill child*, which meant that they focused on the sick child; when the parents were informed that the sibling was the preferred donor, it was obvious that the healthy child should donate stem cells. The parents were *Living with an unreliable future* which describes how they received life-altering information to gain control, but the most important information regarding whether the sick child would survive or not was still missing and left them in a state of uncertainty. To cope with this, they keep their focus on the bright moments. Finally, the parents were *Handling the family and life amid the chaos*, which included a feeling of inadequacy amid the chaos while the family became a fragmented team during hospitalizations.

**Conclusions:** When parents' healthy child is a potential donor to their severely ill child, parents focus on cure for the ill child. Furthermore, they feel no conflicting loyalties for their children, and this highlights the need for a separate advocate for the healthy child. A possible limitation of the study is that some transplants were performed before and some after accreditation according to JACIE International Standards.

EP129/#181 | Poster Topic: AS04 Nursing/AS04.b Research

### EXPLORING ADHERENCE IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT THROUGH REAL-TIME DIGITAL HEALTH INTERVENTIONS: THE BMT4ME USABILITY STUDY

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**Background and Aims:** Due to multifaceted outpatient regimens, children receiving hematopoietic stem cell transplant (HCT) are at high risk of medication non-adherence, leading to life-threatening complications. HCT adherence intervention literature is limited. This study aimed to examine the usability of a digital health intervention (Mobile app: BMT4Me) for adherence reporting to inform BMT4me refinement for efficacy testing.

**Methods:** Parents of children in the acute phase post-HCT were recruited from a Midwestern children's hospital. Parents completed standardized measures of weekly adherence and recorded daily adherence using the BMT4me. Descriptive statistics were used to calculate adherence, barriers, and usability and acceptability over time.

**Results:** Parents ( $n = 14$ ; 78.9% mothers; 71.64% White; 21.4% Black; child age  $M = 8, SD = 5.17$ ) reported missed and late does more frequently in BMT4me ( $n = 17$  (missed),  $n = 468$  (46.9%) (late), than with the weekly self-report adherence measure ( $n = 6, n = 39$ ). Half of parents ( $n = 7, 50%$ ) reported the child was responsible for ensuring medication was taken and 43% ( $n = 6$ ) of children were responsible for knowing when the medication needed to be taken. Missed doses and taking medications late increased over time. The most reported barriers included: "hates taste" ( $n = 8, 67%$ ), "child doesn't want to take" ( $n = 7, 58%$ ), and "hard to wake up" "hard to swallow" ( $n = 6, 50%$ ). Overall, the mean System Usability Scale score was ( $86.15 (SD = 12.8)$ ), and all participants reported BMT4me was easy to use and acceptable. BMT4me motivated 86% of parents ( $n = 12$ ) to stay on schedule with medications. Using reaction cards, parents described the app as "useful", "accessible", "organized" and "appealing".

**Conclusions:** Missed and late doses of medication are problematic post-HCT and worsen with time. Barriers to medication adherence

vary. BMT4me improved accurate real-time reporting of adherence post-HCT. Parents reported BMT4me usable and acceptable. Digital health applications may improve medication adherence and identify barriers, thus enabling healthcare providers to offer tailored interventions for improving adherence and ultimately, outcomes for this vulnerable population.

EP130/#611 | Poster Topic: AS04 Nursing/AS04.b Research

### HOW DO PARENTS' DEAL WITH THEIR MAIN CONCERN WHEN FACING MORAL CHALLENGES IN CHILDHOOD CANCER CARE?

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**Background and Aims:** Childhood cancer are life-threatening diseases that affects the whole family, and quite often parents face moral challenges regarding their child's care. Earlier research reveals that parents' moral challenges arise in connection with experimental treatments and care responsibilities. To explore parents' main concern and how they deal with their main concern when facing moral challenges in childhood cancer care.

**Methods:** The present study is a qualitative and exploratory study based on empirical data. Parents to children with cancer were invited from three childhood cancer centers in Sweden. The data collection was carried out through focus group interviews. A classical grounded theory method was used for the analysis.

**Results:** The data collection resulted in five focus group interviews with 20 parents (fathers n=7 and mothers n=13). The theory explains parents main concern and how they handle their main concern. "Sheltering in chaos" emerged as a core category used to handle the main concern to "Bring the child through the life-saving trajectory". "Sheltering in chaos" includes strategies such as "Balancing control", "Absorbing information", "Deliberating of suffering" and "Valuing the necessity of care actions". This is done in a condition where parents feel that they have no choice and fear loss. The consequences of "Sheltering in chaos" is that parents feel that they are "Torn between roles". "Familiarity" emerged as an influencing variable for the core category and the strategies.

**Conclusions:** The results indicate that parents' care experience is ameliorated by understanding of care actions and familiarity with the healthcare professionals. By detailing the moral challenges as described by parents, the results might inspire and guide ways to offer moral support.

EP131/#886 | Poster Topic: AS04 Nursing/AS04.b Research

### VALIDITY AND RELIABILITY OF A PATIENT-REPORTED EXPERIENCE MEASURE OF HEALTHCARE PROFESSIONALS' EMPATHY LEVELS IN THE CARE OF SWEDISH CHILDREN WITH CANCER OR LONG-TERM ILLNESSES

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**Background and Aims:** Children with long-term illnesses (e.g. cancer) regularly meets with healthcare professionals and requires hospital care. Research shows that these children value participating in empathic and respectful discussions and that most want to be involved in medical consultations. Empathy enables a holistic view of the patient which can improve patient's compliance and treatment efficiency. Patient-reported experience measures allows children to express their experiences with the care received. Previous studies have shown validated patient-reported experience measures are used inconsistently in Swedish paediatric care with only half of the departments surveying children directly. The Visual CARE Measure also called the Paediatric CARE Measure, is a short questionnaire that gives children and parents the opportunity to express how a meeting with a healthcare professional was experienced. The aim of this study was to translate and validate a patient-reported experience measure of the levels of empathy demonstrated by healthcare professionals' as perceived by children during procedures in general pediatric care.

**Methods:** The translation and cultural adaptation of this measure followed the professional society for health economics and outcomes' research principles of good practice. Construct validity, inter-rater reliability and internal consistency were calculated.

**Results:** A total of 290 children 0-17 years and their parents answered the questionnaire. The preliminary results indicated that children and their parents perceived similar levels of empathy from healthcare professionals' during a needle procedure or nasal tube insertion. Between a third and a quarter of the respondents reported the maximum score, indicating that respondents used the entire Likert scale. Most participants answered all items, indicating high acceptability for the Swedish version of the measure.



**Conclusions:** The child-friendly patient reported Visual CARE measure can be used in a general paediatric setting for children with cancer to evaluate their perceived levels of empathy displayed by healthcare professionals'.

EP132/#159 | Poster Topic: AS04 Nursing/AS04.b Research

### BARRIERS TO EFFECTIVE DELIVERY OF PALLIATIVE CARE IN A TEACHING HOSPITAL IN GHANA

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**Background and Aims:** Palliative care a global problem and as such some studies have emphasized that nurses caring for seriously ill children are faced with work related challenges. This has caused many children to have a prolonged hospital stay and suffer unnecessary pains.

The goal of this study was to explore barriers to effective delivery of palliative care in a tertiary hospital in Ghana by pediatric oncology nurses.

**Methods:** A survey amongst 14 nurses at the pediatric oncology unit at Komfo Anokye Teaching Hospital, Ghana from January to April 2022.

According to the survey, a number of barriers must be overcome to address the unmet effective delivery of palliative care of terminally ill children.

Nurses perceptions explored on:

Uncertain prognosis, family not ready to acknowledge incurable disease, language barrier, cultural and social barriers that is believe about death and dying, misconception that improving or increasing dosage to opioid analgesic will lead to increase substance abuse, Insufficient education on pain and time constraints as perceived barriers.

**Results:** From the analysis of the survey, participants were nurses, 4 (28.55%) males and 10 (71.43%) females. All respondents reported 4 of 10 barriers listed in the study questionnaire as frequently or almost always occurring, that is, uncertain prognosis (42.8%), family not ready to acknowledge incurable condition (35.7%), language barriers (14.2%), and time constraints (14.2%).

**Conclusions:** The results point to the fact that; uncertain prognosis, family not ready to acknowledge incurable disease, language barrier and time constraints as frequently or always occurring as barriers to effective delivery of palliative care in Teaching Hospitals in Ghana. It is hoped that by addressing these barriers, there would be an effective care delivery of palliative care which will lead to improving the quality of lives of patients receiving end of life care.

EP133/#1375 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

### IMPACT OF CHILDHOOD CANCER DIAGNOSIS ON PARENTAL RELATIONSHIPS: PARENTAL PERSPECTIVES

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**Background and Aims:** Childhood cancer diagnosis affects not only the child but also parental relationships. Breakdown of the family unit can have far-reaching treatment consequences. The study aimed to determine the impact of childhood cancer diagnosis on parental relationships among parents of children with cancer at the Paediatric Oncology Unit (POU) of the Korle Bu Teaching Hospital (KBTH), Ghana.

**Methods:** Cross-sectional study using a questionnaire administered to parents of children with cancer at the POU, KBTH.

**Results:** Of the 20 respondents, majority (90%) were mothers. Half were married, 40% were cohabiting and 10% were divorced. Worriyngly, 40% had considered separation/divorce since the diagnosis. Before diagnosis, 65% rated their marriage/relationship as "very good", but 80% now rated it as "poor" and the remainder "average". All respondents had been able to make decisions together at least some of the time prior to diagnosis, compared to only 10% after. Few (10%) had ever experienced loneliness prior to the diagnosis, compared to 85% in the aftermath. With tension/ stress between partners, 40% had never experienced this prior, but 90% now experienced this all the time. Almost half (45%) now sought emotional support from others all the time, and the rest, some of the time, whereas 80% had never done this prior to diagnosis. All respondents had trouble communicating with partners all the time after the diagnosis compared to before, where 60% never experienced this and the rest, only some of the time. All but 1 respondent had experienced increased anger at their partner since the diagnosis. Prior, 20% had, some of the time with the rest answering never.

**Conclusions:** Childhood cancer diagnosis places a toll on parental relationships. Support must be provided following the childhood cancer diagnosis to help preserve the family unit.

EP134/#610 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

### CONMEDPED PROJECT: CONTRIBUTING FROM PRIMARY CARE TO THE SPIRITUAL SUPPORT OF CHILDREN WITH ADVANCED CANCER

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**Background and Aims:** In 2019 in the framework of the Panama National Palliative Care Program (PNPCP) a program directed from the primary pediatrician to the children with advanced cancer was created: the Conmedped Project which has the objective of promote the spiritual support within comprehensive pediatric care. During the pandemic, pediatric oncologist asked the project to provide support for those families in trouble caused by global suffering: physical,

psycho-social and existentialist. We saw a very unique experience of improving attention quality,

**Methods:** We collected data from 27 pediatric advanced cancer attended between March 2019 to February 2022 in the PNPCP taking as independent variable having received spiritual support and dependent variable the perception that this had improved the communication between the health personnel and the family taking into account religion, importance, age and diagnosis of the patients

**Results:** The mean age of the patients was 11 years. We have an ecumenical approach; 88.1% of the families were christian. 92.5% of the families responded that was important to include spiritual issues in the conversations with them as well as the child. If we compare the positive answers with the negative ones to the question "Do you think that it is important to bring spiritual issues" we found an OR of 24 in the perception that this matter improved the communication. We also found that 92.3% of families who had taken the decision to attend the last stage of life in home, had have the perception of better communication after spiritual support. It was not found in this sample that there were differences between the perception of improvement in communication if the support was given since the diagnosis or withing the last week of life.

**Conclusions:** We experiment how vital is to ask the family about spiritual matters and include basic-spiritual-support in the "first-aid kit" of quality of life improvement

EP135/#793 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

#### A SURVEY OF PAEDIATRIC HAEMATOLOGY AND ONCOLOGY (PHO) NURSES' PERCEIVED KNOWLEDGE AND ATTITUDES TOWARD IMPLEMENTATION OF FUNDAMENTALS OF PHO NURSING MODULE

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**Background and Aims:** The Universiti Kebangsaan Malaysia Medical Centre (UKMMC), Kuala Lumpur, Malaysia had identified several improvement opportunities as a result of the St. Jude Paediatric Oncology Facility Integrated Local Evaluation (PrOFILe). This includes implementation of a self-paced learning module. The Fundamentals of Paediatric Haematology and Oncology (PHO) Nursing Module aims to improve the PHO nurses' knowledge and specialised skills. This study aims to evaluate the PHO nurses' perceived fundamental PHO knowledge and the attitudes toward the module prior to its implementation, and the association with demographic data.

**Methods:** An online cross-sectional, self-administered survey was conducted among all PHO nurses (n=48) in UKMMC to capture demographic details, perceived PHO fundamental knowledge, and the attitudes toward implementing the learning module. Descriptive analysis, t-test, and one-way analysis of variance (ANOVA) were

performed appropriately. A p-value of  $\leq 0.05$  indicates statistical significance.

**Results:** All nurses (n=48,100%) responded to the online survey. Most nurses rated their perceived knowledge of PHO fundamentals including nursing assessments and care, disease knowledge, oncologic emergencies, and chemotherapy handling as good (Mean  $3.90 \pm 0.59$ ; Likert scale of 1-5; 1=strongly disagree and 5=strongly agree). The nurses agree (Mean  $4.28 \pm 0.72$ ) that this module will give positive impacts on their knowledge, clinical skills, career advancement, and service quality in UKMMC. The level of working experience was significantly related to the perceived knowledge ( $p=0.013$ ). There was no significant association between age ( $p=0.115$ ), gender ( $p=0.775$ ), level of education ( $p=0.139$ ), workstation ( $p=0.259$ ), and perceived knowledge. None of these factors were statistically related to the attitudes toward this module.

**Conclusions:** Most PHO nurses reported good perceived knowledge of fundamentals of PHO nursing and positive attitudes toward implementing this module. The next steps are to implement the fundamental PHO nursing module and objectively assess the effectiveness of the training post implementation. The action plan is important to ensure the nurses are maximally capable to deliver specialised nursing care to their patients.

EP136/#400 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

#### SECOND AMONGST EQUALS? TOWARDS FURTHER PROFESSIONALIZATION OF DOCTOR'S ASSISTANTS IN PATIENT TREATMENT ROOMS AT A PEDIATRIC ONCOLOGY UNIT: AN IMPLEMENTATION PLAN

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**Background and Aims:** The work efficiency of nurses and Doctor's assistants at the day care unit of the Princess Máxima Center has long been considered as suboptimal. This was primarily caused by the fact that for every port-a-cath (PAC) insertion to administer chemo ('chemo-push'), presence of a second nurse was required to approve this action (the 'four eyes check principle'). Doctor's assistants were not permitted to function as an extra set of eyes, nor were they allowed to perform other technical tasks such as removing a PAC needle. As a result, patients and their relatives experienced lengthy waiting times. In the context of a nurse leadership course an implementation plan was developed to further professionalize Doctor's assistants, by training them in tasks to assist during chemo-pushes.

**Methods:** Thirteen Doctor's assistants were selected. Inclusion criteria were: a minimum of nine months working at the Princess Máxima Center and sufficient educational qualifications (intermediate vocational education). The training was given by two nurses and entailed self-study of summaries from protocols within the center, drawing up checklists and providing additional training of three technical nursing actions. These were: i) removing a PAC needle; (ii) heparinizing a PAC needle and (iii) serving as an extra set of eyes in order to perform the

four eyes principle check. The checklist was created in collaboration with the center's academy.

**Results:** The further professionalization of the Doctor's assistants was positively evaluated in team meetings and has resulted in (reported) shorter waiting times for patients, a (reported) reduced workload for the nurses and a broadening of knowledge for Doctor's assistants, who also report more job satisfaction.

**Conclusions:** Doctor's assistants and nurses can collaborate in far more satisfactory ways than is currently practice. By further professionalizing Doctor's assistants through training, better quality of care can be achieved.

EP137/#1729 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

LONG-TERM FOLLOW-UP CONSULTATION IN A NURSE/PHYSICIAN DUO FOR BETTER EFFICIENCY

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**Background and Aims:** The survival of children and adolescents treated for cancer has been steadily increasing. It is estimated that one adult in 1000 is currently a former cancer patient. These young "survivors" need long-term follow-up (LTFU), both medically and psychosocially, follow-up that must be adapted to the specific themes of the AYA (Adolescents and Young Adults, 15-25 years old) age group. Since June 2012 and the establishment of the DAJAC (Device for Adolescents and Young Adults with Cancer) at CLB and IHOPe, more than 1,200 patients have been cared for. The team noted that many former patients contacted them to discuss various problems: return to school/to professional life, need for academic and/or professional reorientation; fertility/sexuality issues; weight problems; difficulties in resuming physical activity; psychological issues.

**Methods:** In this context, LTFU consultations were initiated by a pediatric oncologist for former patients, 5 years after diagnosis. These consultations consisted of a medical interview covering the treatments received and the recommended follow-up, and then a more global interview covering the above-mentioned themes. The team discussed the interest and the place of a nurse coordinator in this consultation.

**Results:** LTFU consultations are carried out by a physician/nurse pair. They take place once a week at a rate of 5 to 6 patients per week. 45 consultations in pairs have been carried out since October 2022 and 400 consultations have been carried out by the physician alone since 2019. A new pathway is thus being established. In case of multiple and/or complex problems, a multidisciplinary LTFU day hospital can be proposed.

**Conclusions:** The creation of this consultation in pairs has allowed an improvement of this very particular care, for patients who are out of care. The objective is to perpetuate this consultation, included in the ten-year strategy of the French National Institute of Cancer.

EP138/#900 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

A NURSING TOOL TO MEASURE DECLINE IN MOTOR AND SENSORY FUNCTIONS IN CHILDREN WITH SPINAL CORD TUMORS

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**Background and Aims:** There is currently no standardized protocol or assessment tool for nursing professionals to measure the motor and or sensory functions in a uniform and concise manner for pediatric oncology patients diagnosed with spinal cord tumors, or those who are at risk of neurological deterioration, both requiring emergent intervention to prevent complete spinal cord dysfunction. Our aims were: 1) to develop a concise neuro assessment tool to be used by nurses to get rapid, simple, consistent neuro evaluations completed, 2) to assess the feasibility to implement the evaluation tool in clinical practice and document results.

**Methods:** A literature search was completed in PubMed and CINAHL databases. An environmental survey of National and International experts in pediatric neurology and oncology was completed via six consultations. Research was completed to determine the right method to deploy the assessment tool.

**Results:** Components of two validated motor and sensory assessment tools were combined (The Medical Resource Council scale and the Erasmus MC modification of the revised Nottingham Sensory Assessment) to create a nursing specific tool that quickly, consistently and concisely identifies a pediatric oncology patient at risk of sensory and motor function decline. Pediatric nurses at the neuro oncology unit will be educated on the tool prior to implementation, utilizing infographics and a supporting educational video to disseminate this information in a rapid manner.

**Conclusions:** The assessment findings will be implemented in the patient chart as a consistent frame of reference for all clinicians and enables the following: consistent reporting of findings by nursing staff during transfer of care, identifying sudden changes that required clinical escalation, in addition to seeing trends over time. Further research will determine the validity of the tool.

EP139/#1290 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

EVIDENCE-BASED PRACTICE: PROLONGED FLUSHING AND LOCKING INTERVAL FOR TOTALLY IMPLANTABLE VASCULAR DEVICES IN CANCER PATIENTS

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**Background and Aims:** Flushing and locking of totally implantable venous devices (TIVDs) is recommended to maintain their patency when not in use. Although manufacturers' recommendations indicate monthly access for maintenance, recent studies have shown that prolonging flush is safe and feasible for patients who complete chemotherapy. We processed evidence-based practice (EBP) projects using PICO model based on current evidence derived from research.

**Methods:** EBP teams were initially tasked to develop clinical practice question into PICO format. P (cancer patients with TIVDs), I (prolonged interval of flushing more than 4 weeks), C (4weeks interval flushing) and O (TIVDs occlusion and infections) was finalized. A systematic search was carried out in PubMed, EMBASE, CINAHL, Cochrane, DBpia, Web of Science and practice guidelines of professional association. Four reviewers independently extracted data and assessed quality. Study findings were summarized and evaluated the quality of evidence using SIGN and GRADE.

**Results:** A total of 11,435 articles were extracted and 12 studies fulfilled the PICO question. Pooled results from 12 studies showed fewer catheter occlusions and infections in favor of prolonged flushing and locking. Meta-analysis showed that frequency of total complication and catheter occlusion rate associated with the 4-week interval were higher than 8-week interval. Moderate-quality evidence suggests that 8-week prolonged schedule flushing and locking intervals has no effect on catheter patency. However, 12-week prolonged flushing and locking intervals is feasible on catheter patency with low-quality of evidence.

**Conclusions:** Extending the flush interval to 8-weeks is safe and feasible with moderate-quality of evidence. But prolonged flushing more than 12 weeks is a recommended level of "C". Implications for Practice: No statistically significant difference in occlusion and infection rate between short and long interval of flushing was found. However, prolonged flushing more than 12 weeks is low-quality of evidence. Therefore, further studies are necessary to strengthen the safe implementation of longer intervals more than 12-week in clinical practice.

EP140/#510 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

#### NURSING LEADERSHIP IN PEDIATRIC ONCOLOGY

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**Background and Aims:** The Princess Maxima Center educates nurses to become specialized Pediatric Oncology Nurses. After finishing the specialization these experienced nurses need to be challenged and must have the possibility for broadening and deepening of their

knowledge and improve nursing leadership. In case of a one-day chemotherapy, the Pediatric Oncology Nurse (PON)<sup>1</sup> is already in the lead however, not in multi-day chemotherapy.

The project 'The PON in the lead' uses the knowledge of the PON, improves nursing leadership, responsibility and ensures uniformity in care for patients with chemotherapy.

**Methods:** In September 2020 the project has started at the solid tumor unit in the Princess Maxima Center for a period of six months. On this ward children, who meet the inclusion criteria with a maximum of seven patients at the same time, are admitted for a multi-day chemotherapy. The PON is in the beginning under supervision of the Nurse Practitioner (NP) and after 2 years under only supervision of the Paediatric Oncologist. In the first two years there was a patient round with the NP on day two of the admission. Since 2022 there is no patient round during admission. In case of complications the patient transfers to regular clinical care and is discharged of the project.

**Results:** This project includes in 2020 77 admissions, seven of them were discharged due to complications. Discharge of the patients is smoother and faster, the daily patient rounds are faster because less patients need to be discussed. In 2021 363 admissions are included and in 2022 355 admissions and just a few patients were transferred to the regular clinical care because of complications.

**Conclusions:** The 'PON in the lead' shows that it is possible and save for the patient. The project is going to be implemented in other wards at the Princess Maxima Center

EP141/#1332 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

#### MANAGEMENT OF NEUTROPENIC FEVER IN THE OUTPATIENT CLINIC: REPORT FROM THE PEDIATRIC HEMATOLOGY AND ONCOLOGY DEPARTMENT OF RABAT - MOROCCO

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**Background and Aims: Introduction:** Toxicity and infection such as neutropenic fever is major cause of early mortality in low and Middle income countries (LMIC). The severity depends on the depth of neutropenia, the duration, type of chemotherapy and quality of management. In LMIC where access to inpatient beds can be limited, managing neutropenic fever in outpatient clinic is a good option but requires a close follow up by trained nurses.

**Objective:** To evaluate the management of febrile neutropenia in the outpatient setting.

**Methods:** This is a prospective and descriptive study carried out in the outpatient unit of the pediatric hematology and oncology department children's hospital of Rabat from December 1<sup>st</sup> 2022 to February 28<sup>th</sup> 2023.

**Results:** We collected information about 43 patients aged 0 to 15 years admitted for neutropenic fever. Among them, 41% of the patients were followed for Acute Lymphoblastic Leukemia of which 31% are in maintenance phase and 18% of patients are followed for Neuroblastoma. 83% of patients received the first dose of antibiotics more than 06 hours after the first fever peak. 74% presented a fever between day 7 and day 15 post chemotherapy. 41% had a temperature of more than 39°C and 67% of patients had respiratory symptoms. 55% of the patients had a profound neutropenia lower than 500/mm<sup>3</sup>. 30% of the patients had a hemoglobin level lower than 7 which required a transfusion of red blood cells. 93% of patients received a 3<sup>rd</sup> generation cephalosporin. Apyrexia was achieved on day 2 in 65% of patients and on day 3 in 9% of patients. 25% of patients required hospitalization. No case of death was reported.

**Conclusions:** Febrile neutropenia remains a frequent diagnostic and therapeutic emergency in patients undergoing chemotherapy requiring rapid management and an adapted antibiotic. In Morocco, outpatient management of neutropenic fever is a frequent situation which is used with high rate of success thank to a trained nurses

EP142/#1351 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

#### TOXICITY RELATED TO CHEMOTHERAPY IN THE OUTPATIENT IN THE PEDIATRIC HEMATOLOGY AND ONCOLOGY DEPARTMENT CHILDREN'S HOSPITAL OF RABAT

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**Background and Aims: Introduction:** Chemotherapy toxicity is one of the major causes of complications and early mortality in low and middle income countries. The severity depends on the duration and type of chemotherapy and the quality of management. Good nursing care in the outpatient setting can reduce the risks related chemotherapy toxicity.

**Objective:** to evaluate the toxicity of chemotherapy received in the outpatient setting in the pediatric hematology and oncology department in Rabat.

**Methods:** This is a prospective and descriptive study carried out in the day hospital unit of the pediatric hematology and oncology department of Rabat children's hospital for a period of one month (Feb 2023).

**Results:** We collected 107 patients aged 0 to 15 years, 44% of the cases having an age of 5 to 10 years and 36% have less than five years. 58% of the patients were followed for Acute Lymphoblastic Leukemia (ALL) of which: 20% presented a hematological toxicity grade 2 and 3.51% presented a digestive toxicity (vomiting) grade 1 and 2.20% of patients followed for neuroblastoma did not present toxicity (grade 0 and 1). 15% of patients followed for neuroblastoma of which: 66% of patients presented a digestive toxicity grade 2. 27% of patients had skin toxicity grade 3. No cardiac, hepatic, or renal toxicity was noted in any of our patients. No patient required hospitalization and there were no toxic deaths. The patients who presented febrile neutropenia were registered in another study done simultaneously.

**Conclusion:** Adherence to the chemotherapy protocol (antiemetic, hydration, and duration of chemotherapy administration) contributed to the control of chemotherapy toxicity and reduction of early mortality. The role of nurses is crucial in the management of chemotherapy induced toxicity

EP143/#442 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

#### "IMPACT OF NURSING INTERVENTIONS ON THE EVOLUTION OF PATIENTS AT HIGH RISK OF CLINICAL DETERIORATION IN A HOSPITAL OF TOLUCA MÉXICO"

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**Background and Aims:** When the EVAT program merges with the nursing process, it allows staff to identify the child with cancer and high risk of clinical deterioration, and to perform positive essential nursing interventions. Aim To evaluate the impact of nursing interventions on the evolution of pediatric patients with cancer and high risk of clinical deterioration assessed by the EVAT scale.

**Methods:** We included patients admitted from the oncology unit in a cross-sectional cohort study, from January 2020 to December 2022. We evaluated the general characteristics, reason for admission, and basic diagnosis. We analyzed high risk of deterioration events by red EVAT. We evaluated characteristics of the event, the type of nursing intervention performed, the rate of deterioration and the outcome of each red EVAT. We realized descriptive statistic

**Results:** During this period, 1895 patients were admitted. Red EVAT was detected in 81 events: 51 males, 30 females, mean age 8 yo, 37% with acute lymphoblastic leukemia, 78% febrile neutropenia as a reason for admission. EVAT score 5 - 8 at the expense of cardiovascular alteration, 70% occurred in evening and night shifts lasting 30' - 14 hrs. The main nursing intervention was continuous monitoring, increase or initiation of oxygen, medication administration, blood products

sampling and venous access facility. 72.9 % evolved to yellow evat and 27.1 % evolved to cynical deterioration: 2 floor intubations, 10 unscheduled transfers to ICU, 8 vasopressors and no patients required cardiopulmonary resuscitation or died during their hospital stay in the oncology unit.

**Conclusions:** In our hospital the nurse detects the risk of deterioration through the EVAT scale and according to the algorithm, through scientific knowledge and clinical judgement performs different interventions mostly classified as independent, while in conjunction with the medical team performs dependent and interdependent interventions that positively impact most of our children with cancer.

EP144/#1780 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

### BUILDING LOCAL QUALITY IMPROVEMENT CAPACITY TO ACCELERATE OWNERSHIP OF QUALITY IMPROVEMENT PROJECTS: THE MEXICO IN ALLIANCE WITH ST. JUDE (MAS) EXPERIENCE

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**Background and Aims:** Aside from supporting the development of healthcare infrastructure and resources within the community, producing local capacity in healthcare involves investing in the education and training of healthcare professionals within the local community. In 2021, we offered the IHI Improvement Coach Program to 100 healthcare professionals from hospitals treating childhood cancer in 5 countries from Latin America, 53 graduated. Based on developed skills, self-motivation, and availability, we selected 11 graduates to be enrolled as coaches for the 2nd MAS Collaborative, the olden Hour, a quality improvement collaborative. Each coach mentors 3-5 QI teams, composed by 4-6 members, to implement the Golden Hour. We aimed to explore local QI coaches' experiences, approaches and strategies to gain an in-depth understanding of factors that lead to a successful implementation and ownership of a QI project.

**Methods:** We conducted semi-structured virtual interviews with the 11 coaches to explore approaches taken to conduct their coaching sessions, successful implementation strategies, and most common encountered barriers. Data were analysed using thematic analysis.

**Results:** Although there was heterogeneity in the approaches to coaching QI teams, the analysis of the 11 interviews yielded three categories as the most effective: goal setting, data-driven action plans, and con-

tinuous improvement cycles. The prevalent barriers to coach still rely on generating key questions for producing changes and methodology adoption. Additionally, and very relevant, coaches expressed having found fruitful and rich knowledge to apply and transfer to their coachees as they understand and know the needs, wishes and demands of local patients and families.

**Conclusions:** Exploring the in-depth experiences of local QI coaches after completing training suggests that communities can become more self-sufficient and less reliant on external support. Training local QI coaches can lead to a more robust healthcare system overall; and, more importantly, sustain improved healthcare outcomes and accelerate QI project ownership.

EP145/#1177 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

### IMPACT OF IMPLEMENTING A QUALITY IMPROVEMENT MODEL FOR OBTAINING BLOOD CULTURES BEFORE ANTIBIOTICS ADMINISTRATION IN HEMATO-ONCOLOGICAL PEDIATRIC PATIENTS

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**Background and Aims:** Background Infectious diseases are the main complication in hemato-oncology patients, and are associated with high mortality. Febrile neutropenia is the most frequent situation, with bacteremia identified in up to 25%. Sensitivity of blood cultures is influenced by type of microorganism, sample volume, time of extraction, and previous antibiotics. Early antibiotic de-escalation, reduction of adverse effects and reduced emergence of resistance are all benefits of identifying causative microorganism. Aim To evaluate the impact of the standardization of samples for blood culture in all the hemato-oncology patients and neutropenic hemato-oncology patients at Hospital Infantil Teletón de Oncología in a lapse of 12 months (April, 2022-March, 2023), and to compare these against a retrospective cohort (November 2020-March, 2022).

**Methods:** Method We used a before-after comparison of the Innovative Series Model developed by the Institute for Healthcare Improvement and a certified quality improvement competency program. We compared between cohorts the proportions of: (1) blood cultures detected in all hemato-oncology patients; (2) blood cultures detected in neutropenic hemato-oncology patients; (3) blood culture

contamination rate, and (4) microorganism detection time; lastly, we made a review about antibiotic requirement.

**Results:** We observed an increment in proportion of blood cultures detected in hemato-oncology patients (4.2% to 9.01%;  $p < 0.001$ ). This increase was most noticeable among neutropenic hemato-oncology patients (7.81% to 23.29%;  $p < 0.001$ ). Adherence to antibiotic administration in the first hour of fever detection raised (71.6% to 86.5%;  $p = 0.035$ ). Blood culture contamination rate were 0.33% and 0.58%. There was no significant difference between detection time of microorganisms, as well in antibiotic administered.

**Conclusions:** We successfully implemented an algorithm for taking blood cultures in febrile hemato-oncology patients as an improvement model without delaying the timely administration of antibiotics in less than 60 minutes.

EP146/#1449 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

#### IMPLEMENTATION OF THE QUALITY IMPROVEMENT MODEL FOR NURSING TRAINING IN THE TIMELY ADMINISTRATION OF ANTIBIOTICS TO HOSPITALIZED PEDIATRIC HEMATO-ONCOLOGIC PATIENTS WITH FEBRILE NEUTROPENIA

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**Background and Aims:** Febrile neutropenia is a life-threatening oncologic emergency in pediatric hematological patients (PHOPf). According to Cieza Tapia (2017), nursing staff is essential for attention, care and prevention of this complication. Early administration of antibiotics in PHOPf in a time not more or equal to sixty minutes from arrival at the emergency department, has been shown to reduce the incidence of sepsis, septic shock and mortality, with the role of nursing being paramount to achieve this. Knowledge gaps exist among nurses who assist PHOPf to address them in the established time. **Aims** Evaluate the results of training implementation for nurses attending hospitalized PHOPf regarding antibiotic Administration Times from Indication (ATI) during a 7-month period.

**Methods:** We performed a before-after comparison. To develop improvement, we applied the Innovative Series Model developed by the Institute for Healthcare Improvement and, a certified quality improvement competency program. From June to December 2022, we tested two different approaches using 3 Plan-Do-Study-Act (PDSA) cycles to conclude inpatient nursing staff training. We applied a twenty-item assessment tool including concepts of febrile neutropenia, bacteremia, vascular access, blood cultures, antibiotic preparation and administration to 85 nurses and 3 paramedics before and after training. For the analysis of nursing skills, ATI was evaluated.

**Results:** We performed 177 assessments and observed 75 PHOPf events before training, the average in nursing staff assessment was 6.9% (IC95: 6.7-7.1) and after applying the PDSA cycles in training, it was 9.1% (IC95: 9-9.2),  $p < 0.001$ . Before training the ATI had an average of 31.34 minutes (41 events) and after it was reduced to an average of 15.82 minutes (34 events) for hospitalized PHOPf.

**Conclusions:** The implementation of training with evaluations of acquired knowledge, using the Improvement Model, decreased antibiotic administration times in PHOPf.

EP147/#1072 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

#### ID-FACTORY WITH PROFESSIONALS IN THE PEDIATRIC ONCOLOGY: TO SHARE EXPERIENCES AND STRENGTHEN OUR KNOWLEDGE TO IMPROVE CARE

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**Background and Aims:** The Princess Máxima Center is organizing a two-day nursing symposium in June.

The first day will be dedicated to presentations closely linked to SIOP themes: nursing leadership, nutrition, pain and palliative care, adolescents & young adults (AYAs) and late effects. The second day is an interactive day to inspire nurses and paramedic, network and innovate together: a great opportunity to shape and shape developments in pediatric oncology. The goal is to achieve continuous improvement and innovation in the nursing profession together.

After all, excellent care for children and parents requires increasing expertise and knowledge.

With the ID-Factory, we generate practical ideas, which nurses and paramedic can apply tomorrow in their own hospital or work setting.

**Methods:** We select 5 themes/ challenges for ID factory:

- THE care innovation in pediatric oncology (think about moving the patient in care, care at home, digitalization in care)
- Directing role of parents
- A challenge on how evidence-based you can work in your department to doing vpk research
- Cultural challenges in the care of the international patient. Cross-pollination occurs between professionals.

Together they create good ideas that are applicable in pediatric oncology.

Together they present the best proposal to a jury After fine-tuning, an innovation proposal emerges in a short time, which can then be further developed/implemented.

**Results:** After the ID-factory, the practical ideas and innovation proposals will be shared at SIOP International as a joint result of the group of nurses from Europe. We would like to share these proposals as a best practice in a presentation, showing the representation of various countries from Europe. We make visible what networking brings and what enthusiasm and motivation this gives to each other.

**Conclusions:** The creative workshop brings professionals together. Nurses from participating centers will get to know each other better and benefit from each other's expertise

EP148/#1265 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

### THE PROJECT IMPACT OF CHILDHOOD AND ADOLESCENTS CANCER FIGHT IN SOUTHERN HIGHLAND ZONE OF TANZANIA: NURSES, ROLE PLAYERS

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**Background and Aims:** Cancer has been a significant problem and global threat to public health with progressive increase of incidence in most of Low and Middle Income. Early detection of cancer in all settings is the fundamental strategy of improving survival for many types of cancers. Tanzania like any other low-income countries, nurses account for more than 60% of the healthcare work force and are frontline workers available at all primary and secondary health facilities. Tanzania National Nurses Association (TANNA) implemented the project of Childhood and Adolescents Cancer Fight in Southern Highland Zone of Tanzania through building capacity to 152 nurses on detection of early warning signs of childhood and adolescents' cancer to 152 nurses, train 16 mentors and conducting community awareness campaign. Evaluation of the project was conducted to determine the project impact for sustainability.

**Methods:** The evaluation was conducted through interview and observation of the project impact to trained nurses, community and stakeholders by the use of developed evaluation tool. The observation focused on project outcome to trained nurses, community awareness and implementation of project sustainability plan. The data were collected and analyzed by using REDCap.

**Results:** Majority (85%) of evaluated nurses demonstrated competence in conducting comprehensive assessment in identifying early warning signs of childhood and adolescents' cancer and 90% provides health education to the community which increased health seeking behavior. Through advocacy to the ministry of health, early identification warning signs of childhood and adolescents' cancer is integrated in the diploma in nursing curriculum and call for the need of expanding scope of nurse in managing Non Communicable Diseases

**Conclusions:** The project has shown significant positive impact in improving nurses' competence in identifying early warning signs of childhood and adolescent cancers. It has further demonstrated the demand for scaling-up and expansion of the project countrywide.

EP149/#1529 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

### NO PLACE LIKE HOME? FOCUSGROUPS IN CHILDREN AND PARENTS ON THE BEST PLACE FOR PEDIATRIC ONCOLOGY CARE

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**Background and Aims:** In the Netherlands, around 600 children are newly diagnosed with cancer each year. Chemotherapy, backbone of many treatment protocols, is usually administered in hospitals. Supportive care such as tube-feeding- and antibiotic care are administered at home, by pediatric homecare nurses. In literature little is known on what children and parents think of the best place of pediatric oncology care. Their opinion is important in search for optimal care for this group.

**Methods:** A semi-structured questionnaire was developed to ask children > 12 years and parents of children < 12 years their opinion about this topic. Parents were invited to participate in on-line focusgroups. Children > 12 years were asked to participate in individual interviews by an independent moderator. Parents and children were recruited among all paediatric oncology patients.

**Results:** Eighteen parents were included for 3 focus groups, each containing 6 parents. Group 1 did not receive homecare, group 2 already received homecare, and group 3 had children who had finished active treatment < 1 year. 13 children were included and interviewed. Ninety percent of the parents and all the children stated that homecare would improve their quality of life. Parents were more reluctant than children, because of safety and quality aspects especially parents of children who had finished their treatment. Parents who had no experience with homecare, were most interested in homecare and saw the least restrictions. Children felt strongly that their care could be transferred to their home since it would allow them more valuable time outside of the hospital

**Conclusions:** The majority of parents and patients are in favor of transferring part of pediatric oncology care to the home setting, if safety and quality of homecare is guaranteed. Possibilities on what care to transfer will be discussed in the broader homecare working group appreciating the wishes of children and parents.



EP150/#1792 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

### PERCEIVED HOSPITAL QUALITY IMPROVEMENT CAPABILITY AND CAPACITY TO SUSTAIN PEDIATRIC EARLY WARNING SYSTEMS IN LATIN AMERICAN PEDIATRIC ONCOLOGY HOSPITALS

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**Background and Aims:** Quality improvement (QI) strives to improve care and clinical outcomes for patients. Without sustaining effective, evidence-based QI interventions, the improved patient outcomes from their implementation can be lost. This study explores the relationship between QI capabilities in resource-variable hospitals in Latin American countries and the relationship to capacity to sustain Pediatric Early Warning Systems (PEWS), an evidence-based intervention to improve early identification of clinical deterioration in pediatric oncology patients.

**Methods:** This is a cross sectional study of Latin American pediatric oncology centers implementing and sustaining PEWS. Clinical staff in multiple roles working across ward, Intensive Care Unit (ICU), and other care settings completed the Clinical Sustainability Assessment Tool (CSAT) a valid and reliable measure of sustainability capacity. Results were calculated by averaging items within each domain and averaging each domain score for the overall capacity score. Participants also answered a subset of questions from the *Change Process Capability Questionnaire*, a QI scale. Both the CSAT and QI scores were assessed using a 5-point Likert scale, with 5 representing high capability or capacity.

**Results:** We received responses from 1,039 clinical staff at 51 pediatric oncology centers in 18 Latin American countries implementing and sustaining PEWS. The Overall CSAT score mean was 4.23 (SD = 0.58) and the overall quality improvement score mean was 4.19 (SD = 0.67). Centers with higher quality improvement capabilities had a higher capacity to sustain PEWS. The correlation between overall CSAT score and total QI score was 0.73 ( $p < 0.001$ ).

**Conclusions:** We describe an association between higher perception of QI capability and higher clinical sustainability score, suggesting capacity for QI may impact intervention sustainability—a relationship that should be explored in future work. This work demonstrates a high capacity to sustain PEWS and offers further evidence for scale-up of PEWS to improve outcomes of pediatric oncology patients.

EP151/#826 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

### USING QUALITY IMPROVEMENT METHODOLOGY TO IMPLEMENT MULTIDISCIPLINARY DAILY ROUNDS IN A PEDIATRIC ONCOLOGY UNIT IN MEXICO: IMPACT ON EFFICIENCY AND PATIENT AND STAFF SATISFACTION

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**Background and Aims:** Multidisciplinary daily rounds (MDR) is a key strategy for real-time communication amongst healthcare team members, patients and families. MDR facilitate delivery of high-quality cancer care by ensuring protocol/guideline use; prioritization of daily tasks/goals of care; discharge planning; and reduction of length of stay (LOS). MDR remain a challenge in low-and middle-income countries given limited human resources, time-constraints and excessive workloads. Our pediatric Oncology Unit at Hospital General-Tijuana was inaugurated in 2008, however MDR were not established.

**Methods:** In September 2019, we used quality improvement (QI) methodology, including Ishikawa and Key-Driver diagrams, to implement MDR at our unit. Our GLOBAL Aim was: Improve care delivery, communication, and patient/staff satisfaction. A multidisciplinary team (pediatrics, oncology, nursing, hematology, infectious diseases, psychology, nutrition) lead by a pediatrician was formed. Roles and responsibilities were assigned. Our SMART Aim was: Increase adherence to the daily-goals sheet to >80% by March 2020. A goals of care sheet was created. Our outcome measure was adherence to the daily-goals sheet. Our process measures were daily team attendance and rounding duration. Balance measures included staff and family satisfaction. We completed 3 Plan-Do-Study-Act (PDSA) cycles: 1) In-person pre-COVID (September 2019-March 2020); 2) Hybrid during COVID (April 2020-March 2022); and 3) In-person post-COVID (April-December 2022).

**Results:** Adherence was 55% in PDSA1, 89% in PDSA2, and 91% in PDSA3. Team attendance was 85% in PDSA1, and 100% in PDSA2-3. Rounding duration was 13min/patient in PDSA1 and 9min/patient in PDSA3. Staff and family satisfaction improved from 42% and 57% pre-implementation to 100% and 93% post-implementation, respectively.

**Conclusions:** We successfully implemented MDR, improved communication and collaboration, and surpassed and sustained adherence to planned daily goals of care. Attendance and satisfaction were high and not influenced by COVID. Rounds duration was not increased post-MDR implementation. Next steps include measuring MDR impact on LOS and consistency of care delivery.

EP152/#1446 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

### THE IMPACT OF DRESSING CARE ON THE DETACHMENT OF DRESSING MATERIAL ON TUNNELED CUFFED CATHETERS IN A PEDIATRIC HEMATO-ONCOLOGY SETTING

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**Background and Aims:** Until September '21, nurses at Pediatric Hemato-Oncology (PHO) of Ghent had a self-developed dressing care to protect the tunneled cuffed catheter. This dressing care was not conform to standards, as the insertion site was not observable. Therefore, we changed the dressing care to a weekly changed, fully transparent upward-facing split dressing with additional fixation by placing strips in an up-and-under curling order. During six months, we optimized several steps in the dressing care. In March '22, we aimed to define crucial steps that had an influence on the good fixation of the IV dressing to be left in place for 7 days.

**Methods:** Within 34 patients, 49 dressings were evaluated.

**Results:** In 7 out of 49 dressings, the split was not facing upwards. In 2 out of these 7 patients, the dressing detached. This is twice as many as the dressings with the split upwards (14% vs 29%). If the thickened part of a double lumen catheter was not under the dressing 66% of the dressings detached. In 4 out of 49 patients, the curl had moved slightly by traction, without traction on the catheter insertion site. Stripping injuries were found in only 3 dressing changes. Shortening the strips did not affect dressing loosening.

**Conclusions:** The place of the dressing split, the position of the thickened part of the double lumen catheter and the strips in an up-and-under curling order are important steps in dressing care that should be well considered to avoid detachment of the dressing. To avoid stripping injuries we added the advice to wait for the disinfectant to evaporate before applying the dressing and to modulate the dressing well without tension. These crucial concerns are taken into account during nurse training.

More research is needed to evaluate Central Line Associated Blood Stream Infections, accidental removals and integrity problems

EP153/#722 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

### BUILDING A GLOBAL NURSING FELLOWSHIP PROGRAM: THE BOSTON CHILDREN'S HOSPITAL EXPERIENCE

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**Background and Aims:** In 2015, Boston Children's Hospital launched the Global Nursing Fellowship in Health Service and Delivery, the first pediatric nursing fellowship of its kind. This collaborative effort between the Global Health Program (GHP) and the Department of Nursing has a mission to reduce the burden of childhood illness in areas with the greatest need through collaborative partnerships with pediatric nurses, clinicians and organizations, modelling excellence in care delivery, education, and research.

**Methods:** Three nurses/advance practice nurses (APNs) are selected annually for the two -year fellowship, which offers education and mentored experiential learning in the development, management and evaluation of global health initiatives aiming to improve child health in resource limited settings. The fellows are granted funding and protected time to pursue global health projects within their subspecialties. Monthly seminars focused on relevant topics related to global health are held, including clinical skills, quality improvement, research methodology and educational strategies. The nursing fellowship director works collaboratively with the Chief Nursing Officer and GHP Medical Director and to develop, monitor and evaluate the program. Each new fellow is assigned a previous fellowship graduate as a mentor.

**Results:** Despite a one-year pause in 2020 due to the pandemic, eighteen nurses/APNs have graduated from the fellowship program since its inception. Nursing and multidisciplinary partnerships have been formed in over thirteen countries, with global initiatives underway involving many pediatric nursing subspecialties.

**Conclusions:** A global nursing fellowship is a unique opportunity to share best practices in clinical care, education, multidisciplinary collaboration and research among nurses from diverse settings with varied resources. Future directions include developing metrics to measure fellowship outcomes, and increase opportunities for dissemination of global nursing efforts.

EP154/#595 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

### NUTRITIONAL MONITORING ON PEDIATRIC WITH NASOPHARYNGEAL CARCINOMA (NPC) AND GASTROSTOMY FEEDING TUBE: WHAT THE NURSE CAN DO?

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**Background and Aims:** Children with palliative care needs present changing challenges in nutritional care as their disease progresses. Nasopharyngeal carcinoma (NPC) is a common tumor of head and neck region but the incidence NPC is quite low in younger age group. Although rare, NPC is one of the most common

cancers with nutritional problems among children. This article was aimed to report challenging of nutritional care and monitoring on pediatric NPC with gastrostomy feeding tube and palliative care.

**Methods:** **Methods** We report a case of a 12-years-old boy with stage IV of NPC and palliative care. He has large mass of NPC that obstructs the airway and can not get nutrition through oral or nasogastric intake. The doctor decided to free the airway obstruction with a tracheostomy and provide nutrition through gastrostomy feeding tube.

**Results:** **Result** The first day of post-gastrostomy care, parents are still confused about the care and administration of gastrostomy. Nurses provide gastrostomy care and nutritional monitoring through gastrostomy cannot be given yet. The second day of treatment is still being monitored because there is a problem with the gastrostomy. On the third day nutrition through a gastrostomy feeding tube was given and nurses provided education to parents. On the sixth day, parents can provide nutrition through a gastrostomy feeding tube properly and are still under the supervision of a nurse. The patient's nutrition can be provided through a gastrostomy feeding tube.

**Conclusions:** **Conclusion** Nurses are in an ideal role to provide pediatric palliative care at the bedside, serve as educators to the parents and family to take care their child at home, and also as supporter to the parents, family and community.

EP155/#676 | **Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project**

#### PARENTAL PERSPECTIVES OF IMPACT OF SIDE EFFECTS OF CHEMOTHERAPY ON CHILDREN WITH CANCER AT A PAEDIATRIC ONCOLOGY UNIT IN GHANA

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**Background and Aims:** Chemotherapy is the bedrock of childhood cancer treatment. Parents play essential roles. Negative parental perception of treatment side effects can lead to missed or interrupted treatment with attendant poor outcomes. The study aim was to determine parental perspective of the impact of side effects of chemotherapy on children with cancer at the pediatric oncology unit (POU) of the Korle-Bu Teaching Hospital (KBTH), Accra, Ghana.

**Methods:** Cross-sectional study using a questionnaire administered to care givers of children with cancer receiving treatment at the POU, KBTH.

**Results:** **RESULTS** Thirty (30) caregivers were included in the study; majority (90%) were female. Of the children, about a quarter (20%) were below 5 years and over half (57%) were female. The most common diagnosis (47%) was acute lymphoblastic leukaemia. All the children were still undergoing treatment, with almost two-thirds (63%) diagnosed within the past 14 months. The most common side-effects experienced were hair loss (80%), febrile illness/infection (77%) and loss of appetite (73%). Notably, half (50%) also experienced darkening of palms/soles and behavioural changes. A large majority (60%)

experienced increased appetite and vomiting (63%). Worryingly, about a quarter (23%) of parents reported that people behaved differently around their child due to visible treatment side-effects such as hair loss. A similar proportion (27%) also said that their child had complained about feeling "different" due to treatment side-effects. One parent (3%) admitted to having with-held treatment on their own volition due to perceived side-effects. Almost all (97%) felt they had been provided with adequate information regarding side-effects prior to treatment. About one-in-four (27%) however felt they had not received enough support to manage them when they occurred

**Conclusions:** Even though initial counselling prepares parents for side-effects of treatment, there is a need to provide ongoing psychosocial and medical support to both parents and the children throughout the course of treatment.

EP156/#667 | **Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project**

#### PSYCHOLOGICAL SAFETY IN CARING FOR CHILDREN AND ADOLESCENTS WITH CANCER

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**Background and Aims:** Working with children and adolescents with cancer can be associated with work-related burnout. Even though children with cancer are increasingly surviving their disease, the work is psychologically challenging as the treatment courses extend over many years and thus imply that the staff gain in-depth knowledge of the family. Sick leave in the Department for Children and Adolescents with Cancer and Blood Disorders was 8.9% in 2022, which is above the Capital Region's target of 4.3%. A good working environment is associated with better patient safety. Furthermore, interprofessional teams with high psychological safety are more efficient and have greater job satisfaction than teams with low psychological safety.

**Methods:** We facilitated two interprofessional workshops with a focus on psychological safety and interprofessional collaboration. A total of 82 healthcare professionals participated representing five different professions; Doctors, nurses, educators, secretaries, and service workers, covering the four different sections in the overall department; bed ward, out-patient clinic, day care unit and a clinical research unit. Participants anonymously completed the Danish version of Edmondson's 'Psychological Safety Scale' before the workshop and again 3 months later.

**Results:** The pre-measurement of psychological safety showed overall high psychological safety, exemplified by the fact that 87.7% of the participants strongly disagreed or disagreed that you are often

blamed if you make a mistake. 87% strongly disagreed or disagreed that it is difficult to ask others in the team for help. Post measurement results are pending as the follow up questionnaire has been sent shortly prior to the abstract deadline. Results will be presented.

**Conclusions:** With a continuous, structured focus on psychological safety, we can create psychologically safe interprofessional teams with increased job satisfaction and we may increase patient safety for children and adolescents with cancer and blood diseases.

EP157/#462 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

PARENTS' PERCEPTION OF THE CHILDHOOD CANCER CENTER'S MOBILE APPLICATION CHILDHOOD CANCER APP AS AN INFORMATION TOOL TO PROMOTE HEALTH LITERACY

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**Background and Aims:** A cancer diagnosis on a child requires a lot of information and knowledge about the diagnosis and its side effects, which places demands on the parent. Understanding information about your child's condition can be a challenge. E-health is becoming more common, which in turn leads to patients finding relevant information easier and becoming more involved in their care. With relevant and easily accessible information, health literacy increases. As a specialist nurse in pediatric care, one of the tasks is to promote health literacy and to personalize the information to the individual and to ensure the individual's receptivity to information. The Childhood Cancer App has been developed so that parents can easily access relevant information about their child's diagnosis. The aim of the study is to describe parents' perception of the Childhood Cancer Center's mobile application The Childhood Cancer App as an information tool to promote health literacy.

**Methods:** A quantitative method with a consecutive sample. A self-constructed online survey is applied as it has been difficult to find a questionnaire that is aimed at the purpose of the study.

**Results:** The results showed that the Childhood Cancer Center's mobile application The Childhood Cancer App was appreciated and needed as it increased trust and security among parents at home. This was demonstrated by the relatively frequent use of the Childhood Cancer App and the fact that parents found the app content to be easy to understand, easily accessible, useful and a good complement to the oral information.

**Conclusions:** The childhood cancer app supports the parent to feel confident in the self-care of their child at home. The app has proven to be important for these parents in their everyday lives to find evidence-based information and follow what is happening inside and outside the hospital. The childhood cancer app is considered useful and easy to understand according to those parents.

EP158/#789 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

SAQI MODEL "SAFELY ADMINISTERED QUALITY INTERVENTIONS TO PEDIATRIC ONCOLOGIC PATIENT"

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**Background and Aims:** Background: It was about the creation and development of a Integrator Model for care, which is called: "Safely Administered Quality Interventions (SAQI) in pediatric oncologic". Children hospitalized with cancer have high risk of clinical deterioration during their hospitalization as a result of cycles of cancer treatment. Early identification of clinical deterioration in hospitalized patients encourage to reduction in mortality. This model considers both the uniqueness and the diversity of the care process, complementarities and antagonisms present when it is developed in the hospital setting, inside a Pediatric Hemato -Oncology Patient Care Unit of the Mexican National Health System. Objectives: Generate an Integrative Model that favors quality interventions safely administered to pediatric oncologic patient in a critical health situation, with the use of validated instruments.

**Methods:** According to the methodological perspective, it was quantitative; design type is transverse mixed with a predominant focus, QUANTI, which, due to its research design, was mixed.

**Results:** They correspond to the research work carried out in the pediatric Hemato -oncology hospitalization unit and the interpretation of quality emerged from the qualitative analysis of the discourses recovered from the questions: What is the quality nursing interventions for you?, Do you consider that the instruments used in your hospital favor the quality of care?, and why?, from which the Ethical Dimension of Quality in Nursing Interventions arose, which grouped three categories with their six subcategories.

**Conclusions:** The care of the oncologic pediatric patients, it has an its essence in ethics and deontology of the nursing. Taking care of oneself and of the others is an ethical, aesthetic and ontological act, which promotes the development of the person, favoring the integration of knowledge in care models.

EP159/#823 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

INADVERTENT INTRATHECAL AND INTRAMUSCULAR INJECTION OF VINCRISTINE AND ROUTE-CAUSE ANALYSIS OF THE MEDICAL ERROR: TIME TO RETHINK OF SYSTEMATIC PREVENTION

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**Background and Aims:** To Err is Human, medical error is one of the 10 leading causes of death in the United States. The treatment for acute lymphoblastic leukemia (ALL) required different routes of chemotherapy administration, including intravenous (IV), intramuscular (IM), and intrathecal (IT) administration. Vincristine is a vinca alkaloid intended for IV use only. However, over six decades vincristine misroutes have still occurred. To establish the systematic prevention, we demonstrate 3 cases of inadvertent vincristine injection misroute (2 intrathecal, 1 intramuscular) and performed route-cause analysis of all events.

**Methods:** We performed route-cause analysis of previously reported of two fatal cases of accidental intrathecal vincristine administration and recently inadvertent intramuscular injection at our institute.

**Results:** The route-cause analysis revealed that all unintentional vincristine-related incidents in our institute were the result of misidentification during the administration procedure by unexperienced physician. The “time-independent” method was established since 2016 as a rule to separate intrathecal chemotherapy administration as a separate procedure that should be performed only after IV or IM chemotherapy. Several methods, such as visual-color labeling for different routes and separate packaging and delivery of chemotherapy, have been used. However, the gap still exists in 2020 we had the incident of inadvertent intramuscular of vincristine in a 4-years old girl with ALL. We found that vincristine was prepared in a 3 mL syringe that resembles a L-asparaginase syringe or other drugs. Hence, as suggested by earlier research, we recommend to prepare vincristine in a 10-mL syringe or small infusion bag instead.

**Conclusions:** The “Five Rights of Medication Administration Principle” has been taught to nurses for years to ensure the right drug, the right dose, the right route, and the right patient at the right time. This knowledge should be applied by all health care personnel. Systematic prevention is needed to minimize the gap for human error.

EP160/#725 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

#### PAEDIATRIC ONCOLOGY NURSING SURVIVAL KIT

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**Background and Aims:** There is often a steep learning curve for novice nurses deployed to the paediatric oncology ward. While they are assigned to a preceptor, they often express difficulty in retaining what was taught. This quality improvement project aims to provide a tool to increase information retention, and reduce the stress experienced by nurses who are new to the paediatric oncology unit.

**Methods:** The Plan-Do-Study-Act cycle was used to guide the project. The team analysed the problems and observed that nurses often kept notes on their mobile phones. Hence, the team developed the “Paediatric Oncology Nursing Survival Kit” as a visual learning tool, tapping on technology to provide essential nursing care information that could be easily accessed and navigated. Expert nurses, who were involved in precepting new nurses, were consulted to determine essential topics for inclusion, and continuous engagement was done to gather their feedback on the created content. The kit was then distributed to 10 newly recruited nurses, and pre- and post-test was conducted to evaluate the kit’s understandability, the nurses’ stress levels, and screen for information retention.

**Results:** With the kit, participants mean score increased from 4 to 8.4 out of 10 in a knowledge test and were able to answer the questions 75% faster than previous. All of the participants strongly agreed that the kit is easy to use and has helped them to pre-emptively prepare for procedures without relying on their memory. The stress level of the participants has also been reported to reduce by 40% after the introduction of the kit.

**Conclusions:** The kit was easy for nurses to understand and use, and has helped to increase new nurses’ preparedness, improve information retention and reduce their stress levels. More intermediate topics could be added to the kit, to expand its reach to all levels of nurses working in the unit.

EP161/#1059 | Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project

#### NURSING LEADERSHIP; TAKE RESPONSIBILITY IN YOUR DAILY NURSING WORK, TO INFLUENCE THE NURSING PROFESSION

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**Background and Aims:** Nurses are the largest profession within the hospital, but often have too little influence on the care processes. It is important that nurses take responsibility for the development of their profession. This allows them to influence the quality of care and work processes in the organization. More nursing leadership is more nursing control.

**Methods:** The Princess Maxima Center has been offering a 6-day nursing leadership training since 2022. Every day started with a motivational speaker. Personal leadership has been discussed, how to influence someone else. Coaching was given about communication techniques and lessons about change management. Each participant has taken on a change assignment in which guidance was offered by professionals. In addition, intervision meetings were offered for the development of personal learning goals.

**Results:** The nursing leadership training has provided tools on how to show more leadership in daily practice. The change assignment as a result of the training involves the collaboration of nurses in different departments in our center. Good collaboration is required for good

care in all departments and to project clarity. In conversation with nurses from the various departments, we looked at what is going well in the collaboration, and what could be improved. These conversations have been analyzed and the outcomes are discussed with the managers. An improvement plan for the collaboration is made with them. Good collaboration has a unifying power, reduces work pressure and leads to better care for patients.

**Conclusions:** It is important that nurses are given more control, and take responsibility for the development of the nursing profession. We would like to share these experiences and knowledge that we have gained during the leadership training with our fellow nurses at the SIOP.

EP162/#1036 | **Poster Topic: AS04 Nursing/AS04.c Quality Improvement/Practice Project**

### PREVALENCE AND FACTORS ASSOCIATED WITH TREATMENT ABANDONMENT OF PEDIATRIC CANCER PATIENTS WITH SOLID TUMORS AT UGANDA CANCER INSTITUTE

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**Background and Aims:** Treatment abandonment is a major cause of treatment failure and poor survival outcomes in children with cancer in low and middle-income countries. Treatment abandonment was a lapse of 4 weeks or longer in treatment. This study aimed at determining the prevalence of treatment abandonment and the associated factors in pediatric patients with solid tumors at Uganda Cancer Institute between January 1st and 31st December 2021.

**Methods:** A total of 76 pediatric patients below 18 years who were histologically diagnosed with solid tumors between January 1st and 31st December 2021 were analyzed retrospectively with data extracted from medical records. Data was analyzed by Qui-square.

**Results:** Data from 76 children diagnosed with solid malignant tumors was analyzed of which 55.3% were female, the average age in years was 8 years (SD= 5.3) and 34 (44.7%) children abandoned treatment. The death rate was 35.3% and 50.0% escaped from the hospital ( $p > 0.001$ ). Among the participants enrolled, Wilms tumor (25.0%), osteosarcoma (19.7%), and RMS (10.5%) were the most common tumors. Of the children who abandoned treatment, 73.5% had peasant caretakers ( $p = 0.004$ ). Most children who abandoned treatment were in the late stages of III (25%) and IV (60.55%) ( $p = 0.039$ ). Most participants received their first cycles of chemotherapy (92.1%) however, 23.5% did not go for surgery, and 29.4% did not receive radiation. Only 52.6% received their complete course of treatment. The survival rate was high among patients who completed treatment at 30.3% ( $p > 0.001$ ).

**Conclusions:** The prevalence of treatment abandonment among patients with solid tumors was high and closely related to socio-demographical factors. Treatment outcomes could be substantially improved by strategies that help prevent abandonment of therapy for example patient tracking and follow-up to improve adherence based on these results particularly for vulnerable populations.

EP163/#1506 | **Poster Topic: AS04 Nursing/AS04.d Baseline Nursing Standards**

### TIMELY IDENTIFICATION OF RECURRENT FEBRILE NEUTROPENIA IN PEDIATRIC CANCER PATIENTS IN THE INITIAL NURSING ASSESSMENT

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**Background and Aims:** Pediatric cancer patients are at risk of presenting neutropenia and fever as a complication associated with chemotherapy. Patients may present more than one event of neutropenia and fever during their treatment, and this is an important factor to consider in the nursing assessment in the emergency room.

**Methods:** Retrospective cohort from 2020 to 2022 of children between 0 and 18 years of age with neutropenia and fever admitted to the emergency department of a pediatric cancer hospital. The results were calculated by averaging the items.

**Results:** We identified 211 febrile events in this period that occurred in a total of 99 patients. The average number of events presented was 2.13 events in two years (in a range of 1 to 7 events). 46% of the patients presented only one event of neutropenia and fever, 20% presented 2 events, 28% presented between 3 to 4 events, and 5% presented between 5 to 7 events. In 84.2% of the cases with repeat events, nursing timely identified the patients through their triage evaluation. In 15.7% of the events, febrile neutropenia was not suspected because it was a recurrent event.

**Conclusions:** Nursing staff must have basic knowledge of the complications associated with pediatric cancer treatment, among which the presence of recurrent febrile neutropenic events stands out.

EP164/#1638 | **Poster Topic: AS04 Nursing/AS04.d Baseline Nursing Standards**

### EATING HABITS IN CHILDREN WITH CANCER

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**Background and Aims:** Malnutrition in children with cancer is a silent emergency, hence the importance early detection for appropriate care to prevent possible consequences. Our study aimed to assess the nutritional status of children with cancer, as well as the disturbances that manifest themselves in their eating habits.

**Methods:** We conducted a cross-sectional prospective study which collected 30 children with cancer undergoing chemotherapy in the pediatric oncology unit in Salah Azaiez Institute over a period of 7 weeks from November 15 to 17 December 2021 and from 17 to 28 January 2022. We used data collected from medical records as well as responses obtained from patient interviews. A dietary survey was carried out. The analysis of the results of the food survey used BILNUT software. Anthropometric measurements of patients were taken and assessed using growth charts.

**Results:** The average age was 10.8 years with a male predominance. The osteosarcoma was the most common cancer. No patient benefited from nutritional education. Thirteen percent of patients were underweight, 13% were delayed in growth and 33% had a lower BMI. Eighty percent of children had lost weight, including 53% more than 10% of their total weight from the start of treatment. Overall, malnutrition was present in 70% of patients. All patients had a change in their eating habits and 74% an intake less than their needs. The duration of disease progression was the only factor contributing to undernutrition in the study multivariate.

**Conclusions:** It is necessary to establish a nutritional strategy to manage children with cancer and nutritional education is mandatory

EP165/#1144 | Poster Topic: AS04 Nursing/AS04.d Baseline Nursing Standards

#### FOUNDATION TRAINING FOR NURSES WORKING IN PAEDIATRIC ONCOLOGY UNIT AT OLA DURING CHILDREN TEACHING HOSPITAL FREETOWN SIERRA LEONE: IMPLEMENTATION EVALUATION

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**Background and Aims:** Sub-Saharan African nursing network developed pediatric oncology foundation training package to nurses new in caring children with cancer relevant to Sub-Saharan Africa setting based on SIOP baseline standards for paediatric oncology nursing. The network which is affiliated to SIOP Africa and supported by World Child Cancer, UK conducted the 'Train of Trainers (TOT)' workshop in Ghana November, 2021 which aimed at capacitating nurses to deliver the training to nurses working at pediatric Oncology unit at Ola During Children Teaching Hospital Freetown, Sierra Leone.

**Aim:** To evaluate the outcome of the implemented pediatric foundation training to nurses working at Ola During Children Teaching Hospital Freetown, Sierra Leone.

**Method:** A cross sectional survey was conducted through administered self-administered questionnaire. Convenience sampling technique to recruit nurses who attended the training in the paediatric oncology unit was used. Data were analyzed using SPSS.

**Results:** Total of 20 nurses were participated in the study. Majority (60%) of participants were new nurses in the unit. Half (50%) of participants reported improved experience. Majority (60%) of participants reported to afraid to administer chemotherapy before training while 40% of participants reported to have increased confidence of administering chemotherapy after training

**Conclusion** – Respondents indicated the foundation training programme had positive value on all the nurses that were trained and also marked an improved experience of newly qualified nurses after their post.

EP166/#967 | Poster Topic: AS04 Nursing/AS04.d Baseline Nursing Standards

#### DIFFERENCES OF OLD VS NEW ALL PROTOCOL

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**Background and Aims: Background/Objectives** In August 2022 the new protocol for treatment of children with Acute Lymphatic Leukaemia was released (AllTogether), our centre has recently started using this for patients with a new diagnosis of ALL however are still using the old protocol (UKALL) for patients who have already commenced treatment. It has been highlighted there are a lot of differences between the old and new protocol and staff are not familiar with these. We recognise this as a barrier and feel a clear, easy to follow poster showing the differences between the old ALL protocol (UKALL) and new ALL protocol (Alltogether) would be beneficial for nursing staff and educate them on the main differences as ALL is the most common cancer type we see and feel this is something that would help improve our service overall. We will also outline how each member of the multi-disciplinary team (MDT) contributes to care throughout treatment this will help educate newly qualified nurses and help signpost them to the correct member of the MDT.

**Methods: Design/Method** We will develop an educational poster showing the points identified above focusing on the main differences between the old and new ALL protocol showing clearly where each of the MDT contributes and what their specific roles are.

**Results: Results** We will implement the poster into the ward and day-care service in Lochranza, we believe this will improve nursing practice and expand knowledge on the new ALL protocol.

**Conclusions: Conclusion** From discussion with nursing staff from the ward, daycare, clinical nurse specialists and research, they agree implementing this would be beneficial for all members of the MDT. We will demonstrate our poster at one of the Thursday teaching sessions on the ward and are happy to receive any feedback from staff.

EP167/#764 | Poster Topic: AS04 Nursing/AS04.d Baseline Nursing Standards

### TRANSLATION AND CULTURAL ADAPTATION OF THE QUESTIONNAIRE "PEDSQL NEUROFIBROMATOSIS MODULE VERSION 3.0 (PEDSQL 3.0) INTO BRAZILIAN PORTUGUESE LANGUAGE

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**Background and Aims:** Neurofibromatosis type 1 (NF1) is a frequent genetic disease without drug treatment, and the quality of life of patients depends on the clinical, psychological, and social conditions.

**Objective:** Translate into Brazilian Portuguese and culturally adapt the "Scaling and scoring of the Pediatric Quality of Life Inventoryã Ped-sQLã Neurofibromatosis" questionnaire for children, adolescents with NF1 aged 5 to 25 years and their parents/caregivers.

**Methods:** The study was developed in phases: 1. Translation into Portuguese 2. Back translation to English language 3. Evaluation of the result by physicians and nurses, from several regions of Brazil 4. Pre-test: application of the questionnaire in patients with NF1. The translations were analyzed by experts and through the content validity index (CVI) and Kappa.

**Results:** The translation and cultural adaptation of the PedsQL™ NF1 questionnaire for patients aged 5 to 25 years with NF1 was performed properly, according to IVC (0.75), KAPPA (0.6) and analysts' opinion. Adjustments were necessary in the family members' questionnaire to facilitate understanding, for example, the word "worrying" was translated into Portuguese as "temer" and later replaced by "tem medo". The pre-test enrolled 46 family members aged between 28 and 54 years, median of 42 years and 42 patients aged between 5 and 25 years, median of 10 years. 5 patients with behavioral changes (autism spectrum disorder - ASD - and hyperactivity were unable to respond to the questionnaire.

**Conclusions:** The translation and cultural adaptation of the PedsQL™ NF1 questionnaire were successfully completed.

EP168/#1553 | Poster Topic: AS04 Nursing/AS04.d Baseline Nursing Standards

### PAEDIATRIC ONCOLOGY EDUCATION AND TRAINING INITIATIVES FOR NURSES. A SCOPING REVIEW

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**Background and Aims:** A number of paediatric oncology education and training programmes have been developed for nurses. This scoping review was conducted to map content, delivery methods, duration and mode of assessment for paediatric oncology nursing education and training programs.

**Methods:** A structured search strategy was conducted in the following data bases: CINAHL, Dimensions, Embase, PubMed and Scopus. Other relevant articles were identified from reference lists of included studies and through hand searching of other databases and journals. Search terms used were: paediatric oncology nursing, childhood cancer nursing, continuing education, orientation training, educational programmes, in-service training. To be included, the article had to describe a paediatric oncology nursing education programme, from any setting and published from 2012 to 2022, Extracted data included authors, year, journal, country, collaborations, project title, theory content, programme delivery methods, programme duration and mode of assessment.

**Results:** Of the 2310 articles screened, 20 articles were included in this review. Content identified for the paediatric oncology education and training programme for nurses include chemotherapy course, supportive care, paediatric oncology overview, common paediatric cancers, management of venous access devices, oncological emergencies, patient and family education, infection prevention and control, nursing considerations, communication, ethical legal issues, grief and bereavement, overview of haematology and haematological cancers. Didactic methods using traditional face to face and virtual approaches were used to deliver theory and practical content of the programmes. The duration for the trainings ranged from two hours to six weeks. Both qualitative and quantitative methods of assessments were utilised before, during and after the interventions.

**Conclusions:** This review provides guidance when planning a paediatric oncology education and training programme for nurses. However, there is a need to consider context specific issues and availability of resources when developing the programmes to ensure relevancy and sustainability. *Acknowledgements* All authors for their contributions.

EP169/#819 | Poster Topic: AS04 Nursing/AS04.d Baseline Nursing Standards

### EFFECT OF IMPLEMENTING CHEMOTHERAPY ADMINISTRATION SOPS ON PEDIATRICS NURSE'S KNOWLEDGE AND ATTITUDE AT LMC IN SUB-SAHARAN AFRICA

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**Background and Aims:** Cancer cases are on arise, it's treatment involves use of chemotherapy. It's administration is complex and high-risk process involving multidisciplinary process that requires high level of competency in its administration. At the study unit, nurses are not specialised in Cancer care but learn on job, no training or monitoring on use of SOPs. Their competency in chemotherapy administration is unknown. The study aims at evaluating effectiveness of implementation of chemotherapy administration SOP on nurses knowledge and attitude of safe chemotherapy administration. This will give opportunity to improve chemotherapy administration competency among pediatrics nurses and ensure best practices in Cancer care.

**Methods:** A descriptive multiple cross-section, semistructured questionnaire containing demographics, questions assessing nurse's knowledge and attitude of chemotherapy administration SOPs at pre and post implementation. Participants selected conveniently. Knowledge questions correctly answered scored one mark, incorrect zero mark. Attitude, items statements on 5\_point liker scale with highest score indicating positive attitude

**Results:** Data presented numerically, graphically and distribution presented in frequency tables, bar charts, pie charts, tables and graphics. Majority of participants were females of reproductive age (22\_29), diploma holders with working experience of 6 years. Ratio of nurse to patient 1:24. Nurses are knowledgeable about antineoplastic drugs (70.8%) and their perceived severity of exposure to chemotherapy still low (50%). A half of them are not acquitted with appropriate guidelines and standards for safe preparation. Over 94% do not know biosafety cabinet and 27% do not feel confident to handle chemotherapy emergencies

**Conclusions:** Despite of pediatric having knowledge about cytotoxic drugs, they expressed concern in managing ontological emergencies. There's need for more training in chemotherapy administration safety me, mentorship and collaboration with experts where they can benchmark and learn from

EP170/#241 | Poster Topic: AS04 Nursing/AS04.d Baseline Nursing Standards

#### STATUS AND CHALLENGES OF VOLUNTEER ACTIVITIES IN PEDIATRICS (INCLUDING ONCOLOGY) DURING THE COVID-19 PANDEMIC (PART 2) - FROM THE PERSPECTIVE OF VOLUNTEER COORDINATORS

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**Background and Aims:** Objective: It is considered that the COVID-19 pandemic has made volunteer activities difficult. We examined the status of such activities in pediatrics, with the aim of contributing to

the improvement of child care environments in consideration of the post-COVID-19 situation.

**Methods:** Qualitative descriptive design. We interviewed volunteer coordinators (VCs), who worked in hospitals specializing in pediatrics, using an interview guide. We organized their statements as narrative records, and categorized those representing the "difficulties faced, measures adopted, and points for improvement noted during the COVID-19 pandemic" based on similarities. Ethical Considerations: This study was conducted with the approval of the Research Ethics Committee.

**Results:** There were 7 VCs, and the mean duration of interviews was 60 minutes. The interview data were classified into 6 categories and 19 sub-categories. 6 Categories: ①[Adopting measures to enable continued sibling support], for example, handmade gifts instead of meetings. ②[Exploring activities that are feasible even during the COVID-19 pandemic] at my home or by mail. ③For [formulating strategies to continue events], we took precautions against infection, and limited the number of people. ④For [preparing for the resumption of events and volunteer activities], participate in planning meetings and conducted publicity activities. ⑤Sharing information with colleagues to increase [motivation VCs]. ⑥VCs activities were [struggling with the disadvantages and advantages of online activities]

**Conclusions:** VCs adopted various measures to enable continued volunteer activities and keep volunteers motivated during the COVID-19 pandemic. There are advantages of online usage for volunteer activities, but it is also necessary to consider individualized approaches and the burden on wards.

EP171/#851 | Poster Topic: AS04 Nursing/AS04.d Baseline Nursing Standards

#### BUILDING A PAEDIATRIC ONCOLOGY NURSING TEAM FOR SHARING OF PATIENTS IN QUETTA PAKISTAN: STRATEGIES AND OUTCOMES

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**Background and Aims:** Shortage of qualified nurses in low and low-to-middle income countries is one of many barriers in delivering quality cancer care, particularly in children. The distribution of trained health-care providers is also unequal, with the province of Balochistan, having only 0.22 registered nurses available for every 1,000 individuals. To prevent patient abandonment, Indus Hospital and Health Network (IHHN) established a Pediatric Oncology Unit (POU) in Quetta, Balochistan to deliver cancer treatment closer to patients' homes. This was achieved through public private partnership with the provincial government.

**Methods:** Nurses were hired and received one week of hands-on training at IHHN Karachi and two weeks of theoretical training in

Quetta, as outlined by established baseline nursing standards. One nurse was dedicated to infection control and two nurses nominated for clinical nursing instructor (CNI) and assistant head nurse (AHN). The nurses were incentivized to work in this remote area with flexible duty hours and transportation to and from the main city. Teleconferencing equipment was used for virtual sessions and regular educational activities were conducted including orientation, basic life support (BLS), CNE sessions and certification courses. A nurse educator from IHHN Karachi visited the POU monthly for in-person mentoring.

**Results:** The POU is operational with a team of 18 nurses and despite interventions, nurse retention was 50% after one year. Almost all (90%) of the nurses are certified for chemotherapy and medication administration and 72% are American Heart Association (AHA) certified BLS providers. All 18 nurses attended two weeks of orientation. On a daily basis, the trained nurses manage 6-8 In-patients, 8-10-day care admissions, 2-3 procedures under sedation, and 15-16 outpatient clinic appointments. Regular hand hygiene audits yield compliance of 80%.

**Conclusions:** A structured model for training and monitoring of clinical nurses for outreach units was created with effective communication and troubleshooting of challenges from the hub center

EP172/#1571 | Poster Topic: AS04 Nursing/AS04.d Baseline Nursing Standards

RISK FACTORS AND CLINICAL PRESENTATION IN THE INITIAL NURSING ASSESSMENT IN PEDIATRIC ONCOLOGICAL PATIENTS WITH SEPSIS AND SEPTIC SHOCK

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**Background and Aims:** Mortality from sepsis has decreased over time in cancer patients due to improvements in management and timely detection. However, sepsis and septic shock continue to be the main complications in this population. It is essential that nursing staff be aware of clinical data and risk factors for early identification.

**Methods:** A retrospective cohort from 2014 to 2022 of children aged 0 to 18 years with sepsis and septic shock admitted to the emergency room in a pediatric oncologic hospital. Results were calculated by averaging items.

**Results:** We identified 1738 febrile events in this period; 52 of these patients were diagnosed with septic shock and 6 with sepsis (incidence of 3.34%), with a predominance of male patients at 60.3% (n=35), adolescents at 65.5% (n=38), and leukemia 60.3% (n=35). The nursing team identified the emergency in 77.5% (n=45) based

on their initial triage assessment, including vital signs and physical examination upon their arrival to the emergency room. The most identified signs in the triage evaluation are related to hemodynamic instability including tachycardia, hypotension, and retarded capillary refill.

**Conclusions:** The pediatric cancer population is at high risk for sepsis and septic shock. The training and practice of early recognition of the initial signs by the nursing staff are essential to guarantee timely management.

EP173/#75 | Poster Topic: AS04 Nursing/AS04.d Baseline Nursing Standards

THE KNOWLEDGE OF STANDARD PRECAUTIONS AMONG NURSES IN PUBLIC AND PRIVATE TERTIARY CARE HOSPITAL LAHORE

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**Background and Aims:** To assess the Knowledge of standard precautions among nurses working at private and public hospitals. Nurses and other healthcare workers are at risk of occupational hazards in the healthcare setting. Nurses are prone to exposure with blood born infection like HIV, HCV and Hb B. Proper implication of standard precaution effectively control the hospital-acquired infections

**Methods:** A cross-sectional study was conducted among nurses in a tertiary care hospital in the private and public sectors. The duration of the study was from February 2018 to May 2018. A self-structured questionnaire was used to obtain information from nurses. Data was analyzed using SPSS version 21 and the level of significance was at pvalue < 0.05.

**Results:** The total number of respondent nurses were 201. The response rate was 98%. The results show 42.3% of the participants in this study had poor knowledge, 40.3% have average knowledge, and 17.4% have good knowledge about the standard precaution. The total number of female participants was 169 (mean knowledge score was 14.14) and male participants 32 (mean knowledge score was 16.13). The results show a significant difference between female versus male participants (p = 0.03). For private hospitals, the participants are 99 mean knowledge score was 13.45 + 3.863 and for a public hospital, nurses included 102 mean knowledge score is 14.66 + 3.167 which is greater than private hospitals. There is a significant difference between public versus private hospitals (p = 0.17).

**Conclusions:** The result indicates poor knowledge of standard precautions among nurses at a private and public hospital. It is suggested to provide training sessions on infection control with hands-on workshops. This is also suggested infection control topics should add in the Nursing curriculum and PNC should take initiative post basic one-year Diploma in Infection Control.

EP174/#1411 | Poster Topic: AS04 Nursing/AS04.d Baseline Nursing Standards

### OBJECTIVE ASSESSMENT OF STANDARDS AND COMPETENCIES OF CHEMOTHERAPY: DOES IT MAKE A DIFFERENCE IN AN LMIC SETTING?

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**Background and Aims:** Chemotherapy administration is the most challenging aspect in the field of paediatric oncology as the nurse needs to attain and maintain a high level of competency to adequately and safely administer chemotherapy. Hence the present study was undertaken to study the impact of standardized chemotherapy training and objective assessments.

**Methods:** This was an observational study carried out in department of pediatric haematology oncology at our institute from August 2021 to August 2022. A 25 pointer chemotherapy competency checklist was created with score of 1 for each step involved before, during and after administration of chemotherapy. Bedside real-time competency was done by team of head-nurse, nurse-educator and a physician. All new nurses were assessed at 4 week and 8 weeks after training. Re-enforcement training was repeated till a score of 100% was achieved. Feedback was collected at end, for usefulness of competency on a score of 10.

**Results:** Twenty new nurses were appointed in the department during study period. Of which 18 underwent chemotherapy competency and 2 nurses opted another unit. At 4 weeks, 55%(10/18) nurses cleared chemotherapy competency in two rounds. Of these, 80%(8/10) nurses had previous experience of oncology outside the unit/elsewhere and 90% had previous clinical experience in paediatrics/adult medicine. However 33% (6/18) and 11%(2/18)nurses required 3 and 4 rounds for clearing competency respectively and 25% had previous clinical experience but none had any oncology experience. At 8 weeks, majority (78%) nurses cleared chemotherapy competency in first round, followed by 22 % in second round. All nurses found chemotherapy competency useful with a median score of 9(9-10).

**Conclusions:** Objective assessment of standards and competencies helped on-boarding nurses improve practice and skill for chemotherapy administration and establish learning and performance goals for themselves. Re-enforcement training could be customised as per individual scores and ensured high-quality, patient-centred care.

EP175/#358 | Poster Topic: AS04 Nursing/AS04.d Baseline Nursing Standards

### FACTORS INFLUENCING RECOGNITION OF IMPORTANCE OF INTERACTION TO OBTAIN IA FROM CHILDREN WITH CANCER IN JAPAN

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**Background and Aims:** In this study, we examined factors influencing recognition of the importance of interaction to obtain informed assent (IA) from children with cancer.

**Methods:** Conducted a questionnaire survey. The study was approved by the Research Ethics Committee.

**Results:** Responses were obtained from 166 nurses (response rate: 53.4%) working at 54 facilities in Japan. The test of proportions (significance level: 5%) revealed significant differences between recognition of the importance of interaction to obtain IA and the following items: personal attributes, age of the child receiving care, availability of guidelines, frequency of IA, and perception of the child.

**Conclusions:** Recognition of the importance of interaction to obtain IA varied according to the age of the child receiving care and the nurse's perception of him/her. Future studies should also examine the associations with the current status of practices related to IA in preparation for model development.

EP176/#359 | Poster Topic: AS04 Nursing/AS04.d Baseline Nursing Standards

### FACTORS INFLUENCING INTERACTIVE PRACTICES TO OBTAIN IA FROM CHILDREN WITH CANCER IN JAPAN

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**Background and Aims:** In this study, we examined factors influencing interactive practices to obtain informed assent (IA) from children with cancer.

**Methods:** Conducted a questionnaire survey. The study was approved by the Research Ethics Committee.

**Results:** Responses were obtained from 166 nurses (response rate: 53.4%) working at 54 facilities in Japan. The test of proportions

(significance level: 5%) revealed significant differences between recognition of the importance of interaction to obtain IA and the following items: personal attributes (sex, age, most recent academic history), education on IA, type of facility as the current workplace, availability of guidelines, frequency of IA, and perception of the child.

**Conclusions:** The results suggest the usefulness of focusing on educational background, practical experience, and manual development as factors influencing IA-related practices, and developing models for nursing interventions with these points taken into consideration as a basis for effective practices.

EP177/#1524 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### SIGNIFICANCE OF BONE MARROW NECROSIS (BMN) IN PEDIATRIC PATIENTS WITH LEUKEMIA TREATED AT A SINGLE COMPREHENSIVE CANCER CENTRE

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**Background and Aims:** Several conditions are associated with BMN, ranging from infections and sepsis to sickle cell disease, metastatic carcinoma and hematological malignancies. However, more extensive BMN is associated with hematological malignancies.

**Methods:** This is a retrospective descriptive study of pediatric patients with acute leukemia (AL) and BMN who were diagnosed and treated at the King Hussein Cancer Center (KHCC) between January, 2016 and February, 2023. We analyzed their presenting symptoms, disease characteristics and treatment outcome.

**Results:** Sixteen patients with BMN were identified. Thirteen patients had Acute Lymphoblastic Leukemia (ALL) (12 Pre B ALL and one T ALL), two patients had AML and one was excluded due to lack of data. At presentation, there were 4 patients with Low Risk (LR), 2 with Standard risk (SR) and 7 with High Risk ALL (HR). BMN was detected at the time of diagnosis in nine patients with ALL and on day 15 of Induction in two patients. BMN was seen at the time of relapse in 2 patients with Pre B ALL and one with AML/M6. Follow up bone marrow examination on day 15 of Induction showed persistent BMN in eight patients and at end of induction (EOI) in four. BMN resulted in Risk group and/or therapy modification in 4 patients. Two patients underwent bone marrow transplantation due to persistent BMN. Four patients with Pre B ALL and the two with AML died of disease.

**Conclusions:** Patients with ALL with BMN were mostly high risk patients and required treatment modifications including BMT. Persistence of necrosis predicted dismal outcome even with the presence of negative MRD. As the occurrence of BMN in childhood leukemia is

rare, it is difficult to identify subsets of patients who will benefit from further treatment modifications. Future studies are needed to better understand the underlying genetic factors in these patients.

EP178/#1197 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### EFFICACY AND SAFETY OF PIPERACILLIN-TAZOBACTAM AND CEFEPIME AS EMPIRICAL THERAPY FOR FEBRILE NEUTROPENIC CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKAEMIA (ALL)

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**Background and Aims:** Background: Infection is a major clinical challenge in ALL treatment. Prompt administration of empirical antibiotic in febrile neutropenic patients has reduced the mortality. Both Cefepime or Piperacillin-Tazobactam has been used as empirical treatment. Objective: To compare the efficacy and safety between Piperacillin-Tazobactam with Cefepime in febrile neutropenic children with ALL.

**Methods:** Materials and methods: This randomized study was conducted from August 2015 to August 2016 in BSMMU. Sixty one episodes of febrile neutropenia in children with ALL, aged 0 to 18 years were included in this study. Patients were randomized into two groups. One group received Piperacillin/Tazobactam and another group received Cefepime and data of 60 febrile neutropenic episodes were analyzed.

**Results:** Febrile neutropenic episodes in the Piperacillin/Tazobactam group were 28 and in Cefepime group was 32 episodes and 34(57.63%) were male and 25 (42.37%) female. Median age was 5 years and 38(62.3%) neutropenic episodes were in induction phase. Majority had fever without focus 21(35%). Microorganisms isolated in 13 (21.66%) patients and majority 6 (46.15%) had blood infection. Most of the isolated organisms were Gram negative 11(84.61%). Overall treatment success without modification in the Piperacillin/Tazobactam group was 17(60.7%) and in Cefepime group 18 (56.3%) and that comparison was not statistically significant ( $p=0.732$ ). Significant difference was also not found comparing the mean duration of fever, neutropenia and hospital stay.

**Conclusions:** Conclusion: Both Piperacillin/Tazobactam and Cefepime were found effective and safe as an empirical therapy for febrile neutropenic children with ALL.

EP179/#877 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
Acute Lymphoblastic Leukaemia

### HIGH FREQUENCY OF TCF3-PBX1 FUSION GENE AMONG IRAQI PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA: A STUDY IN JAPAN

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**Background and Aims:** *TCF3-PBX1* (*E2A-PBX1*) fusion gene associated with t(1;19)(q23;p13) usually represents about 5% of pediatric acute lymphoblastic leukemia (ALL). Genetic analysis is still primitive for diagnosing acute leukemia in Iraq, a country of repeated wars over decades. We aimed to evaluate the cases of *TCF3-PBX1* among Iraqi children with ALL using next-generation sequencing (NGS).

**Methods:** From June 2016 to February 2020, bone marrow paired samples were collected from 55 Iraqi children younger than 16 years with newly diagnosed ALL. FTA cards were utilized to transfer the dried blood spots (DBS) to Japan. We performed whole-exome sequencing, targeted sequencing-based structural variation detection, and whole-genome sequencing on the DNA extracted from the DBS.

**Results:** *TCF3-PBX1* fusion gene was the most recurrent transcript (11/55, 20%), and all were of the balanced type. In addition to a case of *TCF3-HLF* corresponding to t(17;19)(q22;p13). Cross-contamination of samples was excluded because each patient carried a unique chromosomal breakpoint. Our cases had a higher frequency than the high incidence reported in African American and Mexican cases, of 11.8% and 11.5%, respectively. Our frequency was significantly higher than the neighboring Arab countries, such as Saudi Arabia, 3.4%, and Palestine, 7.3%, and higher than our previous report (4.2%). Seven of our 11 *TCF3-PBX1* cases had high-risk clinical criteria. The median WBC and LDH in *TCF3-PBX1* positive-ALL were significantly higher than those without *TCF3-PBX1*. The average number of somatic mutations per case associated with *TCF3-PBX1*-positive ALL was significantly lower than those ALL cases without *TCF3-PBX1*.

**Conclusions:** There is an abundant *TCF3-PBX1* fusion gene among Iraqi pediatric ALL revealed by NGS, a matter with unclear explanations and needs further studies. Geographic or ethnic background and war-related environmental factors might play a role. **Acknowledgments:** We appreciated the 55<sup>th</sup> Annual SIOP acceptance for our abstract to be published in the official congress publications.

EP180/#218 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
Acute Lymphoblastic Leukaemia

### FEBRILE EPISODES DURING DELAYED INTENSIFICATION TREATMENT IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA AND IMPACT ON HOSPITAL - METRICS: IS IT TIME TO RECONSIDER THE DI PHASE?

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**Background and Aims:** Acute Lymphoblastic Leukemia (ALL), most common childhood malignancy and delayed intensification (DI) has improved outcomes, associated with an increased number of febrile episodes (FEs). Emergency Department (ED) visits and hospitalization are unfavorable healthcare financial and quality metrics. This study aims to establish prevalence of FEs and the impact on hospital-metrics including Emergency Department (ED) visits, hospitalization, average length of stay (ALOS), inpatient hospital days, intensive care (ICU) admissions, and death during DI

**Methods:** Retrospective review of children (age 1-14 years) diagnosed with de-novo ALL between 2016-2021. The treatment protocols were based on the Children's Oncology Group AALL0932, AALL1131, and AALL0434 for NCI-Standard Risk B-cell ALL (SR), NCI-High Risk B-cell ALL (HR), and T-cell ALL; respectively. Supportive guidelines did not include prophylactic antibiotics during DI

**Results:** A total of 107 patients were eligible and 87 (80%) experienced FEs during DI. Mean age was 5.6 years, female: male ratio 1.4, 60% SR, 40% HR, and 11% had T-cell ALL. There were 151 FEs in 87 patients with 44% experiencing recurrent FEs. Majority (62%) of FEs occurred during re-consolidation. Recurrent FEs more frequently occurred in re-consolidation (p=0.001) with 27% of FEs occurring during the Ara-C blocks (p=0.006). Hospital-metrics revealed ED visits in 99% of FEs, hospital admissions in 73.5%, ALOS: 8 (5.6-15.8) days, and cumulative inpatient days of 805. Positive microbial culture was reported in 11 (7%) episodes. Of which, 55% were gram-positive and 45% gram-negative organisms. One patient had radiological evidence of fungal infection and one required ICU admission; however, no deaths were observed

**Conclusions:** Febrile episodes occurred in 80% of patients during DI with substantial impact on hospital metrics. Prophylactic antibiotics during DI must be explored through antimicrobial stewardship program and randomized control trials to provide valuable data. Alternatively, with the availability of new therapies, is it time to re-consider the DI phase?

EP181/#1266 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
Acute Lymphoblastic Leukaemia

### SURVIVAL IMPROVEMENT OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA AND TREATMENT ABANDONMENT IN CALI, COLOMBIA

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**Background and Aims:** Treatment abandonment (TxA) remains a challenge in low-and-middle-income countries (LMIC). Children with acute lymphoblastic leukemia (ALL) and TxA have poor overall survival (OS). SIOP defined TxA as  $\geq 4$  weeks of therapy interruption not due to medical reasons. To improve outcomes for children with ALL after TxA, we developed treatment guidelines for this subgroup. We describe the 5-year OS for children with ALL and TxA, pre- and post-guideline implementation.

**Methods:** Treatment guidelines were implemented in 3 pediatric oncology units (POU) in Cali, Colombia and included individualized intensity based on risk, relapse status, and minimal residual disease upon return to the POU after TxA. We analyzed data from 2009 to 2020 in children (<15 years) with ALL included prospectively in VIGICANCER (Childhood Cancer Outcomes Surveillance System). We compared 5-year OS for children with ALL and TxA pre-guideline implementation (Pre:2009-2013) and post-guideline implementation (Post:2014-2020). We used Kaplan-Meier and Cox regression for adjusted survival analyses.

**Results:** During the study period, 743 children with ALL were diagnosed in Cali and registered in VIGICANCER; Pre=296, and Post=447. Patients with T-cell phenotype and NCI high-risk were balanced pre- and post-implementation (9% vs 10%, and 44% vs 46%, respectively). We did not find differences in the 2-year cumulative incidence of TxA (pre=11% vs post=9%;  $p=0.14$ ). Five-year OS in children with ALL and TxA pre-implementation ( $n=31$ ) was 36% (95%CI:19,52) compared to 73% (95%CI:51,86) in children with ALL and TxA post-implementation ( $n=27$ );  $p=0.01$ . This OS difference was independent of potential confounders.

**Conclusions:** We found a 37% absolute increase in the 5-year OS between children with ALL and TxA pre- and post-guideline implementation. Our findings suggest that tailored, individualized chemotherapy regimens for children with ALL and TxA may improve survival. Further research is warranted to test the efficacy of this tailored approach, which could potentially improve OS in LMIC.

EP182/#516 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
Acute Lymphoblastic Leukaemia

### EVALUATING TREATMENT CHALLENGES IMPACTING GLOBAL DISPARITIES IN ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) OUTCOMES TO INFORM DEVELOPMENT OF ADAPTED RESOURCE AND IMPLEMENTATION APPLICATION (ARIA) TREATMENT GUIDELINES

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**Background and Aims:** The ARIA Guide was launched to provide global access to management tools for cancer treatment across all resource settings. In preparation for ALL guideline development, we gathered data regarding treatment challenges in low- and middle-income countries to inform development of a resource-based stratification framework and further treatment modification guidelines.

**Methods:** We identified 34 pediatric hematologists-oncologists, representing diverse geographic regions and World Bank income levels, experienced in ALL treatment and who have been active in developing management guidelines and/or adapting treatment regimens to local context. Using a qualitative mixed methods approach for iterative issue discovery, we conducted semi-structured interviews via video-conferencing between November 2022- March 2023. Open-ended questions covered treatment approaches, modifications with rationales, efficacy of treatment adjustments, and the most critical issues adversely affecting patient outcomes.

**Results:** While relative importance of individual factors varied, common themes emerged in five domains- diagnostics, treatment/supportive care, patient characteristics, facilities/staffing, and social. The high variability in available diagnostics including flow cytometry, cytogenetics, fluorescence in situ hybridization, minimal residual disease, and cerebrospinal fluid cytology impacted risk classification and approach to central nervous system-directed therapy. Factors identified as potential determinants of resource-based treatment strata included blood product availability, fever and sepsis management capabilities, adequate nursing staff, specialty-trained

physicians/nurses/pharmacists, 24-hour emergency access care, and imaging availability. Further treatment modifications must address high dose methotrexate administration capability, and the unavailability of specific chemotherapy drugs, stem cell transplant, therapeutic radiation, inpatient beds, pediatric anesthesia, and tumor-lysis syndrome supportive care. Patient-specific modification guidelines need address malnutrition, pre-existing infections, delayed presentation, lacking transportation and home chemotherapy infeasibility.

**Conclusions:** Through stakeholder discussions, we assembled factors crucial to incorporate into ARIA ALL treatment guideline development. These included primary determinants of a resource-based stratification framework, diagnostic limitation considerations for risk classification, and challenges to address with additional evidence-based treatment modification guidance.

EP183/#271 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### INTERPHASE FISH ASSAY ON AIR-DRIED BONE MARROW AND BLOOD SMEARS: AN EFFICIENT ALTERNATIVE FOR KARYOTYPING TO EVALUATE STRUCTURAL CHROMOSOMAL ABNORMALITIES IN PEDIATRIC ACUTE LEUKEMIA PATIENTS

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**Background and Aims:** Leukemia-associated structural chromosomal abnormalities (SCA) can be identified either by karyotyping or interphase-fluorescence in-situ hybridization (i-FISH) assays. Both karyotyping and i-FISH on mononuclear cell suspension are time, resource, and manpower-consuming assays. In this study, we have compared the results of i-FISH on air-dried bone marrow (BM)/peripheral blood (PB) smears and BM karyotyping in identifying specific leukemia-associated SCA.

**Methods:** The study was conducted among pediatric patients (age <18 years) diagnosed with acute leukemias between January 2018 to December 2022. The results of i-FISH on air-dried BM/PB smears and BM-karyotyping for our SCA of interest (*BCR::ABL1*, *ETV6::RUNX1*, *TCF3::PBX1*, *KMT2A* rearrangement, *RUNX1::RUNX1T1*, *CBFB::MYH11*, and *PML::RARA*) were entered in a contingency table and the agreement of results was calculated. The strength of agreement was assessed by Cramer's V test. The test was two-tailed with a 95% confidence interval and a p-value of  $\leq 0.05$  was considered significant.

**Results:** Among 270 patients, SCA of interest was identified among 26% and 17% of patients by i-FISH on air-dried smears and karyotyping, respectively. Excluding 53 patients with metaphase failure, the remaining 217 patients had 92% agreement (Cramer's V of 0.931 with  $p < 0.000$ ) between the results for specific SCAs identified by both techniques. On excluding samples with cryptic cytogenetic aberran-

cies, there was 99% agreement (Cramer's V of 0.953 with  $p < 0.000$ ) for gross SCA identified by both techniques. In addition, i-FISH on air-dried smears identified SCA in 30% of patients with metaphase failure.

**Conclusions:** I-FISH on air-dried PB/BMA smears is a less-labor & resource-consuming assay and can be considered as an efficient alternative for conventional karyotyping in identifying specific SCA of interest. This assay will be useful for the economical evaluation of specific SCAs by i-FISH in under-resourced laboratories.

EP184/#1674 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### DIAGNOSIS DELAY AND MISDIAGNOSIS IN CHILDREN WITH ACUTE LEUKEMIA IN KINSHASA

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**Background and Aims:** The initial clinical presentation of Acute Leukemia (AL) may simulate other diseases. In the context of limited access to diagnosis tools and high frequency of other common tropical diseases, there can be lot of misdiagnosis of leukemia. This situation increase delayed diagnosis and may lead to underestimating its prevalence. Since 2015, the French -African Pediatric Oncology Group (GFAOP) has been collaborating with our hospital to improve the survival of childhood cancer. The objective of this study is to describe the diagnosis time of AL in Kinshasa.

**Methods:** A retrospective cohort study conducted in the Pediatric Hemato-Oncology Unit of the University Hospital of Kinshasa between January 2005 and December 2018. All patients with more than 25% of blasts in the bone marrow smear were included.

**Results:** There were 105 cases of AL out of 700 registered children with cancer. ALL was predominant with 70.5% of cases and AML represented 29.5%. The median age was 7.5 years. The mean number of health facilities visited without being referred was  $3.7 \pm 1.8$ . The median total time to diagnosis was 83 days (IQR: 40-165), the median patient time was 6 days (IQR: 1.5 -14), and the median healthcare system time was 74 days (IQR: 35-151). Only 13% of patients visited the pediatric oncology unit within 30 days after the onset of symptoms. Some patients (18.1%) went to seek help to herbal healers. All children received antimalarial drugs and antibiotics prior their arrival at the treatment center and 23.8% received corticosteroids. Anti-tuberculosis drugs were prescribed by pediatricians in 63.1% and were given to 36.8% (38/105) of patients. Its average duration was 66 days prior to diagnosis of Leukemia.

**Conclusions:** Delayed diagnosis remains a recurring and worrisome problem. This delay diagnosis results from misdiagnosis and inade-

quate treatment that worsens the prognosis. Increasing awareness may improve the outcome of Leukemia.

EP185/#1228 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

### RISK FACTORS ASSOCIATED WITH L-ASPARAGINASE-INDUCED PANCREATITIS IN MEXICAN PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA TREATED IN THE REMISSION INDUCTION

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**Background and Aims:** L-asparaginase-induced pancreatitis (LAIP) causes discontinuation of L-asparaginase treatment and compromises the effectiveness of chemotherapy in pediatric patients with acute lymphoblastic leukemia (ALL). In this retrospective cohort, the objective was to determine the independent risk factors associated with the development of LAIP in pediatric patients with ALL during remission induction.

**Methods:** Retrospective cohort of pediatric patients with ALL treated with L-asparaginase, the patients come from a cohort that studies adverse reactions associated with chemotherapy in two major pediatric hospitals at Mexico City. Cohort integration was performed during the first dose of L-asparaginase, and follow-up was performed throughout remission induction. Relative Risks (RR) with 95% Confidence Intervals (95% CI) were calculated to determine the risk factors. Independent factors were estimated using Hazard Ratios (HR) with 95%CI using Cox proportional hazards regression.

**Results:** One hundred eleven pediatric patients were included, half were female (51%) and a median age was 5.6 years (range 0.64 to 16.6). The incidence of LAIP was 9.0%. Bivariate analysis identified high-risk ALL (RR 4.05, [95%CI 1.23-13.36]), overweight and obesity (RR 5.96, [95%CI 1.76-60.78]) and steroid-induced hyperglycemia (SIH) (RR 8.58, [95%CI 3.03-24.30]) as risk factors. In the multivariate analysis, both SIH (HR 7.12, [95%CI 1.33-38.26]) and patients with overweight and obesity (HR 5.78, [95%CI 1.11-30.14]) were shown to be independent risk factors for the development of LAIP.

**Conclusions:** SIH, as well as overweight and obesity are independent risk factors for the development of LAIP in Mexican pediatric patients with ALL treated with L-asparaginase during the remission induction.

EP186/#1239 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

### RARE REPORT OF A NOVEL TRANSLOCATION IN INFANTILE B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA (B-ALL) WITH FAVOURABLE OUTCOME

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**Background and Aims:** Infantile acute lymphoblastic leukemia (ALL) is marred by aggressive clinical course associated with KMT2A rearrangements in majority of patients. However, NUTM1 rearranged infantile leukemia tend to have very good outcomes. Here we describe a case of Infantile B-ALL with a novel and hitherto undescribed translocation in literature.

**Methods:** At our center, infants with MLL rearranged lymphoblastic leukemia will be counselled for intensive chemotherapy followed by allogeneic HSCT. Other infant ALL patients would receive high risk arm of institutional modified BFM-95 protocol. The flow-cytometric MRD assessment is done during post-induction (D+35) and post-consolidation (D+70) phase (if MRD positive post-induction). Patients with persistent MRD positivity post-consolidation (D+70) will be counselled for transplant.

**Results:** A 9-month-old infant who presented to us with one month fever and mild splenomegaly had baseline WBC count of 25000/mm<sup>3</sup>. His Bone marrow flow-cytometry was suggestive of pre-B ALL (CD10positive) and FISH didn't reveal MLL rearrangement. Conventional karyotyping showed normal male karyotype with the presence of t(7;15),(46XY, t(7;15)(q32;q22)(17)/46, XY (3). He received modified BFM-95 protocol with good day-8 prednisolone response and complete remission post-induction with flow-cytometric MRD negativity. He has completed the intensive phases of chemotherapy and currently on maintenance therapy and doing well.

**Conclusions:** This translocation (7,15) which is unreported so far, may portend a favorable outcome in Infantile B-cell ALL

EP187/#1137 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

### GENETICS OF CORTICOSTEROID-INDUCED AVASCULAR NECROSIS IN CHILDREN WITH CANCER

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**Background and Aims:** Corticosteroids are commonly used to treat hematologic malignancies in children, but their use can lead to avascular necrosis (AVN), a debilitating adverse reaction whose mechanism has not been fully elucidated. We investigated the impact of clinical and/or genetic factors underlying susceptibility to AVN in children receiving corticosteroid treatment.

**Methods:** Participants were recruited from 10 Canadian Pediatric Oncology Centers. A nested case-control study was conducted of 1370 pediatric patients with cancer who received corticosteroids. AVN was graded using the NCI Common Terminology Criteria for Adverse Events Version 5.0. Genome-wide association study compared children with cancer who developed corticosteroid-induced AVN  $\geq$  grade 2 to those who did not (grade 0). Genomic association tests were performed using genotyped and imputed genotype data (Illumina Infinium GSA array).

**Results:** 108 (7.9%) of patients developed AVN of grade 2 or higher. Age  $\geq$  10 years, female sex, ALL diagnosis, and total cumulative doses of corticosteroids were associated with a higher probability of developed AVN. Genome-wide analysis identified several genetic variants that were significantly associated with AVN ( $p < 5 \times 10^{-8}$ ). The top two loci associated with corticosteroid-induced AVN were an intergenic variant near to the genes *WNT7B* and *PPARA* (OR = 6.9, 95% CI, 3.3-15.1), and an intronic variant in *DEUP1* (OR = 5.5, 95% CI, 3.0-11.6). The primary cilium regulates several osteogenic actions, and the *DEUP1* gene is a key component for cilium formation. *WNT7B* and *PPARA* genes are involved in bone formation, and lipid metabolism, respectively. Corticosteroids have negative impact on bone cell formation/differentiation and can also lead to the accumulation of lipids in the bone marrow, impairing blood flow to the bone tissue.

**Conclusions:** This study identified two genetic variants that substantially increased the risk of developing corticosteroid-induced AVN. These new findings provide evidence of the biological mechanisms of AVN, which may help improve individualized treatment decisions.

EP188/#735 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

HIGH PREVALENCE OF FLT3-ITD MUTATIONS AND CLINICAL CHARACTERISTICS IN MEXICAN PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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**Background and Aims:** Leukemia is the most common pediatric cancer. The presence of genetic alterations is related to the prognosis of patients. *FLT3* is a gene involved in hematopoiesis, the interaction of *FLT3* with its ligand regulates the growth of stem-hematopoietic cells. While alterations such as internal tandem duplication (*FLT3-ITD*) is frequently recognized as a poor prognostic factor in AML, its impact on the clinical prognosis in ALL remains uncertain. The aim of this study is to identify the prevalence of *FLT3-ITD* in pediatric patients with B-ALL at the Hospital Civil Nuevo "Juan I. Menchaca", Guadalajara, México.

**Methods:** *FLT3-ITD* alteration identification was performed by fragment analysis from genomic DNA of patients with B-ALL, the search for genetic alterations was carried out with conventional karyotype, FISH and RT-PCR. The median follow-up time was 60 months and overall survival (OS) was determined with the Kaplan–Meier method.

**Results:** We investigated 80 patients with B-ALL, who presented an average of 7 years at diagnosis, 47.1% being female and 52.9% male, 25.9% presented hyperleukocytosis. Among the 80 patients only 13.75% *FLT3-ITD* were detected, 10.6% hyperdiploidy, 7.1%, *TCF3-PBX1*, 9.4% *ETV6-RUNX1*, 1.2% *MLL/AF4* and 4.7% *BCR-ABL1*.

**Conclusions:** The presence of *FLT3-ITD* in AML is associated with bad prognosis and decreased OS, the frequency of *FLT3-ITD* mutation is around 20%, even in Mexico, meanwhile in ALL is lower (0-5%), but there is a high prevalence of *FLT3-ITD* in pediatric B-ALL in our population with a frequency of 13.75%. In our study we did not find any association with [ICA1] OS. Increased frequency of *FLT3-ITD* mutations in ALL patients in our population, improves the importance of early detection due to in AML is well demonstrated that their presence allows the use of tyrosine kinase inhibitors, could be a perspective of study in ALL.

EP189/#447 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

TRACING BACK OF RELAPSE CLONES BY IG/TCR GENE REARRANGEMENTS REVEALS COMPLEX PATTERNS OF RECURRENCE IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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**Background and Aims:** Relapse remained the major obstacle to improving the prognosis of children with acute lymphoblastic leukemia (ALL). This study aimed to investigate the changing patterns of *Ig/TCR* gene rearrangements between diagnosis and relapse and the clinical relevance and to explore the mechanism of leukemic relapse.

**Methods:** Clonal *Ig/TCR* gene rearrangements were screened by multiplex PCR amplification in 85 paired diagnostic and relapse bone marrow (BM) samples from children with ALL. The new rearrangements presented at relapse were quantitatively assessed by the RQ-PCR approach targeting the patient-specific junctional region sequence in 19 diagnostic samples. The relapse clones were further back-traced to diagnostic and follow-up BM samples from 12 patients.

**Results:** Comparison of *Ig/TCR* gene rearrangements between diagnosis and relapse showed that 57.1% of B-ALL and 33.3% of T-ALL patients exhibited a change from diagnosis to relapse, and 35.7% of B-ALL patients acquired new rearrangements at relapse. The new relapse rearrangements were present in 78.9% of the diagnostic samples as shown by RQ-PCR, with a median level of  $5.26 \times 10^{-2}$ . The levels of minor rearrangements correlated with B immunophenotype, WBC counts, age at diagnosis, and recurrence time. Furthermore, back-tracing rearrangements in 12 patients identified three patterns of relapse clone dynamics, which suggested the recurrence mechanisms not only through clonal selection of pre-existing subclones but also through an ongoing clonal evolution during remission and relapse.

**Conclusions:** Backtracking *Ig/TCR* gene rearrangements in relapse clones of pediatric ALL revealed complex patterns of clonal selection and evolution for leukemic relapse.

EP190/#450 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### HIGH EXPRESSIONS OF P27KIP1 AND HSC70 WERE ASSOCIATED WITH RELAPSE IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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**Background and Aims:** Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy. About 15-20% of patients eventually have a relapse which is a main obstacle to further treatment improvement. Identification of novel prognostic markers for risk refinement represents a significant clinical need to be done. *p27<sup>Kip1</sup>* is involved in regulating many other cellular processes, including regulation of the cell cycle, transcription, cell migration and movement, and autophagy. *Hsc70* functions as a chaperone implicated in a wide variety of cellular processes. The prognostic significance of *P27KIP1* and *HSC70* expression in pediatric ALL remained unclear.

**Methods:** The expressions of *P27KIP1* and *HSC70* were detected in 53 patients by real-time quantitative RT-PCR. The predictive values of both gene expressions in relapse were evaluated.

**Results:** The expression level of *P27KIP1* was significantly associated with *HSC70* expression (Spearman  $R=0.466$ ,  $P < 0.001$ ). The levels of *P27KIP1* or *HSC70* expression in the patients suffering from relapse were significantly higher than that of patients in continuous complete remission (both  $P$  values were 0.002). The receiver operating characteristic curve analysis determined the cut-off levels for *P27KIP1* and *HSC70* expressions with good predictive significance for relapse of ALL (the area under curves were 0.869 and 0.865, respectively). Patients with high-*P27KIP1* expression had higher rates of relapse when compared to patients with low-*P27KIP1* expression (3-year cumulative incidence of relapse rates were  $29.4\% \pm 11.1\%$  and  $2.9\% \pm 2.8\%$ , respectively,  $P=0.001$ ). A higher rate of relapse was found in the high-*HSC70* group than in the low-*HSC70* group (relapse rates were  $30.7\% \pm 11.5\%$  and  $2.9\% \pm 2.8\%$ , respectively,  $P=0.004$ ). Patients were stratified into three groups according to the combined evaluation of the two gene expression, and patients with simultaneous high-expression had the worst outcome (relapse rate was  $50.0\% \pm 17.7\%$ ,  $P=0.001$ ).

**Conclusions:** High expression of *P27KIP1* and *HSC70* predicted the risk of relapse and correlated with poor outcomes in pediatric BCP-ALL.

EP191/#511 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### IMPACT OF MINIMAL RESIDUAL DISEASE ASSESSMENT ON OUTCOMES IN A COHORT OF PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKAEMIA

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**Background and Aims:** Evaluation of Minimal Residual Disease (MRD) at the end of induction (EOI) and consolidation (EOC) is considered to be the most important prognostic factor and is routinely used to risk-stratify and refine treatment in childhood acute lymphoblastic leukaemia (ALL). The aim of this retrospective study was to assess the impact of MRD assessment on outcomes and treatment modification in patients with ALL at a center in North India and compare this with historical data when MRD was not being performed routinely in the unit.

**Methods:** A retrospective audit of all patients 0-19 years that presented to our center was performed. MRD evaluation at and of induction and end of consolidation was adopted w.e.f. November 2016. For patients with standard risk (SR) disease, the second delayed intensification was omitted if MRD was negative at 2 time points. For patients with positive MRD, treatment was escalated wherever feasible. Outcomes of interest were MRD positivity, event free survival (EFS), overall survival (OS), and treatment-related mortality (TRM).

**Results:** Complete data was available for 370 patients treated from 2003-2021. There were 176 patients in the SR arm and 194 in the HR/VHR cohort. 4.16%, 12.2% and 44.4% of SR, HR and VHR patients had positive MRD at EOI. The 5-year EFS was 80% and 89% ( $p=0.19$ ) and OS was 81.4% and 89.8% ( $p=0.31$ ) respectively in the pre-MRD and MRD eras. TRM was 2.7% and 6% in the MRD and pre-MRD cohorts.

**Conclusions:** Though routine assessment of MRD could not impact outcomes significantly, it allowed us to de-escalate treatment and reduce anthracycline exposure in a significant number of patients without compromising outcomes. The de-escalation may have contributed to a lower TRM.

EP192/#1377 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### FORMATIVE EVALUATION OF A STANDARDIZED, MULTIDISCIPLINARY TRAINING PROGRAM FOR ADMINISTERING BLINATUMOMAB IN LOW- AND MIDDLE-INCOME COUNTRIES

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**Background and Aims:** Immunotherapies, like blinatumomab, have improved outcomes in pediatric cancer. However, unique adverse events and administration necessitate multidisciplinary preparation to build knowledge and self-efficacy prior to real-world application of complex therapies. In partnership with a drug-donation effort, we designed a resource-adapted multidisciplinary training program. Five pilot-sites in India and Pakistan participated in the training between 2020-2022. Virtual delivery accommodated travel restrictions and increased program reach.

**Methods:** After training, an electronic survey comprised of multiple-choice knowledge-based questions and nested self-efficacy questions

(based on role-specific objectives) was administered to physicians, nurses, and pharmacists. Self-efficacy questions were scored on a 4-point Likert-type scale (4=very comfortable; 1=very uncomfortable). Local implementation teams further assessed training content and delivery methods through 8 open-ended questions. Miles & Huberman's matrix approach was used for thematic analysis of qualitative data from open-ended responses.

**Results:** Thirty-three providers completed the knowledge and self-efficacy survey (nurses = 6, pharmacists = 7, physicians = 20). Comparing comfort before and after training, mean aggregate self-efficacy scores increased for all providers (nurses 2.89 to 3.63, pharmacists 2.75 to 3.58, physicians 2.36 to 3.91). Thirteen providers completed the training feedback. Positive themes included site-specific discussions, questions specific to local resources, and accessible workflow materials to integrate into care routine. Suggestions included the need for case-based examples, visual aids, variation in training timing and delivery methods specific to nurses' learning needs. Following training, some sites implemented additional local sessions led by senior physicians and nurses to reinforce training principles and onboard new team members.

**Conclusions:** Based on feedback, training materials were modified to include short videos and case-based examples. Additional virtual sessions were added for nurses and pharmacists. A train-the-trainer package for nurses was designed to facilitate future training. Formative evaluation is critical to meet team training needs. This approach can be applied broadly for preparing teams to deliver complex therapies.

EP193/#1134 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### CHANGES OF THE PLATELET COUNT AND RED CELL DISTRIBUTION WIDTH DURING INDUCTION TREATMENT ARE ASSOCIATED WITH FAILURE OF INDUCTION IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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**Background and Aims:** Acute lymphoblastic leukemia (ALL) is the most common cancer during childhood. Recovery of the hematopoietic system during and after induction chemotherapy is one of the prognostic factors for survival in pediatric ALL. The goal of this study is to evaluate the value of different peripheral blood parameters in the prediction of induction remission in these patients.

**Methods:** This study included 100 pediatric ALL patients who were admitted to Shefa Alorman hospital between 2020 and 2022. Data about CBC and bone marrow parameters at day 0, day 8, day 19 and day 42 of induction chemotherapy were collected and analyzed.

**Results:** B-ALL cases represented 75% of cases, and the most common diagnosis among them was common B-ALL (45%). The most common molecular/ cytogenetic findings were t(12;21)(p13;q22) (8%). Ninety four patients achieved complete remission (CR) by the end of induction period. A significant decrease in both platelets (PLT) and red cell distribution width (RDW) were found to increase the likelihood of induction failure (coefficient = -0.01 and -0.24; p = 0.03 and 0.05, respectively). The ROC curve revealed that only PLT had significant discrimination ability between successful and failed induction, with an AUC of 0.64 (p = 0.03).

**Conclusions:** We identified two parameters from that can be used to predict the results of induction treatment in ALL pediatric patients. Decrease of platelet count during induction was an important predictor of failure of induction treatment, and could be one of the early indicators of inability of the bone marrow stem cells to replenish the peripheral blood. Drop of the RDW was another predictor of induction failure. Long term follow up is needed to evaluate the effect of these parameters on disease free survival and overall survival in patient in whom induction was successful or failed to achieve complete remission.

EP194/#1844 | Poster Topic: AS05 SIOP Scientific Program/AS05.a Acute Lymphoblastic Leukaemia

#### RESULTS OF THE DANA FARBER'S ALL TREATMENT PROTOCOL APPLIED IN A HOSPITAL IN MEXICO, A MIDDLE-INCOME COUNTRY

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**Background and Aims:** Acute lymphoblastic leukemia (ALL) is the most frequent cancer in the pediatric age. The use of international protocols with proven survival has been limited in low and middle-income countries due to their intensity, high morbidity, and related mortality. This study presents the results of patients treated with DFCI ALL protocol, at the Teleton Children's Hospital of Oncology in México.

**Methods:** Method Records of patients diagnosed with ALL in the study period were reviewed.

**Results:** From December 2013 to December 2019, were diagnosed 90 patients with ALL, 79 younger than 18 years at diagnosis were included at the present study. The risk factors at diagnosis, 15% had more than 50,000 leukocytes and 8% with more than 100,000; 90% (n=71) of the cases were B lineage, 5% (n=4) expressed T, by karyotype,

8.9% (n=7) presented hyperdiploidy, DNA index of 1.02, 12.6% (n=10) expressed ETV6-RUNX/t(12:21) TEL-AML1, 10% (n=8) IAMP21, 8.9% (n=7) E2A/PBX t(1:19), none express MLL t(4:11). By risk group 51% (n=41) was standard risk (SR), 47% (n=37) high risk (HR), only one very high risk (VHR) case, at the end of induction with minimal residual disease (MRD) at day 32, the risk was reclassified in 10 cases, 2 cases from (SR) to (HR) and 6 to (VHR), from the HR group two cases were reclassified as VHR and one was reduced to SR. Only 7.5% (n=6) of the cases have died, reporting an overall survival OS at 3y of 84.8% for all risks, 97.1% for SR, 85.7% for VHR and 78.6% for HR. Event Free survival (EFS) at 3y for SR 90.9%, VHR 84.6% and HR 57.1%.

**Conclusions:** Conclusion: We believe that the results obtained with this protocol are closely related to supportive treatment, antimicrobial prophylaxis and proper management, time care, as well as personnel trained in the management of critical hemato-oncology pediatric patients.

EP195/#1875 | Poster Topic: AS05 SIOP Scientific Program/AS05.a Acute Lymphoblastic Leukaemia

#### OUTCOMES RELAPSED CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA: TELETHON CHILDREN'S HOSPITAL OF ONCOLOGY EXPERIENCE

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**Background and Aims:** Even though the treatment outcomes of ALL have improved recently, relapse of the disease still remains a challenge in developing countries. The objective of this study is to analyze the incidence of relapse and survival rates in childhood ALL on our hospital.

**Methods:** Retrospective study of 108 children with novo ALL december 2013 to june 2021 was conducted. Data on age, gender, relapse site, the timing of relapse (very early, early or late), and the phenotype of the disease were analyzed, considerate important prognostic factors for determining post-relapse survival rate.

We carried out this research to analyze the incidence of relapse and survival rate in childhood ALL. We considerate our findings will contribute to further improving the treatment outcomes in children with ALL.

**Results:** total of 18 (16.6%) patients, with m:f ratio of 1.6:1. The relapse rate in the high- and very-high-risk group was 3 times higher than in the standard-risk group (75% vs. 25%). The most common relapse site was isolated CNS 35.2%, followed by the isolated the BM 29.4%, and the rest was represented by the CNS/ BM (11.8%); testicle/ BM (11.8%) and BM with other sites (11.8%). The median OS is 27 months (95% CI 18-35%) with a probability of 41% of patients are alive, the DFS in a mean 37.9 mon (95% CI 22.5-53.3%) with a survival probability of 47.8%. For isolated CNS relapses, the estimated survival is 60%

with a mean follow-up of 42.9 mo (95% CI 27.9-70.4%). In combined relapses, the estimated survival was 66.7% with a mean follow-up of 30.1 months (95% CI 14.5-45.8%).

**Conclusions:** To intensify therapy to the CNS with 2 cycles HD-methotrexate and increase the number of IT as well as delaying the first intrathecal according to peripheral blood blast clearance and platelet count >50,000/mm<sup>3</sup> and use immunotherapy can improve the overall survival rates in relapsed.

EP196/#112 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

### ROLE OF INOTUZUMAB OZOGAMYCIN IN TREATMENT OF CHILDREN WITH RELAPSED AND REFRACTORY B-LINEAGE ACUTE LYMPHOBLASTIC LEUKEMIA

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**Background and Aims:** Current results of acute lymphoblastic leukemia (ALL) therapy are encouraging, however 10-15% patients relapse. The application of immunotherapy made possible to achieve minimal residual disease (MRD) - negative remission in relapsed/refractory (R/R) patients. Inotuzumab Ozogamycin (InO) is an anti-CD22 monoclonal antibody conjugated to the cytotoxic agent calicheamicin using as such therapy. We analyzed the efficacy and toxicity of anti CD22 conjugate inotuzumab in group of children with R/R acute lymphoblastic leukemia

**Methods:** We report the usage of InO in 17 patients under the age of 18 with R/R forms of precursor B-cell ALL (pB-ALL) at the Dmitry Rogachev National Medical Research Center of Pediatric Hematology, Oncology and Immunology from 01.10.2016 to 01.09.2022. The efficacy and toxicity of therapy were estimated by morphological response, MRD-negativity, overall survival (OS) and CTCAE 4.03 (Common Criteria for Adverse Events) respectively. Statistic results were processed by XLSTAT 2016 software.

**Results:** The majority of patients (75%) responded to the therapy. MRD-negative status was achieved in 41.2% of responders. One-year overall survival was 40.3% (95% CI: 14.8-65.7%). The treatment was well-tolerated, but 33% of patients with post-InO hematopoietic stem cell transplantation (HSCT) developed sinusoidal obstruction syndrome. This study demonstrated high efficacy as a "rescue" therapy in patients with R/R pB-ALL, as well as "bridge therapy" before hematopoietic HSCT transplantation and also need for future studies.

**Conclusions:** The use of inotuzumab ozogamycin in the treatment of refractory acute lymphoblastic leukemia in children is effective for achieving remission before HSCT, but the toxicity and optimal timing of its use requires further study

EP197/#1012 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

### EARLY TOXICITY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA TREATED ACCORDING TO THE ALLTOGETHER TREATMENT PROTOCOL

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**Background and Aims: Background** The ALLTogether treatment protocol for children with acute lymphoblastic leukemia aims to decrease toxicity without compromising the survival in the low-risk patients and to intensify treatment for high-risk patients. The induction differs from the previous NOPHO ALL2008 protocol by earlier initiation of asparaginase, use of dexamethasone to all patients, and omission of anthracycline for low-risk patients. The consolidation-1 phase is in the ALLTogether protocol based on the Induction-1B-phase by the BFM-group whereas in the NOPHO ALL2008, consolidation-1 was based on high-dose methotrexate, mercaptopurine and asparaginase. **Aim** To compare the prevalence of 14 predefined toxicities between the ALLTogether and ALL2008 protocols during early treatment (days 1-78): asparaginase allergy, thromboembolism, bleeding, CNS-toxicity, electrolyte disturbances, hyperglycemia, severe infection, liver toxicity, intensive care, surgery, osteonecrosis, pancreatitis, peripheral neuropathy and kidney dysfunction. In-patient days and weight change during early treatment were also registered.

**Methods:** Retrospective data from all Swedish pediatric oncology centers were collected from medical records of patients treated with the ALLTogether protocol (n=106) before the first amendment (from August 2019 to May 2021) and matched controls treated with the ALL2008 protocol (n=159).

**Results:** The average number of toxicities did not differ between the protocols: 2.48 and 2.40 events/patient in the ALLTogether and ALL2008 protocols respectively. Hyperglycemia, osteonecrosis, weight gain, and thromboembolism were more frequent in the ALLTogether protocol (p<0.05). Bleeding episodes and neutropenic infections were

more frequent during the ALL2008 protocol ( $p < 0.05$ ). No differences were seen regarding days of in-patient care (mean 33- and 36 days in ALLTogether and ALL2008, respectively).

**Conclusions:** The toxicity profile following the ALLTogether protocol differs from the ALL2008 protocol, although the overall frequency of toxicities remains unchanged. The increase of hyperglycemia and thromboembolism in the ALLTogether protocol is likely related to the early initiation of asparaginase, whereas the decrease in infections may be related to omitting anthracycline from low-risk induction.

EP198/#1415 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### CLINICAL, IMMUNOPHENOTYPIC, CYTOGENETIC AND MOLECULAR CHARACTERIZATION AND RESPONSE TO TREATMENT AT THE END OF INDUCTION IN PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA/LYMPHOMA

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**Background and Aims:** Acute lymphoblastic leukemia/lymphoma (ALL) is the most common malignancy in children. The current results show an event-free survival of 90% in developed countries. In low- and middle-income countries, the reported results are lower, due to multiple factors, such as late diagnosis, lack of resources for diagnosis and treatment, higher early mortality, a higher percentage of relapses, and lower adherence to treatment. The objective is to clinically, cytogenetically and molecularly characterize pediatric patients with ALL and to evaluate the response to treatment at the end of induction in an in the Department of Pediatric Hemato-Oncology of the Hospital de Clínicas of the Faculty of Medical Sciences of the National University of Asuncion

**Methods:** Observational, descriptive, prospective study, between June 2019 and December 2022

**Results:** 138 patients with ALL were diagnosed, 72 patients were male (52,2%). The mean age was 6.8 years (11 months to 17.8 years). 132 patients (95.7%) were of lineage B. 111 patients presented with WBCs of  $< 50,000/\text{mm}^3$ . 113 patients with B cell ALL were evaluable for the determination of molecular and cytogenetic alterations: ETV6::RUNX1 29 (25,7%); TCF3::PBX1 in 8 (7,1%); BCR::ABL in 3 (2,6%); MLL::AE4 in 1 (0,9%), Hypodiploidy in 2 (1,8%). No cytogenetic alterations were detected in 70 cases (61,9%). 130 patients (94.2%) were evaluable by MRD at the end of induction. 2/2 of patients with BCR ABL were MRD positive, while 1/2 patients with hypodiploidy and 3/6 patients with T-cell ALL were MRD positive. 14/70 patients (20%) were MRD

positive in the group of patients with no molecular and cytogenetic alterations.

**Conclusions:** Despite the low number of patients in some groups, the results are consistent with those reported in the literature. We consider expanding the determinations made in our patients to achieve an early identification of patients with a higher risk of relapse allows treatment to be adjusted.

EP199/#1499 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### EFFECT OF DIETARY ASPARAGINE ON BLOOD ASPARAGINE AND GUT BACTERIA

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**Background and Aims:** Peg-asparaginase converts serum asparagine (Asn) into aspartate, killing leukemic but not healthy cells. Dietary Asn and gut microbial communities possibly metabolizing Asn could be confounding blood Asn levels, impacting peg-asparaginase efficacy. We aimed to understand the relationship between gut and blood Asn and the potential to modify Asn levels through diet and the microbiome using mice.

**Methods:** Baseline blood and stool samples were collected from C57BL/6 mice prior to starting an Asn-depleted (0%) or Asn-rich diet (4%), and 72 days later. Stool and blood samples were analyzed using LC/MS-MS for the metabolome, and stool samples were further analyzed using bacterial 16S and meta-genome sequencing.

**Results:** Blood Asn levels were similar between diets after 72 days, indicating either the diets had no effect or the animals' physiology maintained a steady state level. On day 72, The Asn-depleted mice had significantly more stool Asn, and the Asn-rich mice had significantly more blood aspartate. We identified difference in bacteria between diets, leading us to hypothesize that the Asn-rich diet was selecting for bacteria with asparaginase activity. However, meta-genome sequencing did not show a significant difference in the relative abundance of asparaginase or Asn synthetase.

**Conclusions:** Dietary Asn was unable to directly influence blood Asn levels after 72 days. It is possible that an impact may be evident in a shorter period of time. Mice on the diet high in Asn had lower gut Asn levels in comparison to the diet high in Asn was suggestive of Asn metabolism in the gut; however, we were unable to trace these changes back to the bacteria. It remains possible that enzymatic activities are not reflected in the relative gene levels, but absolute gene copy numbers are not available. Further research into the relationship between blood and gut amino acid levels and microbial metabolism is warranted including during Peg-asparaginase treatment.

EP200/#91 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

POPULATION PHARMACOKINETICS AND  
 PHARMACODYNAMICS OF L-ASPARAGINASE AND ITS IMPACT  
 ON THE DEVELOPMENT OF PANCREATITIS AND  
 HYPERSENSITIVITY REACTIONS IN CHILDREN WITH ALL  
 UNDER TREATMENT

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**Background and Aims:** L-Asparaginase (L-Asp) is essential in the treatment of patients with acute lymphoblastic leukemia (ALL), commonly associated with adverse effects (AEs). Immunogenicity and pharmacokinetic differences could predispose to the development of AEs due to L-Asp. **Objective:** to determine the population pharmacokinetics/pharmacodynamics (PK/PD) of L-Asp and its impact on the development of pancreatitis or hypersensitivity in children with ALL.

**Methods:** Thirty-six children with ALL treated with L-Asp were included, from the Pediatric Hemato-Oncology Service of the State Cancer Center (CECAN) of Durango, Mexico. One to three blood samples were randomly obtained from each patient, at times from 0 to 30 hours, up to a total of 108 samples. L-Asp enzymatic activity, Asparagine (Asp) concentration and anti-L-Asp antibodies were quantified. Population PK/PD modeling of L-Asp was developed to determine the association of covariates with PK/PD parameters of L-Asp.

**Results:** Significant associations were found between the presence of anti-L-Asp antibodies with increases in both L-Asp clearance (Cl) ( $r = 0.813$ ,  $p = 0.01$ ) and L-Asp intercompartmental clearance (Q) ( $r = 0.7164$ ,  $p = 0.04$ ); likewise with the decrease of volume of distribution (V1) of L-Asp ( $r = -0.7230$ ,  $p = 0.003$ ). On the other hand, the female sex was associated with the increase in V1 ( $r = 0.7390$ ,  $p = 0.01$ ) and the age from 1 to 7 years was associated with the decrease in V1 ( $r = -0.6564$ ,  $p = 0.05$ ). Regarding the PD of L-Asp, it was found that both the presence of anti-L-Asp antibodies and the female sex were related to the increase in the concentration of L-Asp necessary to deplete 50% of Asp (IC50) ( $r = 0.7341$ ,  $p = 0.01$  and  $p = 0.6990$ ,  $p = 0.01$ ), respectively. All patients with pancreatitis have a complete depletion of Asp before the first 24 hours after infusion of L-Asp.

**Conclusions:** The influence of the variables on the increase or decrease of the PK/PD parameters have implications for the safety and efficacy of the drug.

EP201/#1155 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

BURDEN OF SEPSIS SYNDROME IN CHILDREN WITH ACUTE  
 LYMPHOBLASTIC LEUKEMIA IN ARGENTINA. REVIEW OF TEN  
 YEAR FOLLOW UP

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**Background and Aims:** Sepsis syndrome (SS) is one of the most important causes of death in Acute Lymphoblastic Leukemia (ALL); it has been recognized as a medical emergency. There are a paucity of data concerning outcomes of infection-related-deaths (IRD) in patients with ALL in low-middle-income countries. Reports of IRD rates are 2-3% in high-income-countries. The objective was to analyze the IRD rates, and related risk factors influencing outcomes in patients with ALL in Argentina

**Methods:** Prospective observational study; 2233 Pts were accrued from January 2012-November 2021 from ALLIC-GATLA-2010 Protocol. SS is defined according to Surviving Sepsis Campaign as the presence of infection together with systemic manifestations, organ dysfunction or hypoperfusion

**Results:** In total, there have been 288 deaths, of which 133 (46.0%) were disease-related and 155 (54.0%) were caused by treatment related mortality (TRM). SS was the most common cause of TRM, with 95 deaths. This constitutes 4.25% of all trial patients, 33% of the 288 deaths overall. At 5 years, the cumulative incidence from death from all causes was 13% (CI 95% 12.8-13.11) and 4.2% from IRD (95% CI 4.0-4.4) In the univariate model we found significant differences on the risk of IRD in patients with Down syndrome (DS), T-ALL, infections during induction phase, poor response to steroids and minimal residual disease levels, but in the multivariate analysis, Down syndrome retained significance as risk factor for IRD (odds ratio [OR], 3.74; 95% CI, 2.76-4.71  $P < .0001$ ), followed by level of MRD (OR, 1.85; 95% CI, 1.55-2.14;  $P < .0001$ .)

**Conclusions:** Higher rates of cumulative infection incidence in children with ALL in Argentina, and higher a IRD risk. Our data, confirm Down syndrome and high levels of MRD as a risk factor for IRD.

EP202/#1166 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

SEPSIS SYNDROME AND TREATMENT RELATED MORTALITY  
 RATES IN DOWN SYNDROME TREATED FOR ACUTE  
 LYMPHOBLASTIC LEUKEMIA IN ARGENTINA

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**Background and Aims:** Sepsis Syndrome (SS) is defined as the presence of infection together with systemic manifestations of infection; sepsis-induced organ dysfunction or tissue hypoperfusion is referred to as severe sepsis. Children with Down syndrome (DS) with acute lymphoblastic leukemia (ALL) are more vulnerable to SS and show higher rates of treatment related mortality (TRM). There is lack of information concerning TRM and SS in DS and their related risk factors in middle-low-income countries Objective To describe SS and TRM identify risk factors in children with DS during chemotherapy for ALL.

**Methods:** Prospective interventional study. Cohort of 2105 ALL Pts from 38 institutions in Argentina, accrued from January 2010-November 2021 and reported to ALLIC-GATLA-2010 Study. Patients received full chemotherapy doses, no randomization.

**Results:** Forty-six patients had DS (2%). Mean age 9 years old.(SD +/- 4.2), 54%male. 76% were intermediate risk; 96% had prednisone good response; 67% have low-intermediate minimal residual level on day 15th and 98% had B-lineage ALL. Overall survival was 0.56% (IC 95% 0.50 -0.61 in DS at 28 months. (Median Survival time was not achieved); OS was lower compared to non-DS children (0.89% (CI 95% 0.875-0.903) (log rank p <0.001). Ten pts with DS had SS and died 10/46 (22%), compared to 144/2169 (6.7%) (p 0.0001) in non-DS with sepsis syndrome. 2/46 (4.3%) of Pts with DS had TRM Death risk was assessed for DS pts on logistic regression univariate analysis: SS and relapse had significant effects but only relapse retained significance for death risk on multiple variable analysis (OR 7.3 (CI 95%, 1.64 -32.5)

**Conclusions:** DS patients had significant shorter median time for survival than non DS children. Relapse and SS rates were more frequent in DS Pts and significantly increased risk of death in this population. Results are in concordance with literature and future studies should include optimization of supportive care.

EP203/#1576 | **Poster Topic: AS05 SIOP Scientific Program/AS05.a Acute Lymphoblastic Leukaemia**

#### OUTCOME OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) IN SRI LANKA: A SUCCESS STORY OR AN OPPORTUNITY LOST?

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**Background and Aims:** Sri Lanka is a Lower Middle Income Country with a health system that provide free coverage of childhood ALL treatment. A guideline adopted from the UKALL 2011 protocol is currently used to treat childhood ALL in Sri Lanka. This study sets out to describe the baseline status of childhood ALL outcomes in Sri Lanka which can inform future quality improvement initiatives.

**Methods:** Data was collected retrospectively from all patients less than 19 years. from 2014-2019 registered with the only 2 childhood cancer treatment centres in the country. Only children with confirmed diagnosis through a bone marrow aspiration, peripheral blood flow cytometry or CSF analysis were included.

**Results:** While 1319 patients were eligible to be enrolled, evaluable data was available only in 1264. Median age at diagnosis was 4.65 years and 54% were boys. B lineage ALL was the commonest category with 79%. Malnutrition was a major concern in this cohort with 34% of patients showing evidence of wasting. The NCI standard risk patients formed 54% of the cohort. Central Nervous System involvement was seen only in 6%. Treatment abandonment rate stood at 6% and out of this 90% occurred within 2 weeks of initial diagnosis. Five year overall survival and relapse free survival of the cohort was 73% and 65% respectively. Patients with B-ALL did significantly better than T-ALL (79% vs 62%, P = 0.006). No difference in outcomes was observed according to age, sex, area of residence, parental education. In this study 212 treatment related deaths were identified and 88% of those deaths happened within first six weeks of starting treatment with 91% happening due to infections and 96% having a respiratory system focus.

**Conclusions:** Sri Lanka has achieved satisfactory outcomes in childhood ALL even with limited resources. However, high treatment related mortality malnutrition at presentation are barriers in further improving survival.

EP204/#934 | **Poster Topic: AS05 SIOP Scientific Program/AS05.a Acute Lymphoblastic Leukaemia**

#### PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY (PQCT) TO ASSESS THE MUSCLE-BONE UNIT AND DETECT SARCOPENIA AND SARCOPENIC OBESITY IN LONG-TERM SURVIVORS OF PEDIATRIC CANCER

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**Background and Aims:** Sarcopenia, a systemic loss of skeletal muscle mass (SMM) and function, and sarcopenic obesity (SO) with concomitant gain in fat mass, are prevalent findings in survivors of pediatric cancer, but are difficult to detect in a clinical setting, limiting



opportunities for intervention. We explored whether pQCT can identify sarcopenia in a cohort of long-term survivors of pediatric acute lymphoblastic leukemia (ALL), and to shed further light on the “functional muscle-bone unit”<sup>1</sup> in this population.

**Methods:** pQCT at 2 diaphyseal and 3 metaphyseal sites of upper and lower non-dominant limbs was performed on 70 patients greater than 10y from diagnosis (55.7% male). Metrics assessing bone quality and strength were obtained at each site and calf muscle cross-sectional area (CSA) at the mid-calf (38% tibia). Their correlations were assessed using linear regression and Pearson coefficients. Muscle CSA and CSA Z scores by ALL risk stratification and presence of SO were compared using t-tests and regression techniques.

**Results:** There is a strong correlation between calf muscle CSA and previously measured appendicular lean mass index (ALMI), a surrogate marker for SMM ( $r=0.585$ ,  $p<0.0001$ ), and bone mineral content at the 38% tibia ( $r=0.726$ ,  $p<0.0001$ ). Calf muscle CSA Z scores were correlated strongly and significantly with numerous metrics of bone health and strength. No significant difference in CSA Z scores was noted between ALL risk groups; however, Z scores are markedly higher in those without SO (odds ratio: 0.388, 95%CI: 0.093-0.586,  $p=0.014$ ).

**Conclusions:** Our results are supportive of a functional muscle-bone unit in long-term survivors of pediatric ALL, with strong correlations between calf muscle CSA and measures of bone quality and strength. Calf muscle CSA Z scores may represent a useful clinical measure to assess nutritional status and are predictive of SO in this population. 1. Schoenau E. *J Musculoskelet Neuronal Interact* 2005; 5: 232-238.

EP205/#873 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### INVESTIGATING THE POTENTIAL THERAPEUTIC ROLE OF ENERGY METABOLISM SIGNALING PATHWAY IN T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

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**Background and Aims:** T-cell acute lymphoblastic leukemia (T-ALL) is a common pediatric malignancy, characterized by the abnormal presence of immature T-cell progenitors. Conventional treatments for T-ALL fail to prevent or cure the disease, with a high-risk of recurrence after the first remission. Thus, medical options are in demand to develop novel therapies for patients suffering with T-ALL. Niclosamide, a traditional oral anti-helminthic drug, has been reported to be a potential anticancer agent that regulates intracellular signaling pathways. Few studies have yet investigated the effects of niclosamide on the development of T-ALL. Here, the present study aimed to investigate the anti-leukemia effects of niclosamide on T-ALL.

**Methods:** T-ALL cell lines, Jurkat and CCRF-CEM, were treated with different doses of niclosamide for 24 h. Cell proliferation was measured by Ki-67 staining. Energy metabolism markers such as transketolase (TKT), transketolase like 1/2 (TKTL1/2) and transaldolase (TALDO)

expressions were measured by western blotting. The mTOR pathway proteins were also detected by western blotting.

**Results:** In our study, we found that niclosamide can effectively reduce the expression of TKT, TKTL1/2 and TALDO in the pentose phosphate pathway. In addition, niclosamide decreases the expression of the mTOR pathway downstream protein, p-4E-BP1, leading to inhibit T-ALL cell proliferation.

**Conclusions:** Our study indicated that niclosamide could inhibit the cell proliferation of T-ALL by regulating energy metabolism signaling pathway. We conclude that niclosamide plays an anti-leukemia role, and that it represents a novel approach for the treatment of T-ALL.

EP206/#600 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### PROGNOSTIC IMPACT OF MINIMAL RESIDUAL DISEASE ON LONG-TERM SURVIVAL OUTCOMES IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA DIFFERS ACCORDING TO CYTOGENETIC SUBTYPES

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**Background and Aims:** To investigate the effect of minimal residual disease (MRD) levels with different cytogenetic subtypes on the long-term prognosis of children with acute lymphoma, to better stratify the treatment.

**Methods:** From March 1, 2008, to December 31, 2012, CCLG-2008 regimen was used in Beijing Children's Hospital, Capital Medical University to treat 723 newly diagnosed acute lymphoblastic leukemia (ALL) children. Univariate and multivariate analyses were used to analyze the influencing factors of ALL recurrence, and then the influence of MRD levels with different genotypes on the long-term prognosis was evaluated to determine the respective MRD stratification standards.

**Results:** With a median follow-up time of 130.5 months, the 10-year overall survival (OS), event-free survival (EFS) and cumulative incidence of relapse (R) of 723 patients were  $85.4\pm 1.3\%$ ,  $80.1\pm 1.5\%$  and  $12.0\pm 1.3\%$ , respectively. Univariate and multivariate analyses demonstrated that MRD grouping was independent prognostic factors for long-term prognosis in children with ALL. There were significant differences in MRD levels with different cytogenetic subtypes in the early stage of treatment ( $P < 0.001$ ). Through analysis, it was concluded that the prognostic significance of MRD level for recurrence with different subtypes was also different. Based on the above criteria, we designed a formula to assess the risk of recurrence: Risk index = clinical risk (score 1 for SR, 2 for IR and 3 for IR) + MRD-group (0 for MRD-LR, 1 for MRD-VVR)  $\times$  B (1.572 for BCR/ABL; 1.853 for TEL/AML1; 1.552 for T-ALL). The predictive value of the risk index for relapse was tested by the ROC curve, which indicated that the predictive efficiency of the new risk index for relapse was better than that of clinical risk stratification.

**Conclusions:** The prognostic significance of different genotypes of MRD is significantly different, suggesting that genotyping should be based on different genotyping criteria, which can be verified in a new multicenter study.

EP207/#817 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### ASPARAGINASE-ASSOCIATED TOXICITY AND HYPERSENSITIVITY REACTIONS IN DOWN SYNDROME CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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**Background and Aims:** Children with Down Syndrome (DS) and acute lymphoblastic leukemia (ALL) have high treatment associated mortality. We aimed to determine: 1) the incidence of pegaspargase (PEG)-associated toxicity in patients with DS-ALL and, 2) whether premedicating patients with DS-ALL using histamine-1 (H-1) and histamine-2 (H-2) blockers prior to PEG decreases hypersensitivity reactions (HSR).

**Methods:** Prospectively enrolled patients with ALL at six centers received H-1 and H-2 blockers prior to PEG in consolidation and subsequent cycles. Therapeutic drug monitoring was performed 7-10 and 14-17 days after each PEG dose. Patients were monitored for HSR and PEG-associated toxicities.

**Results:** Nine patients with DS-ALL and 68 non DS-ALL were enrolled between 10/2019 and 1/2022. In patients with DS-ALL, the median age at diagnosis was 5.0 years [IQR: 4.3, 14.9], 4 were NCI High Risk (HR), 4 were Hispanic, and none were obese. Patients with DS-ALL experienced high rates of PEG-associated toxicities, with 13 Grade  $\geq$  3 toxicities in 5 DS-ALL patients (5/9; 55.6%). The cases of toxicities included: 2 pancreatitis, 9 hepatotoxicity, 1 thromboembolism, and 1 hypoglycemia. All four patients with NCI HR DS-ALL experienced PEG-associated toxicities. No patient with DS-ALL experienced HSR compared to 19 (27.9%) of the non DS-ALL,  $p=0.10$ . One patient with DS-ALL had accelerated PEG clearance. Mean asparaginase activity (AA) level at 7-10 days was 0.82 IU/ml for DS-ALL versus 1.05 IU/ml for non DS-ALL,  $p=0.05$ . By days 10-14, the AA was 0.57 IU/ml for patients with DS-ALL and 0.69 IU/ml for non-DS-ALL,  $p=0.25$ .

**Conclusions:** There were no HSR to PEG in patients with DS-ALL premedicated with H1 and H2 blockers. Patients with DS-ALL achieved therapeutic AA, with exception of one who experienced accelerated clearance. Five (55.6%) patients with DS-ALL experienced Grade  $\geq$  3 PEG-associated toxicity, with 4 being NCI HR. We recommend research in a larger population to confirm these findings.

EP208/#1230 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### ROLE OF INTERLEUKIN-6 AS AN EARLY PREDICTOR OF BACTEREMIA IN FEBRILE NEUTROPENIA AMONG THE CHILDREN WITH ACUTE LEUKEMIA

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**Background and Aims:** Culture is the gold standard method for detection of bacteria but is time consuming. Studies showed that Interleukin-6 may have the properties to act as an early and convenient marker in predicting bacteremia among children with hematological malignancy with febrile neutropenia. This study was aimed to determine the role of Interleukin-6 in predicting bacteremia in febrile neutropenia in children with acute leukemia.

**Methods:** This cross-sectional study was conducted at the department of Department of Pediatric Hematology and Oncology, Bangabandhu Sheikh Mujib Medical University (BSMMU) on 50 children with acute leukemia who developed febrile neutropenia Following informed written informed consent from parents or guardians, a detailed history and thorough clinical examination were carried out along with relevant investigations

**Results:** Mean age of the study patients was  $5.96 \pm 3.69$  (SD) years with male predominance (62% male and 38% female). Of all, 46% of the patients had microbiologically documented infection (MDI), 30% had clinically documented infection (CDI) and 24% had fever without focus (FWF). Among the isolated organism of patients with MDI, 69.56% were gram-negative (*Pseudomonas*, *Serratia*, *Klebsiella*, *Escherichia coli*, *Acinetobacter*). Mean rank of Interleukin-6 among the patients with MDI, CDI and FUO were 34.65, 21.83 and 12.54. Interleukin-6 was statistically higher among patients with microbiologically documented infection ( $p < .001$ ). In ROC curve, Interleukin-6 showed 87% sensitivity, 76% specificity at a cut-off value of 141.95 pg/mL with an area under curve.843. An increasing level of interleukin-6 showed significantly higher Odds for occurrence of bacteremia according to both univariate [OR 1.004, 95% CI (1.001-1.006),  $p < .05$ ] and multivariate logistic regression [OR 1.004, 95% CI (1.001-1.007),  $p < .05$ ]. No difference of Interleukin-6 was observed between the gram-positive and gram negative bacteremia patients ( $p \geq .05$ ).

**Conclusions:** According to this study findings interleukin-6 might play a crucial role in predicting bacteremia among febrile neutropenic

patients with acute leukemia. However, further multi-center case control study is recommended.

EP209/#1710 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### TREATMENT OUTCOMES OF ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) AND MAGNITUDE OF ALL RELAPSE IN CHILDREN TREATED AT TIKUR ANBESSA SPECIALIZED HOSPITAL (TASH), ETHIOPIA

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**Background and Aims:** ALL is the commonest childhood cancer globally with an overall survival (OS) rate above 80% and cumulative relapse of 10 -15% in high-income countries but remains significantly lower in low income countries. There is paucity of data with regard to ALL OS and event-free survival (EFS) outcomes in Ethiopia. TASH conducted a retrospective cross-sectional study to assess treatment outcomes and relapse.

**Methods:** All cases from January 1, 2014 to December 30, 2019 were included in the study. Data were analyzed using SPSS version 26. Descriptive analysis was used to summarize data, and the Kaplan-Meier method was applied to estimate probabilities of survival. EFS and OS were compared with the log-rank test. A p-value <0.05 was considered significant. Narratives, tables and figures were used to present the results.

**Results:** One hundred sixty four children were analyzed. Median age was 6 years, males accounted for 66.5% and male to female ratio was 2:1. Seventy-five percent presented within 8 weeks of symptoms. According to NCI Risk Stratification, 49.4% and 50.6 % were standard and high-risk ALL, respectively. The induction mortality was 14.7%. EFS at 1 and 3 years were 64% and 54%. The OS at 1, 3 and 5 years were 79 %, 62 %, and 55 % respectively. Age above 10 years, male sex, high- risk and treatment discontinuation were associated with mortality. Relapse rate was 21.4%. Isolated BM relapse was 63.3%, followed by isolated CNS relapse (16.7%). ALL relapse induction mortality was 28% and OS at 3 years was 39%.

**Conclusions:** The 5- years OS rates of children with ALL was 55%. Age above 10 years, male sex, and high- risk were statistically associated with mortality. ALL relapse was 21.4% with higher re-induction

mortality. Pediatric ALL treatment outcomes were low but better than anticipated.

EP210/#971 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### INVESTIGATING BACTERIAL CHAPERONE HIGH-TEMPERATURE PROTEIN G (HTPG) DURING INDUCTION CHEMOTHERAPY IN PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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**Background and Aims:** Bacteria in the gastrointestinal tract (GIT) contain heat shock protein (HSP) genes, which allow them to respond to environmental stresses and help maintain cell homeostasis. One HSP is HtpG, a homolog of eukaryote HSP90. HSP90 plays an important role in growth and survival of cancer cells. Understanding how the microbial HSP gene community changes with treatment is important in understanding if bacterial HSPs could be important to the tumor microenvironment and leukemia treatment.

**Methods:** We examined bacterial chaperone HtpG gene abundance using shotgun metagenome sequence data in 48 stool samples from 30 pediatric patients with ALL. Following ethics approval, samples were collected pre-treatment (13 samples, 13 patients) or during induction-therapy (35 samples, 23 patients). Days from chemotherapy start and antibiotic use were collected. Taxonomic composition, and Shannon diversity was assessed from each sample. Data was normalized to account for differences in sequencing depth. We used Wilcoxon test to assess differences in means between pre-treatment and induction samples, and linear models to examine relationships between days of induction and HtpG gene count and taxa.

**Results:** Between pre-treatment and induction samples we identified a significant decrease in mean counts of HtpG ( $p=0.0024$ ), while we did not find significant differences in Shannon diversity ( $p=0.28$ ), or taxonomic levels (phyla, family, or species  $pBH>0.05$ ). HtpG gene counts also decreased significantly ( $F=12.8$ ,  $p=7.5e-4$ ,  $R^2=0.27$ ) as did Bacteroidetes ( $F=18.5$ ,  $pBH=8.6e-4$ ,  $R^2=0.34$ ) with days in induction.

**Conclusions:** HtpG genes were decreased over induction therapy, likely the result of decreased Bacteroidetes due to chemotherapy as these bacteria carry multiple copies of this gene. This may result in reduction of circulating bacterial HtpG. As HtpG responds to environmental stress which may occur as a result of leukemia we recommend further study of HtpG in children with leukemia and its relevance as a possible marker of disease.

EP211/#1022 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
Acute Lymphoblastic Leukaemia

### A SURVEY OF CLASSES OF ANTIBIOTIC RESISTANCE GENES IN THE GUT MICROBIOME OF PEDIATRIC PATIENTS WITH LEUKEMIA AND LYMPHOMA

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**Background and Aims:** Cancer treatment increases risk of infectious complications in children with leukemia and lymphoma.  $\beta$ -lactam and glycopeptide antibiotics are frequently used to treat infections in this susceptible population. However, the use of antibiotics can result in an increase in antibiotic resistance genes (ARGs) in the microbial resistome, which increases the potential for antibiotic resistant bacteria. We surveyed the gut microbiome resistome of pediatric patients with leukemia and lymphoma to assess which antibiotic classes and ARGs were present in this vulnerable population.

**Methods:** After ethics approval, we compared shotgun metagenome sequence data from 127 stools samples collected at various time-points before and during chemotherapy treatment from 39 pediatric patients with leukemia and lymphoma to a pediatric oncology ARG database previously generated in our group. Stool sample sequences were mapped to the database, and those with  $\geq 60\%$  identity to ARGs were included in our survey. ARGs identified were assigned to antibiotic classes using the comprehensive antibiotic resistance database. We classified ARGs for  $\beta$ -lactam related antibiotics as a single class ( $\beta$ -lactams) and ARGs for multiple unrelated antibiotic types as multidrug.

**Results:** The 39 patients include 22 males and 17 females, with 29 patients over the age of 3 and 10 patients under 3. We identified 264 ARGs spanning 24 antibiotic classes present in at least 1 of the 127 patient samples. Most ARGs (n=93) were in the multidrug class, followed by  $\beta$ -lactam (n=24), aminoglycoside (23), glycopeptide (n=23), tetracycline (n=22), peptide (n=14) and fluoroquinolone (n=11) classes. For the remaining 17 antibiotic classes, between 1 and 7 ARGs were identified.

**Conclusions:** It is understandable, yet concerning, that 53% of all ARGs identified were within the multidrug,  $\beta$ -lactam and glycopeptide antibiotic classes. Further investigation is essential to understand gut microbial dysbiosis and the impact of chemotherapy on ARGs in relation to treatment related infections.

EP212/#260 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
Acute Lymphoblastic Leukaemia

### A COST-EFFECTIVE METHOD FOR MONITORING HIGH DOSE METHOTREXATE IN RESOURCE CONSTRAINED AREAS BY TESTING SLCO1B1 GENE

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**Background and Aims:** High dose methotrexate (HDMTX) is defined as methotrexate (MTX) dose of  $> 500\text{mg/m}^2$  which is given in hematological malignancies. It causes serious toxicities in 10-12% patients which requires serum MTX level monitoring. It is unavailable and unaffordable in many centers, so HDMTX was either avoided or given compromised doses. The SLCO1B1 gene studies showed that it predicts HDMTX toxicity. We studied whether SLCO1B1 gene can be utilized in patients receiving HDMTX without MTX monitoring

**Methods:** Its a retrospective study of patients with acute lymphoblastic leukemia (ALL), Burkitts lymphoma (BL) treated at our center from January 2020 to April 2022. Serum SLCO1B1 gene was tested prior to HDMTX therapy. Patients with functional gene received HDMTX and vice versa. Serum MTX level was not tested, but daily serum creatinine, potassium and clinically monitored

**Results:** The study included 25 patients, among 15 (60%) were males and 19 (76%) were  $< 18$  years. Patients with B ALL, were 14(56%), T ALL were 8(32%), and BL were 3(12%). The SLCO1B1 gene was functional (low risk of toxicity) in 21(84%) patients. HDMTX was given in 21 (84%), and avoided in 4 (16%) patients due to nonfunctional gene. The HDMTX related grade 3 or 4 mucositis was seen in 1 (5%) patient, nephrotoxicity with AKIN stage I in 1 (5%) and II in 2(9%) patients. But no grade 3 or 4 hematological toxicities, hepatic toxicity, sepsis and mortalities. HDMTX toxicities were managed with further hydration, leucovorin until normalized. The cost of SLCO1B1 testing was 50 USD, and the entire cost for MTX monitoring in consolidation per patient was 1505 USD. The cost saving by SLCO1B1 gene testing and avoiding MTX level testing was 1455 USD per patient

**Conclusions:** By utilizing SLCO1B1 gene, HDMTX can be safely given without MTX level monitoring. It is cost effective and alternative method in resource constrained areas

EP213/#164 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
Acute Lymphoblastic Leukaemia

### PROGNOSTIC AND PHARMACOTYPIC HETEROGENEITY OF HYPERDIPLOIDY IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA

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**Background and Aims:** High hyperdiploidy is the largest subtype in childhood acute lymphoblastic leukemia (ALL), and is typically associated with highly favorable outcomes. However, there is significant biological and prognostic heterogeneity across this large subtype, and the optimal definition of hyperdiploidy remains uncertain. Moreover, the pharmacological basis of this heterogeneity remains poorly understood. We therefore aimed to comprehensively compare the survival outcomes across various definitions of hyperdiploidy, and to determine the correlations of hyperdiploidy with drug sensitivity profiles to uncover the basis of their prognosis.

**Methods:** We analyzed survival outcomes of two Total Therapy ALL cohorts, across six different definitions of hyperdiploidy (chromosome number 51 to 67 (Chr51-67); DNA index (DI)1.16-1.6); UKALL low-risk hyperdiploid, trisomy of 17 and 18, or +17 or +18 without +5 and +20; single trisomy of 18; Double trisomy, trisomy of 4 and 10; and Triple trisomy (TT), trisomy of chromosomes 4, 10 and 17). We also characterized their ex vivo pharmacotypes across 8 main cytotoxic drugs of ALL therapy.

**Results:** Survival outcomes of 1,096 children were analyzed. In univariate analysis, compared to the remainder of B-ALL, TT was the most favorable criterion for event-free survival (10-year EFS 97.3% vs 86.8%,  $P=0.0003$ ) and cumulative incidence of relapse (10-year CIR 1.4% vs 8.8%,  $P=0.002$ ). In multivariable analysis accounting for patient numbers using the Akaike Information Criterion (AIC), DI1.16-1.6 was the most favorable criterion and had the best AIC for both EFS (hazard ratio [HR],0.45) and CIR (HR,0.45) while Chr51-67 had the worst AIC for both. Subgroups with favorable prognosis exhibited notable sensitivities to asparaginase and thiopurines. In particular, asparaginase sensitivity was linked to Chr 16 and 17, and mercaptopurine or thioguanine to gains of Chr 6, 10, 14, and 17.

**Conclusions:** Among different definitions of hyperdiploid ALL, DNA index has the strongest prognostic impact. Hyperdiploid ALL exhibited particular sensitivities to asparaginase, mercaptopurine, and thioguanine, with chromosome-specific associations.

EP214/#1782 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

### IMPACT THE POLYMORPHISMS RS7799039 THE LEP GENE AND RS1137101 THE LEPR GENE ON NUTRITIONAL STATUS AND PRESENCE OF ADVERSE EVENTS IN PATIENTS WITH PEDIATRIC ALL

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**Background and Aims:** Acute lymphoblastic leukemia (ALL) is the most common pediatric malignancy. Dysregulation of adipokine pathways is implicated in carcinogenesis. Leptin shows both proinflammatory and anti-inflammatory properties, has been associated with protection against lethality induced by LPS or TNF $\alpha$ , and it has been reported that leptin levels are increased in ALL and that an insufficient increase is a risk factor. unfavorable outcome (death) in states of acute systemic stress. The objective was to associate the presence of polymorphisms rs7799039 of the *LEP* gene and rs1137101 of the *LEPR* gene with nutritional status and the presence of adverse events in pediatric patients with ALL.

**Methods:** 59 patients with ALL treated at the State Cancer Center of Durango were studied. It was approved by the Research Ethics Committees of the General Hospital of Durango and the State Cancer Center. Nutritional status was estimated by BMI and genotyping by qPCR.

**Results:** The most frequent sex was male with 35 cases and 24 female. The global nutritional status was; 60% normal nutritional status, 23% overweight, 6% obesity and 11% malnutrition. Lethality was associated with the rs7799039 GA genotype of the *LEP* gene in males ( $p<0.01$ ) and GG in females ( $p<0.05$ ), with malnutrition ( $p<0.01$ ) and with the presence of moderate adverse events in males ( $p<0.01$ ). The presence of the G allele of the rs1137101 polymorphism of the *LEPR* gene was associated with survival ( $p<0.05$ ) and mild to moderate adverse events in both sexes ( $p<0.05$ ).

**Conclusions:** The rs7799039 GA polymorphisms is associated with overweight and obesity, it is a risk factor for lethality and the presence of moderate adverse events in men. The rs1137101 polymorphisms is not associated with nutritional status, genotype GA/GG is associated with survival and mild to moderate adverse events in both sexes.

EP215/#1833 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

**DEVELOPING AN ACUTE LYMPHOBLASTIC LEUKEMIA  
 TREATMENT PROTOCOL IN A MIDDLE-INCOME COUNTRY  
 WITH NATIONAL DISPARITIES**

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**Background and Aims:** The treatment of acute lymphocytic leukemia, standardized in Brazil since the 1980s with the efforts of the Brazilian Group for the Treatment of Childhood Leukemia (GBTLI), improved survival from 25% in 1980 to 68% in 1999, remaining stable since then. In 2005, through a partnership with SJCRH, a protocol was developed in a single center in northeastern Brazil, considering local difficulties (RE-ALL 05), improving survival rates from 68% to 82%. We describe a strategy for implementing the new national protocol, assessing lessons learned from the development of RE-ALL 05 and the six ALL GBTLI studies.

**Methods:** To develop the new ALL GBTLI protocol, onco-hematologists from all Brazilian regions met with colleagues from St. Jude and Ospitale San Geraldo and reviewed the long-term results of the ALL GBTLI 2009 and RE-ALL 05 protocols. They identified opportunities for improvement and adapted the treatment according to regional resources. Partnerships ensured a minimal high-quality diagnostic was available. The Brazilian Society of Pediatric Oncology, St Jude Global, Keira Grace Foundation, and Confederation of Foundations of Brazil (CONIACC) supported a data managers project.

**Results:** Hospitals from all regions requested participation in the Brazilian protocol (n=62). As of February 2023, 25 hospitals have completed the regulatory process and are recruiting patients. In addition, a group of experts meets weekly online to discuss cases in real-time. Twenty-nine patients were already included from January 1st, 2023, to March 20th. 55% male, mean age of 5 years old. This preliminary small sample's median white blood cell count is 31.610 for B cells and 112.920 for T cell patients

**Conclusions:** Implementing a collaborative protocol in a country of continental dimensions and immense social/economic disparities is challenging, but it provides local specialists with opportunities for collaboration and learning.

EP216/#1621 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

**CHROMOSOME 1 ABNORMALITIES IN CHILDHOOD  
 B-LYMPHOBLASTIC LEUKEMIA – AN ANALYSIS WITH RESPECT  
 TO CLINICAL VARIABLES AND SURVIVAL OUTCOME**

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**Background and Aims:** Chromosome 1 abnormalities (C1As) are common genetic aberrations in hematological malignancies. We sought to evaluate the significance of these abnormalities with reference to clinical characteristics and survival outcome in a pediatric B-Lymphoblastic Leukemia (B-ALL) cohort.

**Methods:** This is a retrospective, observational study conducted in hematology department of Indus Hospital and Health Network. Following ethical approval, the hospital's electronic medical record was reviewed from October 2020 to July 2022. Data extracted for childhood B-ALL cases exhibiting C1As. Chromosome analysis performed on Cytovision MB8 using G-banded metaphases derived from unstimulated bone marrow culture. Results were recorded according to the International System for Human Cytogenetic Nomenclature (ISCN-2020). Data analyzed using SPSS, version 24.0.

**Results:** C1As were observed in 60/450 (13.3%) cases of B-ALL. Among C1As, 29 (48%) cases had t(1;19). There were 13 (45%) balanced and 16 (55%) unbalanced translocations. The aberrations without t(1;19) were seen in 31 (52%) cases including 1q duplication with concomitant hyperdiploidy and complex karyotype in 14 (45%) and 4 (13%) cases respectively. The median age for C1As with and without t(1;19) was 8 years vs. 6 years (p=0.018) while the median leukocyte count was  $32 \times 10^9/L$  vs.  $17 \times 10^9/L$  (p=0.042). Disease-free survival (DFS) for cases with t(1;19) was 72% (62% vs. 81% in balanced vs. unbalanced translocations) while it was 74% for cases without t(1;19). Median follow-up was 14 months.

**Conclusions:** C1As are widely studied in multiple myeloma and solid tumors however, data are limited in childhood B-ALL. Our study demonstrates that this genetic aberration often occurs within this entity. The high frequency of 1q duplication and the survival difference in the balanced and unbalanced t (1;19) are

the study highlights, hence justify large-scale studies for further insight.

EP217/#1630 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
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### HEMATOLOGICAL PROFILE, CLINICAL CHARACTERISTICS AND POST INDUCTION REMISSION STATUS OF MIXED PHENOTYPE ACUTE LEUKEMIA, A RARE AND CHALLENGING ENTITY

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**Background and Aims:** Mixed-phenotype acute leukemia (MPAL), is a heterogenous group of leukemias recognized by the WHO Classification as a rare subtype, comprising  $\leq 4\%$  of all leukemias. Given the rarity of the disease, the diagnosis and treatment are extremely challenging particularly for low middle income countries. Controversies exist globally with no consensus on the best approach to manage this subgroup. We aimed to determine the diagnostic profile and early outcome in terms of post induction remission status in our settings.

**Methods:** A retrospective study included all newly diagnosed cases of MPAL, aged 1-17 years from January 2020 to September 2022. Diagnosis was established using 8-color flowcytometry on peripheral blood or bone marrow aspirate (BMA). NCI criteria used for initial risk-based induction chemotherapy according to modified BFM protocol. In B/myeloid cases, post induction (day 35) MRD was performed by flowcytometry. Remission status of T/myeloid was determined by morphological assessment of day 35 BMA.

**Results:** Total 30 cases of MPAL with median age 7.5 (IQR 3-12 years) were included. T/myeloid and B/myeloid were 17 (57%) and 13 (43%) respectively. Cytochemical MPO was positive in 12/30 (40%) cases while 100% cases were MPO positive by flowcytometry. Cytogenetic aberrations were observed in 23% cases of B/myeloid and BCR-ABL1 by FISH in two cases (7%). All patients were treated with ALL protocol, two were shifted to AML protocol while two were kept on palliative care. In B/myeloid, post induction MRD was positive in 7/9 (54%) cases; it was not applicable in 4 cases due to abandonment and induction death. Three cases of T/myeloid and 1 case of B/myeloid showed induction failure.

**Conclusions:** T/myeloid was found to be higher in frequency with inferior outcome as compared to B/myeloid cases. No significant association observed with clinical characteristics and cytogenetics. Remission status was decisive in re-stratification and appropriate protocol selection of MPAL patients.

EP218/#1653 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
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### CD4+ T CELL CYTOKINE IMBALANCE ON CASES OF PEDIATRIC ACUTE LEUKAEMIA IN MAPUTO, MOZAMBIQUE

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**Background and Aims:** CD4+ T cells play a major role in controlling the proliferation of leukemic cells and also modulating the immune response with the secretion of cytokines which controls cell recruiting and activation. The present study aims to evaluate the CD4+ T cell cytokines balance in pediatric subjects with Acute Leukemia (AL).

**Methods:** Bone marrow (BM) and peripheral blood (PB) samples of diagnosis of 82 patients from Hemato-Oncology Pediatric Service at Maputo Central Hospital, was used for the analysis of Th1, Th2, and Th17 cytokines (INF- $\gamma$ , TNF- $\alpha$ , IL-1 $\beta$ , IL-2, IL-4, IL-5, IL-6, IL-17, IL-2, IL-10, and IL-21) by Luminex assay as mean fluorescence intensity (MFI). Patients were aged below 14 and grouped as negative (n=41) or positive (n=51) cases of AL, and 56% of them were diagnosed with AL Lymphoblastic Type B (ALL-B). Information regarding group risk and the number of deaths was collected for positive cases. The ratio between cytokines was determined to study Th1/Th2 and Th1/Th17 balance. Association and correlation between variables were assessed using Man Whitney and Spearman Rank, tests respectively.

**Results:** No differences were found between cases positive and negative for AL when comparing the median MFI of single cytokines for both BM and SP samples ( $p > 0.05$ ). BM samples of positive cases of AL presented a higher median ratio of TNF $\alpha$ /IL-10 ( $p = 0.024$ ) and TNF $\alpha$ /IL-21 ( $p = 0.003$ ) when compared to negative cases. Thirty-seven deaths (45.12%) were reported during the study period and were found to have a higher BM median MFI ratio of TNF $\alpha$ /IL-10 compared to survivors ( $p = 0.0125$ ) and no differences were found between groups on the PB samples.

**Conclusions:** Study findings suggest a Th1/Th2 and Th1/Th17 cytokine imbalance with a decrease of Th1 cytokine in cases with AL. There is evidence of an association between TNF $\alpha$ /IL-10 ratio and AL disease diagnosis and outcome.

EP219/#1125 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
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OUTCOMES OF ACUTE LYMPHOBLASTIC LEUKEMIA PEDIATRIC PATIENTS WITH MINIMAL RESIDUAL DISEASE REEMERGENCE TREATED WITH A CONSERVATIVE APPROACH: A RETROSPECTIVE STUDY

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**Background and Aims:** The reemergence of acute lymphoblastic leukemia (ALL) after achieving complete remission (CR) remains an unresolved issue in clinical practice, as there are no guidelines for management if diagnostic relapse values are not reached. This study assessed the outcomes of patients with reemergence who were treated conservatively.

**Methods:** A retrospective analysis of ALL patients treated at our center, diagnosed between 2010 and 2020, was conducted. Reemergence was defined as disease reappearance after achieving CR with negative minimal residual disease (MRD), detected by flow cytometry (FC) or molecular studies using PCR, below 5%. Reemergence detected within the first six months post-hematopoietic stem cell transplantation (HSCT) or post-CAR-T were excluded, as they have specific management.

**Results:** Out of 255 ALL patients, 20 experienced reemergence. Four occurred in the context of extramedullary relapse, one reached relapse cut-off levels in the second evaluation, two occurred in pre-HSCT evaluation, and 13 achieved negative MRD again without changing their initial treatment and without receiving transplantation. Examining the characteristics of these 13, detection was performed by FC in 11 cases (median MRD 0.04%) and molecular study in 2. Seven patients had B-cell ALL, five T-cell ALL, and one ambiguous lineage. None had high-risk cytogenetic rearrangements. Two patients experienced relapse (median of 22 months), with one dying due to progression. The overall survival of the 13 relapses treated with conservative approach was 92% with a mean follow-up of 8.2 years from diagnosis.

**Conclusions:** This is the first study to show the follow-up of MRD reemergence managed conservatively. Data suggests that closely monitoring MRD without modifying treatment may be safe and effective in patients without reaching relapse cut-off levels (MRD >5%). However, validation requires a prospectively designed study with a homogeneous and systematic MRD follow-up after CR, including

patients with risk cytogenetics, who inherently have a higher risk of relapse.

EP220/#1477 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
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FEASIBILITY OF CENTRALIZED ACUTE LYMPHOBLASTIC LEUKEMIA TESTING IN MEXICO IN ALLIANCE WITH ST. JUDE (MAS) INSTITUTIONS THROUGH A QUALITY IMPROVEMENT METHODOLOGY APPROACH

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**Background and Aims:** The Bridge Project (BP) is a multi-site collaboration and quality improvement project to centralize diagnostic studies for children with suspected acute lymphoblastic leukemia (ALL) within the Mexico in Alliance with St. Jude (MAS) collaborative group. It has exposed the variability of techniques used to obtain samples, packaging, and shipment processes. We present the results and experiences of four of the fifteen participating institutions that have implemented the Quality Improvement (QI) methodology to achieve standardization.

**Methods:** We utilized the Model for Improvement: defined aim, theory of change, a family of measures, and iteration for improvement through Plan-Do-Study-Act (PDSA) cycles. Patient samples were shipped from the treatment facility to the central laboratory. Upon arrival, the laboratory evaluated the samples against 14-item criteria (9 critical and 5 non-critical based on the impact on sample viability/reliability) and collected de-identified information in a database. Hospitals designed and registered PDSA cycles to decrease the number of errors.

**Results:** We collected data from 327 patients with suspected ALL from four institutions from June 2019 to February 2023. All patients benefited from a complete diagnostic report; 273 (83%) cases were confirmed ALL and 844 samples were shipped. After the QI intervention in January 2021 we observed improvement in most outcome, process, and balance measures. We documented a reduction in prevalent critical errors; 7% in labeling and temperature and 8% in volume.



Participants reported high satisfaction with the project (>90%). Successful QI change ideas were registered in a repository to guide implementation in new participating centers.

**Conclusions:** Our results show that centralization of specialized diagnostic services is feasible, can effectively build local capacity, standardize the process of sample procurement, packaging, and shipment, and increase access to a standardized diagnostic panel for children with suspected ALL. A replica of the model across other specialized laboratories in Mexico is underway.

EP221/#268 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
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### SIGNIFICANT DOSE REDUCTION IN MERCAPTOPYRINE (6MP) AND METHOTREXATE (MTX) REQUIRED IN CHILDREN WITH ALL FROM TWO POPULATIONS IN ASIA

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**Background and Aims:** Antimetabolite therapy remains the backbone of ALL maintenance. Low tolerance of recommended doses in patients from the Middle East and South Asia has been anecdotally reported. This study provides real-life data from two distinct populations.

**Methods:** Mean weekly doses of oral 6MP and MTX for children diagnosed with ALL from 2011-2015 at KFMC, Riyadh and AKUH, Karachi were retrospectively retrieved for weeks 1, 5 and 9 in maintenance cycles 2, 4 and 6. Platelet and neutrophil counts, toxicities, reasons for dose reduction, and patient outcome were collected. The dose quantum and trends and their association with survival and relapse were evaluated.

**Results:** For the 207 patients, (KFMC: 125; AKUH: 82) median [range] age at diagnosis was 56 months (4-195; KFMC 51 [4-169]; AKUH 63.5 [15-195]) and T-ALL accounted for 16.6%. Across 3 cycles the mean tolerated dose of 6MP was 43.3mg/m<sup>2</sup> (KFMC 44.74±16.59; AKUH 42.25±22.28) and for MTX was 13.2mg/m<sup>2</sup> (KFMC 16.93±3.03; AKUH 8.09±4.2). The mean tolerated dose increased over time for 6MP (40.1mg/m<sup>2</sup> to 47mg/m<sup>2</sup>; p<0.001), with proportion tolerating full dose (75 mg /m<sup>2</sup> for 6-MP, 20 mg/m<sup>2</sup> for MTX) increasing from 7.2% to 22.2% (p<0.001); for MTX dose increased from 12.3mg/m<sup>2</sup> to 14mg/m<sup>2</sup> (p<0.001) with 15.5% to 29% (p<0.001) tolerating full dose. Neutropenia was the main reason for reduced doses: only 12.6% had an ANC>1500. The 5-year RFS in KFMC/AKUH was 87.8% /88.0%, whereas OS in each of the hospitals was 93.8%. Continued dose reduction for 6MP or MTX due to neutropenia at cycles 4 and 6 seems not to infer a relapse or survival disadvantage.

**Conclusions:** Significant dose reductions during maintenance are needed in this population to maintain appropriate neutrophil and

platelet counts. Revised guidelines for dosing are suggested. Population based pharmacokinetics and genetic testing for polymorphisms in drug metabolism genes (e.g., TPMT; NUDT-15) is recommended.

EP222/#1892 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

### PULMONARY COMPLICATIONS AND OUTCOMES OF ACUTE LYMPHOBLASTIC LEUKEMIA IN A TERTIARY TEACHING HOSPITAL IN ADDIS ABABA, ETHIOPIA

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**Background and Aims:** Acute lymphoblastic leukemia (ALL) is the commonest malignancy of childhood. Pulmonary complications are frequently reported and could result in high morbidity and mortality. Phase of ALL treatment, absolute neutrophil count, duration of neutropenia, thrombocytopenia, malnutrition and timing of antimicrobial therapy are some of the factors associated with pulmonary complications. We present data on 97 ALL patients who presented with or developed pulmonary complications during treatment at Tikur Anbessa Specialized Hospital (TASH) between December 2019 to October 2020. TASH is Ethiopia's largest referral hospital, serving the nation's population of 120 million persons.

**Methods:** A cross-sectional study collected retrospective data from patient charts at the TASH pediatric oncology unit. All patients whose records met our inclusion criteria were reviewed. The data was analyzed using SPSS version 25 and summarized using descriptive statistics and tabular and graphic presentations. Binary and multiple logistic regressions were used to determine the statistical significance and independent association between independent and dependent variables.

**Results:** From 216 charts reviewed, 97 (45%) patients developed 103 pulmonary complications, including hyperleukocytosis, hemorrhage, edema, pneumothorax and pneumonia. Infections (bacterial, fungal and viral) accounted for 79.6 % (N: 82), followed by pulmonary edema 11.3% (N:11). Oxygen saturation levels below 90%, severe acute malnutrition, aspergillosis, and pulmonary hemorrhage were significantly and independently associated with mortality

**Conclusions:** Pulmonary complications are a source of morbidity and mortality in pediatric ALL patients. Infection and pulmonary edema constituted the majority of pulmonary complications in our ALL patients. Low oxygen saturation, malnutrition, aspergillosis, and

pulmonary hemorrhage were independent determinants of outcome. Early identification and timely management of pulmonary complications in ALL patients can significantly improve patient outcome.

EP223/#416 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
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#### GENETIC MUTATIONAL ANALYSIS OF MALAYSIAN CHILDREN WITH RELAPSED ACUTE LYMPHOBLASTIC LEUKAEMIA USING WHOLE EXOME SEQUENCING; A SINGLE CENTER EXPERIENCE

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**Background and Aims:** Relapsed acute lymphoblastic leukaemia (ALL) remains the cause of death in children with haematological malignancy. We aim to identify genetic biomarkers that could predict a high likelihood of relapse in Malaysian children with ALL through whole exome sequencing (WES).

**Methods:** DNAs were extracted from bone marrow and peripheral blood samples using QIAGEN AllPrep DNA/RNA Mini Kit. WES was performed using the Illumina NovaSeq-PE150 platform on paired blood samples collected at diagnosis and relapsed for two patients. The Panel of Normal (PoN) analysis was performed on diagnosis samples only for six patients who relapsed and relapsed samples only for four patients.

**Results:** Two paired samples had 806 somatic mutations with 390 single nucleotide variants (SNVs) and 416 InDels. There were 22 synonymous and 48 nonsynonymous SNVs. One of the patients had a pathogenic variant of the tumour suppressor gene, *TP53*. About 73 variants were identified in coding regions. SIFT and PolyPhen-2 scores showed that 21 genes were deleterious. Both patients have recurrent somatic SNV of *RPL10* which is reported as a recurrent somatic mutation in ribosomal proteins. Over 60% of somatic alterations identified in relapsed samples are not reported in dbSNP.

PoN analysis for four relapse samples revealed 7,081 somatic mutations with 6,500 SNVs and 581 InDels, with 20 frameshift deletions and 8 frameshift insertions found in coding regions. There were 417 synonymous and 809 nonsynonymous SNVs. Relapsed samples manifested about 19 alterations. Two of the four relapsed patients had recurrent somatic SNV of *FCGR3A*, which could be a potential

biomarker for cancer detection. Around 50% of somatic alterations identified in four relapsed samples are not reported in dbSNP. The study's main downside was its smaller sample size, which was further limited by the unavailability of samples at diagnosis and/or relapse.

**Conclusions:** Our preliminary findings indicated that *RPL10* and *FCGR3A* may contribute to ALL relapse.

EP224/#414 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
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#### OUTCOMES FOR CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA STRATIFIED FOR AGE: AGE IS NOT JUST A NUMBER!

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**Background and Aims:** It is well recognized that higher age at diagnosis is an adverse prognostic factor for Acute Lymphoblastic Leukemia and all current treatment protocols intensify treatment for this. It is also well appreciated that this subgroup has higher treatment-associated morbidity. Data from India for children aged 10-19 years is limited. This study aimed to assess the outcomes of this cohort with appropriately intensified treatment at a center in North India.

**Methods:** Retrospective audit of clinical details, clinical course and outcomes of all patients less than 10 years and 10-19 years treated from 2003-2021 was analyzed. Treatment was stratified for age with older children receiving 4-drug induction, BFM consolidation, and higher cumulative doses of Methotrexate and Asparaginase. Outcomes of interest were presence of high-risk factors such as white cell count >50,000, positive end-of-induction (EOI) minimal residual disease (MRD), treatment related mortality (TRM), event-free survival (EFS) and overall survival (OS).

**Results:** A total of 393 patients presented to the center of which 372 patients took complete treatment at this center and all follow up data was available. 279 were below 10 years of age. The M:F ratio was 1.8:1 vs 3.1:1 in the younger/ older cohort respectively (p 0.06). The proportion of patients with WBC >50,000 was similar. Patients > 10 years were more likely to have T-cell disease (p<0.001). Positive MRD at EOI was seen in 36% vs 17.4% in the older cohort of the patients for whom this data was available. The TRM was similar. The 5-year EFS was 84.1% vs 73.4% (P0.02), and OS 86.4% and 77.1% (p 0.013) of the younger and older cohorts respectively.

**Conclusions:** Despite intensifying treatment for age, children over 10 years of age had inferior outcomes. Treatment for this cohort needs to be further optimized in our setting.

EP225/#483 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
Acute Lymphoblastic Leukaemia

### IMPACT OF EARLY MORTALITY AND TREATMENT ABANDONMENT ON THE PROGNOSTIC VALUE OF MINIMAL RESIDUAL DISEASE AND IMMUNOPHENOTYPE IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA IN SUB-SAHARAN AFRICA

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**Background and Aims:** In acute lymphoblastic leukemia (ALL), immunophenotype and end of Induction (EOI) Minimal Residual Disease (MRD) are significantly prognostic. Data on these factors in sub-Saharan Africa (SSA) are very limited. We report outcomes of pediatric ALL in Malawi and evaluate the prognostic value of immunophenotype and EOI MRD.

**Methods:** We conducted a retrospective cohort study of children (<18 years) who received a risk-adapted treatment for ALL as per the UKALL2011 protocol, between 2016-2022, at Kamuzu Central Hospital, Malawi. Diagnosis was based on morphology, and immunohistochemistry or flow cytometry when available. Flow cytometry interpretation was by experts based in Texas and Uganda; MRD defined as <0.01%. Survival outcomes were described.

**Results:** A total of 118 patients were identified - 49 (41.5%) B-ALL, 27 (22.9%) T-ALL and 42 (35.6%) unspecified. Of the 61 patients with EOI MRD, 17 (28%) were positive. The 24-month OS and EFS for all patients was 51% and 41%. The OS was 52% in B-ALL vs. 65% in T-ALL ( $p=0.35$ ); with EFS of 39% vs. 45% respectively. For MRD negative, OS of 61% vs. 53% for positive, ( $p=0.37$ ); and EFS 47% vs. 48%, respectively. Sub-group analysis of MRD based on immunophenotype showed EFS of 67% (MRD negative) vs. 33% ( $p=0.04$ ) in B-ALL; and 71% (MRD positive) vs. 32% ( $p=0.07$ ) in T-ALL. Nineteen patients (16.1%) abandoned treatment, and 58 (49.0%) died - 33 (56.9%) occurring  $\leq 50$  days from diagnosis. Most deaths were treatment-related ( $n=47$ , 81.1%) and 11 (18.9%) died from disease progression. Median time-to-relapse was 16 months.

**Conclusions:** In B-ALL, EOI MRD was prognostic, but survival was unexpectedly higher in T-ALL. While immunophenotype and MRD remain prognostic, they may be limited by high early mortality and abandonment in low-resource settings. Therefore, current efforts in SSA should target addressing these factors to improve outcomes for ALL.

EP226/#1715 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
Acute Lymphoblastic Leukaemia

### INVESTIGATING THE TOLERANCE TO MAINTENANCE THERAPY AMONG PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS AND ITS POTENTIAL EFFECT ON TREATMENT OUTCOMES

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**Background and Aims:** Acute lymphoblastic leukemia (ALL) accounts for 70–80% of all leukemias in children. Despite the remarkable progress in ALL treatment with cure rates of over 80%, Low-and-Middle-Income-Countries register lower cure rates. Maintenance therapy backbone drugs; 6-Mercaptopurine (6MP) and Oral-Methotrexate (MTX), often cause neutropenia, necessitating dose reductions. Given the narrow therapeutic window, efficacious doses are close to toxic doses, raising concerns about dose reductions. Aim: To investigate tolerance to maintenance therapy; (6MP and MTX) among pediatric ALL patients by measuring the percentage of time each patient received 100% (6MP and MTX) during the first year (PTPM) and its potential impact on treatment outcomes.

**Methods:** A retrospective treatment chart analysis of patients' first-year maintenance therapy at Mulago National Referral Hospital, Uganda, following IRB approval. To control neutropenia, doses were adjusted based on neutrophil and platelet counts at each visit or review. PTPM was calculated.

**Results:** Enrolled 46 Patients with ALL in first year of maintenance. Median age was six years. 74% patients were male, 26% female. The average-PTPM for our patients was 57% interquartile-range (IQR)(38–76). Only five patients (10%) had a PTPM of 100% in their first year of maintenance treatment. Escalation beyond 100% wasn't possible. For 37 (78%) patients in clinical remission (CR), the average-PTPM was 59.4, IQR (20–75). Whereas for 9 (22%) patients who relapsed (RP), average-PTPM was 49.9 IQR (39–77). The difference between PTPM for CR and RP wasn't significant. ( $U=138$ ,  $p=.44$ ,  $r=0.12$ .) Furthermore, the (median-PTPM for males was 55.88, slightly lower than the females' (median-PTPM (58.1). ( $U=192$ ,  $p=.775$ ,  $r=0.04$ .)

**Conclusions:** Tolerance among patients varies widely and tends to be lower than in previous studies conducted outside of Africa.

Consequently, more extensive research is required to investigate tolerance, as well as the correlation between relapse and dosage in Africa.

EP227/#1755 | Poster Topic: AS05 SIOP Scientific Program/AS05.a Acute Lymphoblastic Leukaemia

#### INVESTIGATING THE TOLERANCE TO MAINTENANCE THERAPY AMONG PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS AND ITS POTENTIAL EFFECT ON TREATMENT OUTCOMES

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**Background and Aims:** Acute lymphoblastic leukemia (ALL) accounts for 70–80% of all leukemias in children. Despite the remarkable progress in ALL treatment with cure rates of over 80%, Low-and-Middle-Income-Countries register lower cure rates. Maintenance therapy backbone drugs; 6-Mercaptopurine (6MP) and Oral-Methotrexate (MTX), often cause neutropenia, necessitating dose reductions. Given the narrow therapeutic window, efficacious doses are close to toxic doses, raising concerns about dose reductions. Aim: To investigate tolerance to maintenance therapy;(6MP and MTX) among pediatric patients with ALL by measuring the percentage of time each patient received 100% (6MP and MTX) during the first year (PTPM) and its potential impact on treatment outcomes.

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**Results:** Enrolled 46 ALL patients in first year of maintenance. Median age was six years. 74% patients were male, 26% female. The average-PTPM for our patients was 57% interquartile-range (IQR)(38–76). Only five patients (10%) had a PTPM of 100% in their first year of maintenance treatment. Escalation beyond 100% wasn't possible. For 37 (78%) patients in clinical remission (CR), the average-PTPM was 59.4, IQR (20–75). Whereas for 9 (22%) patients who relapsed (RP), average-PTD was 49.9 IQR (39–77). The difference between PTM for CR

and RP wasn't significant. (U=138, p=.44, r= 0.12.) Furthermore, the median-PTD for males was 55.88, slightly lower than the females' median-PTM (58.1).(U=192, p=.775, r=0.04.)

**Conclusions:** Tolerance among patients varies widely and tends to be lower than in previous studies conducted outside of Africa. Consequently, more extensive research is required to investigate tolerance, as well as the correlation between relapse and dosage in Africa.

EP228/#1600 | Poster Topic: AS05 SIOP Scientific Program/AS05.a Acute Lymphoblastic Leukaemia

#### FLOW-CYTOMETRY DEFINED REMISSION IN PEDIATRIC T-ACUTE LYMPHOBLASTIC LEUKEMIA CAUSES DURABLE REMISSIONS BUT INCURS HIGH TOXICITIES- EXPERIENCE FROM A LARGE TERTIARY CANCER CARE CENTER FROM INDIA

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**Background and Aims:** Pediatric T-Acute Lymphoblastic Leukemia (T-ALL) has good outcomes with contemporary protocols, however patients fare poorly if flow-cytometry (FCM)-defined Minimal Residual Disease (MRD) negative remissions are not achieved with initial intensive treatment, or relapsing disease within 3 years. Intensifying protocols to achieve and sustain remission also carry significant toxicities. We studied the impact of uniformly treated T-ALL at a single center on ICiCLE-2014 protocol

**Methods:** Consecutive children below 15-years with newly-diagnosed T-ALL between Jun 2018- March 2022 who completed evaluation and initiated treatment were included. Patient records were scrutinized for demographic data, disease/ host factors and outcomes. Next-Generation Sequencing (NGS) Panel was used for detecting somatic mutations in DNA extracted from bone marrow with an assay utilizing 1015 hybrid capture oligonucleotides. Sequencing was done on an Illumina Miseq using V2-300-cycle chemistry. Analysis was by descriptive statistics, Kaplan-meir method for survival, and statistical analyses using Jamovi-2021.v1.6.

**Results:** Of 224 eligible patients, 181(81%) were male at median age 8.6 yrs (range:0.5-15), 174(78%) were T-ALL, and the remaining Early-T-Precursor (ETP)-ALL. Median Leukocyte count was  $1.099 \times 10^5$ /mL, with 101(45%) having bulky disease, and 14(6%) with Central Nervous System (CNS) involvement at presentation. NGS available in 83(37%) patients revealed Notch1-24(34%), FBXW7-22(31%), RAS-pathway-10(14%), PHF6-13(18%), PTEN-8(11%), and others-15(21%) of those tested. While 97(44%) patients had MRD of 0.01% or more at

end-induction, only 5 remained positive by end-consolidation. Of 75 deaths or palliative outcomes 29(39%) were due to relapse/progression, while the remaining occurred in remission. At median 222.5 months follow-up Event-free (EFS) & Overall Survival (OS) were 69% and 76%, respectively. No impact was seen of diagnostic phenotype, bulky disease, or genomic profile on outcome.

**Conclusions:** Pediatric T-ALL remains difficult-to-treat with intensive chemotherapy resulting in adequate remissions of curative potential, but at the cost of significant toxicity. With high non-relapse mortality, prognostic significance of host and disease factors lose their predictive impact.

EP229/#1531 | Poster Topic: AS05 SIOP Scientific Program/AS05.A  
*Acute Lymphoblastic Leukaemia*

#### RELAPSES IN ACUTE LYMPHOID LEUKEMIA IN CHILDHOOD: EXPERIENCE OF A BRAZILIAN INSTITUTION AND ITS CHALLENGES

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**Background and Aims:** Relapse is the main reason for treatment failure in childhood acute lymphoblastic leukemia (ALL). Despite improvements in the ALL therapy, survival after relapse is still poor especially in low/middle-income countries.

**Methods:** This was a 5-year retrospective cohort study in a single Brazilian institute that aimed to estimate treatment outcomes and relapse rates of newly diagnosed ALL in children treated according to the IC-ALL Berlin-Frankfurt-Münster (BFM) 2009 as up-front protocol.

**Results:** Altogether, 8 patients (6.5%) relapsed out of 122 between 2018 and 2022 with a male-to-female ratio of 1,25:1. Here, 6 (75%) and 2 (25%) had B-cell and T-cell phenotypes, respectively. The cytogenetic risk factors are significant markers. The most common cytogenetic and molecular findings among our population was hyperdiploidy and t(12;21)(p13;q22), respectively. From patients with relapse, we noticed one patient with hypodiploidy. Moreover, in one case, *ETV6::RUNX1* was shown, which is considered a favorable prognostic factor. The relapse rate in the high-risk group was 1.6 times greater than in the intermediate-risk group (62.5% vs. 37.5%). The median time from diagnosis to relapse was 25 months (early relapses after 18 months of diagnosis occurred in 25% of patients, and late relapses after 36 months in 37.5%). Regarding the relapse site, isolated bone marrow (BM) was the leading site (75%). The 5-year event-free survival among all patients was 86% and the median post-relapse survival time was 5.4 months. Amid the relapse group, there was a

high incidence of deaths in the re-induction phase mostly related to infection, and only 37.5% of the patients was submitted to hematopoietic stem cell transplantation and are alive without disease.

**Conclusions:** In addition to limited access to immunotherapy for clinical remission with good performance status, a major challenge is still the reduction of re-inducing death with morbidity and mortality associated with treatment or opportunistic infections.

EP230/#779 | Poster Topic: AS05 SIOP Scientific Program/AS05.A  
*Acute Lymphoblastic Leukaemia*

#### PHYSIOTHERAPY NEEDS AND PERSPECTIVES OF PARENTS OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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**Background and Aims:** A Canadian children's hospital has been conducting a physiotherapy program to monitor the impact of cancer treatment on the physical function of children with acute lymphoblastic leukemia. The program has been successful in identifying deficits associated with chemotherapy; however, children with identified physiotherapy needs who are referred to the service do not always access care, and the reasons why are unknown.

**Methods:** Twenty parents of children undergoing or having completed chemotherapy treatment were recruited to complete a cross-sectional survey to gather data regarding (1) their views towards physiotherapy service delivery for their child, (2) existing barriers and facilitators to participation in physiotherapy, and (3) the best methods and time to introduce physiotherapy services. Survey questions were designed based on the Theoretical Domains Framework (TDF)— a tool to help apply theoretic approaches to behaviour change interventions. Survey responses were mapped to the component of the Capability, Opportunity, Motivation -Behavior Change (COM-B) Model.

**Results:** A total of 19 out of 20 parents have completed the survey. All parents indicated they would consider accessing physiotherapy for their child; however, resources such as convenient location (74%) and options for physiotherapy delivery (e.g., virtual: 47.4%) need to be in place. Fifty-two percent of parents would prefer their child to take part in physiotherapy during the maintenance phase of chemotherapy. While some parents identified availability of time and resources as facilitators to the delivery of their child's exercises at home,

others identified a lack of motivation without therapist support and distractions as barriers to the home environment.

**Conclusions:** Understanding parents' perspectives towards physiotherapy services is essential to help meet the needs of children with cancer. Results from this study will inform the design of a future physiotherapy intervention trial for children with acute lymphoblastic leukemia.

EP231/#544 | Poster Topic: AS05 SIOP Scientific Program/AS05.a Acute Lymphoblastic Leukaemia

### BLINATUMOMAB SINGLE CENTER EXPERIENCE

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**Background and Aims:** The survival rate for patients with LAL is 90% but unfortunately 20% of cases relapsed with a 50% OS in first relapse, worsening with the subsequent relapses. Blinatumomab is a monoclonal antibody designed to treat relapsed patients with the intention to reduce de MRD. This retrospective study shows the experiences of this drug in a single pediatric center

**Methods:** 10 patients were treated in Uruguay in Perez Scremini foundation in the period between March 2020 and October 2022. They were under 18 years old with the diagnosis of LAL B in first remission or relapsed. The main objective is to determine the overall free survival and the event free survival of this patient. The second objective is to determine adverse event according to CTCAE grading

**Results:** 10 patients were treated with a median age of 10 years old. All patients were submitted for the 28 days administration, half of the performed 1 cycle and the other half 2 cycles. 6 patients experience their first relapse, 1 relapse was lymphoid, another was an infant with a testicular relapse and 2 patients did it at first induction due to severe toxicity during induction. 80% experience adverse event, all were mild. 2 interrupted treatment. 9 out of 10 patients had complete remission, the lymphoid relapse was refractory. The OS was 80% and EFS 70%.

**Conclusions:** blinatumomab is a safe and effective option in children, especially those with positive MRD. In our experience most of patients experience a mild toxicity, most of them reaching complete remission. More studies need to be performed to determine the extramedullary setting and the utility to use it upfront in the cases of severe toxicity,

EP232/#1588 | Poster Topic: AS05 SIOP Scientific Program/AS05.a Acute Lymphoblastic Leukaemia

### EVALUATING THE USEFULNESS OF THE PEDIATRIC EARLY WARNING SYSTEM (PEWS) FOR PREDICTING CLINICAL DETERIORATION AND MORTALITY IN FEBRILE NEUTROPENIA

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**Background and Aims:** Children with febrile neutropenia are at high risk for rapid deterioration and mortality. PEWS is a bedside scoring tool associated with action algorithms that aid in the early identification of clinical deterioration in hospitalized children. Correlation between PEWS score to clinical deterioration

Correlation of PEWS with pSOFA score

Correlation of PEWS patients with adverse outcome with Serum Albumin

**Methods:** This is a prospectively done study between August 2022 to February 2023. Patients diagnosed with paediatric cancer admitted for febrile neutropenia (aged 0 - 18 years) and started on antibiotics as per institute protocol were enrolled. Clinical observations were done by PEWS four times a day from admission to discharge/death; standard protocol for blood count parameters; inflammatory biomarkers and antimicrobials were used. Standard diagnosis and treatment guidelines were followed.

**Results:** During study period, 44 febrile neutropenic episodes in 33 patients were evaluated. The median age was 8 years (range: 1 - 16 years). M: F ratio was 4:1. The most common primary diagnosis was BALL (59%) followed by AML (9%). Biochemical parameters revealed hyponatremia in 28 (63%), hypokalaemia in 11 (25%), hypoalbuminemia in 14 (31%) and low IgG in 3 patients. 95% of children were malnourished. 1 death was recorded in this study. The mortality rate for PEWS above 10 was 82%. The average PEWS score for 'recovered' cases is 0.98, whereas that for 'death' cases is 12.9 which was statistically significant. The correlation between the Average PEWS score and Albumin levels is -0.23. The negative correlation implies increasing albumin reduced the PEWS score. The correlation between the PEWS score and pSOFA score is +0.27; a positive correlation.

**Conclusions:** This score is simple to use and if found effective can be taken as the standard of care in children receiving treatment for febrile neutropenia. This would especially be helpful in low and middle-income countries with limited manpower, intensive care facilities and supportive care.

EP233/#1378 | Poster Topic: AS05 SIOP Scientific Program/AS05.a Acute Lymphoblastic Leukaemia

### L-ASPARAGINASE INDUCED PANCREATITIS DURING CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA THERAPY, A PROSPECTIVE STUDY FROM SOUTH INDIA

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### **Background and Aims:** L-ASPARAGINASE INDUCED PANCREATITIS DURING CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA THERAPY - A PROSPECTIVE STUDY FROM SOUTH INDIA BACKGROUND

L-Asparaginase is one of the integral drugs used in the induction and the reinduction phase of treatment of Acute lymphoblastic leukemia (ALL) in children. L-Asparaginase induced pancreatitis is seen in 2-18% of patients receiving L-Asparaginase during the treatment of ALL. This prospective study analysed the profile and outcome of L-Asparaginase induced pancreatitis during the treatment of childhood ALL.

**Methods:** METHODOLOGY All children (0-14 years) with newly diagnosed ALL treated between 1st June 2021 and December 30th 2022 were monitored for pancreatitis during the induction and reinduction phases with appropriate biochemical and radiological investigations. The toxicities were graded according to CTCAE.4.0. L-Asparaginase doses were temporarily withheld in Grade 2 pancreatitis and subsequent doses of L-Asparaginase were suspended in grade-3 /4 pancreatitis.

**Results:** A total of 132 children received L-Asparaginase during the study period in the 2 phases of chemotherapy. Eighteen children developed pancreatitis (13.6%) during the Induction period while none developed pancreatitis in the reinduction phase. The mean age of the children was 6.75 years with a male female ratio of 1:1.5. The mean Sr Amylase and Sr Lipase levels were 331.9 U/L (Range 142-2134 U/L) and 2251.83 U/L (Range 461-10,116 U/L) respectively. Radiological evidence of pancreatitis was seen in 7/18 (39%) of them. Five children developed grade 2(28%) and 6 children developed grade 3 toxicities (33%). All 7 children with grade 4 pancreatitis (39%) developed severe hemodynamic instability and sepsis while two among them died due to Candida sepsis and Acute respiratory distress syndrome respectively.

**Conclusions:** Children receiving L-Asparaginase during ALL therapy develop pancreatitis that can lead to raised Sr amylase/lipase with or without radiological evidence. Monitoring of biochemical parameters is of paramount importance for early identification of pancreatitis to guide further therapy.

EP234/#1202 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

### **INFLUENCE OF NUTRITIONAL STATUS OF CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA (ALL) ON TREATMENT OUTCOME AFTER COMPLETION OF INDUCTION**

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**Background and Aims:** *Background:* Malnourished and cancer influences both tolerance and response to treatment especially acute lymphoblastic leukemia. Malnutrition increases morbidity, mortality,

reduces the effectiveness of treatment and impairs the quality of life significantly. **Objective:** Assessment of the nutritional status and its influence on treatment outcome children with Acute Lymphoblastic Leukemia (ALL) before and after induction chemotherapy.

**Methods:** This prospective observational study included 72 children with ALL, aged 1-15 years, was conducted from January to December 2014 in the Department of Pediatric Hematology and Oncology, BSMMU. The anthropometric measurements, hematological and biochemical parameter were measured. Anthropometric indices are calculated using reference median as recommended by NCHS (WHO-2000), NHANES. Children < -2 SD below the reference median are considered as underweight (weight-for-age), stunted (height-for-age) and wasted (weight-for-height), MUAC for age (<-2SD) malnutrition, BMI for age <5<sup>th</sup> centile considered underweight respectively. The children got induction chemotherapy according to the UK ALL 2003 (modified) protocol.

**Results:** Among the study population, 18(39.1%) were underweight, 8(17.4%) were stunted, 16(34.8%) were wasted, MUAC for age 14(56.0%) and BMI for age 12(57.1%) were malnourished, 10.9% had low total proteins (<5.7g/dl), 37.0% low serum albumin (<3.2g/dL). Mean anthropometric measurements and biochemical parameters were higher among the survivors compared to non-survivors. Significant difference was found between the well-nourished and the malnourished group according to WAZ. Complications like febrile neutropenia, treatment delay, number of transfusion (PRBC) requirement were more in malnourished group.

**Conclusions:** Malnutrition is widely prevalent in children with ALL and a major determining factor in treatment planning, complications and final outcome.

EP235/#1867 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

### **PHILADELPHIA CHROMOSOME AND PH-LIKE ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN WITH CANCER: SINGLE-CENTER EXPERIENCE IN NORTH-WESTERN MEXICO**

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**Background and Aims:** In high-income countries (HIC), Philadelphia chromosome (Ph+) and Philadelphia-like (Ph-like) subtypes are present in 3-5% and 10%-15% of children with Pre-B Acute Lymphoblastic Leukemia (ALL), respectively. Higher incidence of Ph-Like ALL (~35%) has been reported in Hispanics in the U.S. Children with

Ph+/Ph-like ALL experience poor outcomes. However, using tyrosine-kinase inhibitors can increase overall survival (OS) to >70%. There is scarce data on OS in children with Ph+/Ph-like ALL in low-and-middle-income countries (LMIC). We describe OS in a cohort of children with Ph+/Ph-Like Pre-B ALL in Northwestern Mexico.

**Methods:** ALL cases in children aged 0-18 years from January 2013 to December 2022 were reviewed retrospectively. Clinical features and treatment data were collected. Kaplan-Meier was used to estimate OS.

**Results:** 148 children were diagnosed with Pre-B ALL during the study period. Chromosome and molecular analysis were performed in >90% of cases. Eleven patients (7%) were diagnosed with Ph+/Ph-like Pre-B ALL, of those 10 (91%) were males and 1 (9%) was female (Ph-like). Ph+ chromosome (BCR-ABL) was found in 6 patients and Ph-like abnormalities in 5 (CRLF2 rearrangements (n=2), ABL1-class rearrangements (n=2) and immunoglobulin heavy-chain rearrangement (n=1)). In addition to backbone high-risk chemotherapy, children with Ph+ ALL received Dasatinib (n=4) and Imatinib (n=2). Children with Ph-like ALL received Dasatinib (n=3), Ruxolitinib (n=1), and neither (n=1). Five-year OS was 57% for children with Ph+/Ph-like Pre-B ALL.

**Conclusions:** Ph+/Ph-like subtypes were less prevalent in our cohort compared to reports from HIC. In Mexico, data on OS for this population is lacking given very limited access to diagnostic panels and/or to targeted therapy. We show feasibility of providing state-of-the-art diagnosis and standard treatment with tyrosine-kinase inhibitors in children with Ph+/Ph-like ALL in a LMIC. Systematic detection and targeted therapy are needed to improve survival in children with Ph+/Ph-like ALL in LMIC.

EP236/#901 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### ANALYSIS OF TREATMENT AND OUTCOME OF RELAPSED ACUTE LYMPHOBLASTIC LEUKEMIA ACCORDING TO IMMUNOPHENOTYPE IN SPAIN

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**Background and Aims:** Relapse of acute lymphoblastic leukemia (ALL) is one of the leading causes of cancer death in children. The prognosis varies according to prognostic factors such as time to relapse, site of relapse and leukemia immunophenotype, being worse in ALL

with T immunophenotype (ALL-T) than in B cell precursor ALL (ALL-pB). Our aim was to compare the clinical presentation, treatment and outcome of children diagnosed with relapse of ALL in Spain, and to analyze whether the leukemia immunophenotype influenced the choice of treatment (standardized versus individualized).

**Methods:** Data were retrospectively collected from two registries: the "SEHOP-PETHEMA 2013" guideline and registry of the Spanish Society of Pediatric Hematology and Oncology (SEHOP) for first-line treatment of ALL, and the "SEHOP-PETHEMA 2015" guideline and registry for relapsed ALL. This later guideline was considered the standard treatment for relapse and patients undergoing alternative treatment were classified as individualized treatment. Risk-group allocation at relapse, treatment and indication for SCT were based on the IntReALL SR and HR trials (non-investigational treatment arms). Chi-square test and overall and event-free survival analysis (OS and EFS) were performed using R v3.3.0.

**Results:** A total of 110 cases were included, of which 88 (80%) were pB-ALL and 22 (20%) were T-ALL. Patients with T-ALL tend to be treated on an individualized basis (45.45% vs 25%, p=0.1037) without translating into survival improvements (OS 10% vs 21.2% p=0.363 EFS 25% vs 10% p=0.429). Patients with T-ALL obtained significantly worse OS (15.6% vs 48.7% p=0.001); EFS was also lower, although this difference was not statistically significant (17% vs 30.6%, p=0.069).

**Conclusions:** Treatment outcome of children with ALL after relapse is poor, particularly in T-ALL. Individualizing treatment approaches in T-ALL did not translate into a significant advantage and preclude the evaluation of results. Novel immunotherapy approaches in pB-ALL probably contributed to rescue patients after subsequent relapse.

EP237/#1301 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### CLINICAL AND GENETIC CHARACTERISTICS OF LEUKEMIA IN CHILDREN WITH DOWN SYNDROME: A RETROSPECTIVE STUDY

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**Background and Aims:** Children with Down syndrome (DS) have an increased risk of developing leukemia compared to the general population. We aim to assess clinical and genetic characteristics, treatment outcomes and complications in children with DS diagnosed with leukemia, at King Hussein Cancer Center in Jordan.

**Methods:** Between January 2017 and January 2023, we retrospectively reviewed medical records of children with DS diagnosed at our center. Data on demographics, clinical characteristics, laboratory



results, genetic testing, treatment outcomes, and complications were collected and analyzed the data using descriptive statistics.

**Results:** Between 2017-2023, 667 pediatric patients were diagnosed with acute leukemia, of those 13 had DS. Of the 13 children, 6 were female (46%) and the median age at diagnosis was 2.5 years (IQR, 1.7-3.4). Two had congenital heart defects. Diagnoses included B-ALL (N=8,62%), AML-M7 (N=3,23%), MDS (N=1,7.7%), and TAM (N=1,7.7%). Somatic mutations in GATA-1, GATA-2, TP53, KRAS, MPL, and RAD2 were detected by sequencing, and different combinations were found in 4 patients. Alterations affecting ETV6/RUNX1 or 2 were detected in 5, while trisomy 8 was detected in 2 patients. The median Follow-up was 1.9 years. At diagnosis, the median white blood cell count was 14k/microL (IQR,9-44). Eight patients achieved full remission after induction chemotherapy, while the remaining patients had residual disease either molecular (N=3) or morphological relapse (N=2). During therapy, complications included gram-negative bacteremia (N=4), gram-positive bacteremia (N=9), viral infections (N=5), fungal infections (N=1), ICU admissions (N=2), acute kidney injury (N=2), and grade III/IV mucositis after HDMTX (N=4). Towards the end of our study, only 1 patient had a relapse, 4 patients completed therapy, 6 were still undergoing treatment, and 2 were lost to follow-up.

**Conclusions:** Our study provides insight into clinical and genetic characteristics, as well as treatment outcomes and complications of children with DS with leukemia. Our study highlights the importance of careful monitoring and management of infections and other complications during therapy in this population.

EP238/#1645 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
Acute Lymphoblastic Leukaemia

#### IMPORTANCE OF KARYOTYPE AND FISH CORRELATION FOR COMPREHENSIVE DIAGNOSIS OF PEDIATRIC PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA: BRIDGE PROJECT MEXICO IN ALLIANCE WITH ST. JUDE COLLABORATION

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**Background and Aims:** In Mexico, approximately 7,000 children develop cancer each year. Of these, close to 40% are diagnosed with acute lymphoblastic leukemia (ALL). Genetic markers are relevant for diagnostic and prognostic research of hematological malignancies. Fluorescent in situ Hybridization (FISH) and karyotype contribute to the diagnosis, staging, and prognosis of hematologic malignancies. The Bridge Project is a Mexico in Alliance with St. Jude (MAS) initiative that aims to improve access to a consensus-derived diagnostic panel for children with suspected ALL in Mexico. We report the cytogenetic findings of karyotype and FISH panels and their importance in the diagnosis of Mexican patients with ALL.

**Methods:** Bone marrow samples of children with suspected ALL from participating institutions were processed in the Molecular Genetics laboratory of the Hospital Infantil Teletón de Oncología. Cell cultures for karyotyping were performed and FISH technique used an embedded B-cell lymphoid panel (KMT2A, ETV6/RUNX1, BCR/ABL1, TCF3/PBX1) and a T-cell lymphoid panel (KMT2A, BCR/ABL1, TLX1, TLX3, CDKN2A-TRA/D rearrangements).

**Results:** ALL was confirmed in 429 patients from July 2019 to February 2023. ALL-specific structural and numerical changes were identified. 49% of karyotypes were positive for at least one cytogenetic alteration. We found that hyperdiploidy (n=72) was the most common alteration, followed by complex karyotypes (n=44) and karyotypes related to non-common genetic alterations (n=41). FISH alterations were found in 70% of the samples; gene gains (n=115), t(12;21) (p13;q22) (n=69) and iAMP21 (n=40) were the most common alterations.

**Conclusions:** Complex karyotype and non-common genetic alterations findings in this study emphasize the karyotype diagnostic scope in pediatric ALL, being the only diagnostic methodology up to date capable of analyzing the whole genome within its resolution. FISH and karyotype techniques add diagnostic and stratification value in childhood ALL.

EP239/#778 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
Acute Lymphoblastic Leukaemia

### ANTIBIOTIC USE AFFECTS METABOLITE ABUNDANCES IN THE GUT OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS AND IS ASSOCIATED WITH TAXONOMIC AND FUNCTIONAL METABOLIC PATHWAY DIFFERENCES

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**Background and Aims:** The human gastrointestinal tract (GIT) microbiome consists of metabolically active microbial organisms and modulates host physiology. As the microbiome composition changes, abundances of GIT metabolites change and may have physiological consequences. Children with Acute Lymphoblastic Leukemia (ALL) receive treatments that alter the GIT microbiome, which could affect metabolism. This study aimed to examine stool samples from patients with ALL for metabolites that differed significantly with antibiotic use. Metabolites were assessed for associations with taxonomic and functional metabolic pathways.

**Methods:** After ethics approval, 43 stool samples from 17 pediatric patients with ALL treated at the IWK Health Centre in Halifax, Canada were assessed. Mass spectrometry was used to determine intensity of 159 metabolites. Linear models with covariate adjustment, corrected for multiple tests multiple tests ( $\alpha_{BH} < 0.05$ ), was used to assess metabolites that differed significantly with antibiotic use, while accounting for age and treatment intensity. Taxonomic and functional pathway abundance was determined from metagenome sequence data, and subsequently, associations with metabolites were determined using Spearman correlation ( $\alpha < 0.05$ ).

**Results:** With antibiotic use, 20 metabolites decreased and 9 increased significantly. Functional pathways that decreased with decreased metabolites included many degradation pathways. Those that increased with increased metabolites included several nucleoside and nucleotide biosynthesis pathways, and other biosynthesis pathways. In addition, Bacteroidetes and a subset of Firmicutes decreased with decreased metabolites. Actinobacteria, Proteobacteria and a different subset of Firmicutes increased with increased metabolites.

**Conclusions:** Antibiotic use significantly affects GIT metabolites in pediatric ALL patients. We found that the subset of metabolites with increased intensity with antibiotic use were associated with oral-related Firmicute and Actinobacteria taxa and biosynthesis pathways. The metabolites that decreased with antibiotics were associated with decreased Bacteroidetes and Firmicutes taxa and degradation pathways. Understanding how treatment impacts the GIT microbiome and

metabolome allows us to gain insight into short- and long-term health consequences.

EP240/#751 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
Acute Lymphoblastic Leukaemia

### MOLECULAR AND IMMUNE LANDSCAPE OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA IN ARGENTINE PATIENTS FROM THE ALLIC-GATLA-2010 PROTOCOL

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**Background and Aims:** Acute Lymphoblastic Leukemia (ALL) is a genetically heterogeneous entity. Its molecular features can be prognostic and set the basis for therapeutic decisions. We aimed to find clinically relevant biological signatures using a comprehensive molecular characterization of childhood B-ALL that includes features from both the leukemic cells and the tumor microenvironment (TME).

**Methods:** We studied single nucleotide variants (SNVs), fusion genes and CD20 isoform abundance in 39 patients recruited under the ALLIC-GATLA-2010 protocol. We analyzed the transcriptome of bone marrow samples at time of diagnosis. *RNAmut* was used to evaluate SNVs/InDels in 114 genes and 79 fusion genes. Discovery of fusion genes was complemented with *STAR-Fusion*. Variants were filtered based on an in-house pipeline. Quantification of isoforms was performed using *Salmon*. The immune component of the TME was estimated by *MIXTURE*, and the abundance of cytotoxic cells was assessed by a gene expression-based cytolytic score.

**Results:** We identified 20 SNVs/InDels in 14/33 patients. We found variants in *CREBBP*, *CSF3R*, *ETV6*, *TP53*, *ATM* and *DUX4* that were not previously described in ALL. We also detected 7 previously reported and two novel fusion genes in 11/33 patients. *CX3CR1*, *HAVCR2*, *CCL4*, *XCL2* and *IL7* RNA levels were increased in patients with high vs low cytolytic score ( $p\text{-val} < 0.05$ ); suggesting an inflammatory and exhausted phenotype. The abundance of CD20 RNA isoforms was highly variable among patients, including an isoform lacking the rituximab-binding epitope and non-coding variants.

**Conclusions:** We characterized SNVs and fusion genes in 19/33 (58%) of samples. The TME immune component showcased high heterogeneity among patients. The assessment of CD20 isoforms at diagnosis could be of clinical utility in the context of clinical trials including CD20-targeted therapies because it might identify non-responders or resistant patients.

EP241/#1092 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

**IMPACT OF LOW QUALITY ASPARAGINASE BIO-GENERIC  
 AND DRUG SHORTAGES ON TREATMENT OUTCOMES FOR  
 CHILDHOOD LEUKAEMIA IN LOW- AND MIDDLE-INCOME  
 COUNTRIES**

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**Background and Aims:** Asparaginase is a key component for the treatment of acute lymphoblastic leukemia (ALL), which affects 100,000 children per year in low- and middle-income countries (LMIC). Due to limited availability of the innovator native *E. coli* asparaginase, bio-generic formulations are used in LMIC, that vary in quality and therapeutic efficacy. We aim to highlight the impact of low-quality asparaginases on treatment outcomes.

**Methods:** Literature review of PubMed indexed articles from LMIC about different bio-generic asparaginase formulations that reported asparaginase activity, bioavailability, immunogenicity and outcomes.

**Results:** Seven publications met eligibility criteria and reported clinical and laboratory data. Three articles reported limited access to the innovator compound and subtherapeutic activity of generic *E. coli* asparaginases when compared to the innovator compound. One reported bioavailability of the biosimilar being 1/3 of that of the innovator asparaginase. One paper reported 19% incidence of clinical hypersensitivity with biosimilar native asparaginase. Increased incidence of allergic reactions with intravenous administration was described in one paper. Three studies showed the presence of multiple spurious host cell proteins in many of these generic *E. coli* asparaginases (as high as 37% of the total peptides identified by mass spectrometry). One study reported clinical outcomes, comparing generic against the innovator compound showing an 8% decrease in 3-year OS (91.8% vs 83.8%) and 3-year EFS (84.8% vs 76.1%).

**Conclusions:** Compared to the innovator, generic asparaginases show decreased asparaginase activity, low bioavailability, increased immunogenicity and poorer outcomes. Increasing access to high-quality asparaginases by use of innovator compounds and biosimilars by adequate regulatory oversight, quality control, and TDM of asparaginase activity would improve EFS and prevent 8000 relapses each year

among children with ALL in LMIC. This intervention alone would raise the global cure rate for childhood cancer by 2% and provide substantial impetus to reaching the 2030 targets of the WHO Global Initiative for Children with Cancer.

EP242/#1525 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

**OUTCOME OF RELAPSED CHILDHOOD ACUTE  
 LYMPHOBLASTIC LEUKEMIA (ALL) TREATED WITHOUT HSCT: A  
 REAL-WORLD EXPERIENCE FROM A TERTIARY CANCER  
 CENTRE IN SOUTHERN INDIA**

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**Background and Aims:** More than 50% relapsed paediatric ALL patients achieve long term remissions with salvage therapy including chemotherapy, hematopoietic stem cell transplant (HSCT) and immunotherapies in developed countries. However, in developing countries, access to paediatric HSCT and immunotherapy is limited. We looked into the clinical profile and outcomes of relapsed paediatric ALL patients treated at our centre with salvage chemotherapy.

**Methods:** We conducted a retrospective audit of relapsed ALL treated with BFM-REZ-90 protocol from January 2017 to December 2022. Outcome was assessed in terms of event free survival (EFS) and overall survival (OS) using Kaplan-Meier survival analysis.

**Results:** A total of 81 ALL patients relapsed during the study period, of which 64(79%) were B-ALL and 17 (21.0%) were T-ALL. Among the relapsed ALL patients, 21 (26%) were very early, 35 (43%) were early, 25(31%) were late relapses. Isolated medullary relapse was the most common (72%), followed by isolated central nervous system (CNS) (16%), combined relapse (6.%) and isolated testicular (4%) relapse. Fifteen cases (18%) were treated using BFM-REZ salvage protocol, while others opted for palliation or further therapy at another centre with HSCT. Of the relapsed ALL patients treated, 14 (93%) were B-ALL. 80% were late relapses and rest (20%) were early relapses. Half of these cases were isolated medullary relapses, while 25% were combined relapses and 19% were CNS relapses. Six children (37.5%) had second relapse while on salvage protocol of which four children (26.7%) died. Two-year EFS was 61.0 ± 14.2% and OS was 70.06 ± 12.6%.

**Conclusions:** In resource poor setting, late B-ALL relapses can be salvaged with BFM-REZ 90 protocol.

EP243/#1330 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### RELUCTANCE, NOT REFUSAL: PATIENT AND PUBLIC INVOLVEMENT WORK ON MEDICATIONS IN THE MAINTENANCE PHASE OF ACUTE LYMPHOBLASTIC LEUKAEMIA

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**Background and Aims:** Acute lymphoblastic leukaemia (ALL) is the most common childhood cancer. UK treatment protocols include a maintenance phase lasting between 18 months and 3 years during which oral chemotherapy is administered by the family at home. Approximately one third of children and young people (CYP) with ALL are described as sometimes "refusing" to take their oral medication, which can be a source of stress for families. Patient and Public Involvement (PPI) work was undertaken to inform future research into the issue.

**Methods:** Semi-structured PPI interviews were conducted with a convenience sample of 17 families at outpatient clinic visits to Alder Hey Children's Hospital, Liverpool, UK. Questions regarding the issue were also presented to a local Young Persons Advisory Group (YPAG).

**Results:** The terms "reluctance" or "hesitance" to describe when CYP may not want to take prescribed medication were more acceptable to families and young people in the YPAG than those such as "refusal" used in existing literature. Medication reluctance was experienced at some point during maintenance by 14/17 (82%) of families interviewed. Frequency and severity of reluctance were variable, with some families requiring insertion of nasogastric tubes to ensure medication administration. Palatability of liquid formulations and adverse effects (dexamethasone particularly) were widely reported to contribute to reluctance. Switching to tablet formulations, offering an element of control to CYP and incorporation into everyday routine were commonly used management strategies. Results about preferred methods to explore the experience of maintenance medication were as follows: questionnaire format was acceptable to all families; semi-structured interviews were acceptable to most families; visual art mediums (e.g., photo-elicitation interviewing) were mostly acceptable but varied between families.

**Conclusions:** This PPI work yielded novel findings about patient-focused terminology. The proportion of families experiencing reluctance was greater than that described in existing literature, possibly related to change in terminology, interview format or patient population.

EP244/#943 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### MULTIDISCIPLINARY APPROACH IN DEVELOPING PHILIPPINE CLINICAL PRACTICE GUIDELINES FOR THE DIAGNOSIS AND MANAGEMENT OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA IN A LIMITED RESOURCE SETTING

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**Background and Aims:** Acute Lymphoblastic Leukemia (ALL) is the most common childhood cancer. Survival rate is more than 80% in high income countries but less than 20% in limited resource settings. The Southern Philippines Medical Center Children's Cancer Institute (SPMC-CCI) is a public, tertiary, end-referral center for pediatric cancer in Mindanao. While there are international guidelines available, the local context and availability of resources differ. There is a need to develop country-specific guidelines that can be implemented in various settings to improve survival and quality of life for patients and their families in the Philippines. This study aims to develop clinical practice guidelines (CPG) applicable in a limited resource setting for childhood ALL.

**Methods:** A Steering Committee was formed from SPMC-CCI followed by the formation of the ALL Technical Working Group (TWG) for guideline development. The multi-specialty team was composed of pediatric oncologists, general pediatricians, pathologists, palliative care specialists, family physicians, nurses, clinical pharmacists and other allied health professionals. Key questions on pediatric ALL were formed upon consultation with care providers, patients and families. Search for literatures, selection, appraisal and abstraction of the evidence were done using AGREE and GRADEPro tools. Formulation and grading of recommendations were evaluated for practical application to different settings through consensus panel voting and externally reviewed by relevant pediatric professional societies.

**Results:** A total of 33 key recommendations were developed for clinical decisions encountered in the areas of screening and prevention,

assessment and diagnosis, pharmacologic intervention, complications and prognosis, supportive and palliative care and health system support for newly diagnosed childhood ALL.

**Conclusions:** A multidisciplinary health care team approach to CPG development thoroughly informs provision of care for childhood ALL patients in a limited resource setting.

EP245/#1725 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### A STUDY OF ROLE OF CARDIO PROTECTION (ACEI PLUS BETA BLOCKADE) IN EARLY CHEMOTHERAPY INDUCED CARDIOTOXICITY IN PEDIATRIC LEUKEMIA DURING CHEMOTHERAPY

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**Background and Aims:** Use of biomarkers and frequent echocardiography may lead to early detection and reversal of Chemotherapy induced cardiotoxicity (CIC). In this study, patients of acute leukemia were prospectively evaluated for cardiac damage, treated early with ACE inhibitors and beta blockers either before (Preventive) or after (Treatment) developing ventricular dysfunction.

**Methods:** CIC was evaluated by biomarkers (NT pro BNP & troponin) and echocardiography before each chemotherapy cycle and at onset of febrile neutropenic episodes. Cardiac dysfunction was diagnosed with a fall in Ejection fraction (EF) by 10% (Preventive arm) or a fall in EF below 50% (therapeutic arm). Both arms were treated with ACE inhibitors and Beta blockers.

**Results:** 186 children with acute leukemia were enrolled (137 patients with ALL /T NHL and 49 patients with AML). Twelve (6.4%) entered the Preventive arm. NT pro BNP elevation occurred in 7 patients before EF drop was detected. The mean fall in EF was to 48.2%. Cardioprotection was given to these patients and chemotherapy was not interrupted. Cardiac function recovered in all patients. Twenty six patients entered the Therapeutic Arm. The EF dropped to mean of 40.5%. EF recovered in all except one patient. Chemotherapy was interrupted and resumed on improvement of cardiac function. The NT pro BNP mean was elevated in 22 of 26 patients. Troponin elevations were not found in both groups. Three patients died, one relapsed and one defaulted. Febrile neutropenia was not a predictor of cardiac dysfunction. In the patients without any cardiac involvement, the EF remained stable.

**Conclusions:** Early anthracycline toxicity picked up by very frequent echocardiography can be reversible. There is a role for ACE inhibitors and beta blockers for both prevention and treatment of cardiotoxicity. NT pro BNP elevation occurs in many patients with cardiac dysfunction but its role needs further evaluation.

EP246/#1240 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### CYTOGENETIC PROFILE OF CHILDREN WITH ACUTE LYPHOBLASTIC LEUKEMIA (ALL): EXPERIENCE FROM A TERTIARY CARE CENTRE IN INDIA

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**Background and Aims:** Cytogenetics plays a vital role in diagnosis and prognosis in ALL. We aimed to study the prevalence of different cytogenetic abnormalities and their correlation with treatment outcomes in patients with ALL at our tertiary care hospital.

**Methods:** In this observational study, retrospective data analysis were done for Pediatric ALL patients, who were diagnosed and treated from January 2012 to December 2021 at B.J. Wadia Hospital for children. FISH & conventional karyotyping were used for cytogenetic analysis. Patients were divided into 2 cohorts: 1) who had completed treatment till 2019, their outcomes were analyzed as 3 years EFS and OS; 2) who had diagnosed and treated after 2019, their short-term outcomes were analyzed as post induction MRD and major events like relapse or expiry.

**Results:** Out of total 382 patients, 321(84%) had B-ALL phenotype and 61(16%) had T-ALL. Maximum number of patients were between 1-10 years, male to female ration was 1.9:1. In B-ALL group EFS was 81% and OS was 84%. Cytogenetic profile analysis denoted 40% hyperdiploidy (commonest), 15% t(12;21), 7% hypodiploidy, 7% t(1;19), 6% MLL rearrangements, 4% t(9;22), 0.5% t(17;19), 0.5% i (AMP) 21. Correlating these cytogenetics abnormality with outcome, we found that our patients with hyperdiploidy & t(1;19) had best outcome (EFS=90%), followed by t(12;21) (EFS=72%), hypodiploidy (EFS=60%), MLL rearrangements (EFS=50%), while t(9;22) (EFS=33%) & t(17;19) performed worst. In T-ALL group, 9 were early T cell leukemia (ETP-ALL) phenotype, 22 (36%) had some chromosomal abnormalities identified, most common being 9p deletion in 17 (28%), followed by TCR rearrangements in 7 (11%). Surprisingly none of the patients with 9p deletion had ETP-ALL phenotype and they performed well with OS of 100%, however low sample size was the strongest limitation here.

**Conclusions:** Detailed cytogenetic study is recommended at the diagnosis in ALL for prognostication. More importantly risk adapted treatment with the use of cytogenetics can definitely improve outcomes.

EP247/#552 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### CLINICAL CHARACTERISTICS AND TREATMENT OUTCOME OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA IN TANZANIA FROM 2016 TO 2020

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**Background and Aims:** The regular assessment of local resources and disease outcomes is important in pediatric oncology of low to middle-income countries. The Tanzanian government opened its first pediatric oncology ward in 2004, and progress has been made on its medical infrastructure in the past decade. This research aims to describe the current clinical outcome of childhood acute lymphoblastic leukemia (ALL) in Tanzania from 2016 to 2020.

**Methods:** This was a retrospective cohort study on pediatric patients who were treated for ALL from January 1, 2016 to December 31, 2020 at Muhimbili National Hospital (MNH). During the study period, MNH was the only facility in the country that could offer ALL chemotherapy. We obtained information of patient demographics, disease presentation, diagnosis and outcome through comprehensive chart review. We estimated the overall survival (OS) and event-free survival (EFS) from the date of treatment initiation using the Kaplan-Meier method. Univariable and multivariable Cox proportional hazards models were used to calculate the hazard ratios (HRs) of each prognostic factors on survival.

**Results:** A total of 202 patients were eligible for the study. Median follow-up time was 39 months. Median age was 6 years (range 1-19), and 84 were females (42%). B-lineage and T-lineage accounted for 70% and 30% respectively. After remission induction treatment, 126 patients achieved remission (65%); and of those, 96 patients achieved minimal residual disease negativity. Median OS was 499 days (95% confidence interval (CI): 296-755) and the 2-year OS was 43% (95%CI: 37-50). Median EFS was 312 days (95%CI: 223-475), and the 2-year EFS was 37% (95%CI: 30-43). Edema (HR 1.93, p=0.003), sickle cell anemia (HR 1.81, p=0.076) and 2-hours travel time from home to the hospital (HR 1.57, p=0.052) were positively associated with mortality in multivariable analysis.

**Conclusions:** Biological and social factors affect the prognosis of Tanzanian pediatric ALL population specifically in its own medical setting.

EP248/#1574 | **Poster Topic: AS05 SIOP Scientific Program/AS05.a Acute Lymphoblastic Leukaemia**

**A COST-UTILITY ANALYSIS OF NELARABINE FOR THE FIRST-LINE TREATMENT OF NEWLY DIAGNOSED PEDIATRIC T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA**

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**Background and Aims:** The Children's Oncology Group (COG) AALL0434 trial investigated the addition of nelarabine to standard of care (SOC) chemotherapy in patients aged 1-30 with newly diagnosed T-cell acute lymphoblastic leukemia (T-ALL). Though AALL0434 demonstrated superior outcomes and a reduction in CNS relapses, nelarabine is not currently funded by many health systems, in part due to a lack of cost-effectiveness data. We thus estimated the cost-utility of nelarabine for this indication from a Canadian public health care payer perspective.

**Methods:** A microsimulation model with a lifetime horizon followed a hypothetical cohort of patients with newly diagnosed T-ALL from post-induction therapy to death. Three health states were included: relapse-free post-induction, relapse, and death. Efficacy was estimated through multistate modeling of AALL0434 data. Drug and resource-related costs were obtained from Ontario-based sources. Utility estimates and long-term mortality risks were sourced from the literature. Total health care costs, quality-adjusted life years (QALYs), and incremental cost-effectiveness ratios (ICER) were reported. One-way probabilistic sensitivity analyses and scenario analyses were conducted.

**Results:** Incorporating nelarabine increased costs by \$102,304 CAD/patient but resulted in 1.93 more QALYs and thus an ICER of \$53,102/QALY. The bulk of the identified cost and benefit were accrued within the AALL0434 trial period (first 11 years from diagnosis) and while patients were in the relapse-free health state. Across multiple scenario analyses, the ICER was stable under the \$100,000/QALY threshold.

**Conclusions:** Incorporating nelarabine into SOC, as first demonstrated by AALL0434, was cost-effective across different scenarios and assumptions. These results support the funding of nelarabine by public and private payers.

EP249/#625 | **Poster Topic: AS05 SIOP Scientific Program/AS05.a Acute Lymphoblastic Leukaemia**

**IMPACT OF MINIMAL RESIDUAL DISEASE ON OUTCOME OF ADOLESCENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA**

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**Background and Aims:** Adolescents with acute lymphoblastic leukemia (ALL) have inferior outcomes when compared with younger children. Methods to identify patients expected to fail on current protocols are required, so that alternative therapy can be introduced as early as possible. This study aimed to assess impact of minimal residual disease (MRD) as well as other prognostic factors on outcome of adolescents with ALL.

**Methods:** 301 patients with newly diagnosed ALL, aged 13-18 years, were treated on a protocol adopted from St. Jude total-XV at Children's Cancer Hospital Egypt between 2007 and 2017.

**Results:** The 5-year event-free survival and overall survival were 58.1%±2.8% and 64.1%±2.8%, respectively. The cumulative incidence of any relapse (CIR) at 5 years was 23.6% (95% CI, 19%-28.6%), isolated CNS relapse 5.3% (95% CI, 3.2%-8.3%) and toxic mortality 14.3% (95% CI, 10.6%-18.5%). There were no significant association between CIR and gender or phenotype, while initial WBC  $\geq 100 \times 10^9/L$  was significantly associated with higher CIR;  $p=0.018$ . The 5-year CIR was 13.6%±3.8%, 23.6%±4.4%, and 33.9%±4.7% with MRD day15 <0.01%, 0.01-1%, and  $\geq 1\%$ , respectively;  $p=0.007$  and it was significantly higher with any detectable residual leukemia  $\geq 0.01\%$  at end of induction (EOI) being 19.8%±2.9%, 39.1%±7.7%, and 39.3%±9.5% with MRD <0.01%, 0.01-1%, and  $\geq 1\%$ , respectively;  $p=0.011$ . Adolescents with B-ALL having favorable genetic features and negative EOI MRD were successfully treated on low-risk therapy with CIR comparable to other adolescents treated on the standard-risk arm, 21.4%±11.5% and 20.8%±3.6%, respectively. B-Precursor ALL had significantly higher CIR with MRD  $\geq 0.1\%$  on day15;  $p=0.029$  and  $\geq 0.01\%$  at EOI;  $p=0.036$ , while T-cell ALL had significantly worse outcome if MRD day15 was  $\geq 1\%$ ;  $p=0.026$  or EOI  $\geq 0.1\%$ ;  $p=0.011$ .

**Conclusions:** MRD and initial WBC retained their prognostic significance in adolescents with ALL by multivariate analysis. Novel approaches should be considered for adolescents with EOI MRD levels  $\geq 0.01\%$  in B-precursor ALL and MRD  $\geq 0.1\%$  in T-cell ALL.

EP250/#1507 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### RELAPSED ACUTE LYMPHOBLASTIC LEUKAEMIA: IS IT WORTHWHILE TREATING IN LOW-RESOURCE SETTING? EXPERIENCE FROM UGANDA

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**Background and Aims:** Acute lymphoblastic leukaemia (ALL) is highly curable but relapse remains an important cause of treatment failure. In most resource-limited settings relapsed ALL isn't salvageable, with treatment often not attempted. We describe the characteristics and outcomes of children treated for relapsed ALL at our centre.

**Methods:** A retrospective cohort analysis of children with relapsed ALL between February 2019 and January 2023 at Mulago National Referral Hospital, Uganda. Kaplan-Meier estimate was used to examine overall survival following relapse.

**Results:** Thirty-four children (71% male) were diagnosed with relapsed ALL, with median age of 9 years (IQR = 6,12). Most patients (20/34, 59%) relapsed within 18 months of diagnosis; median time to relapse was 13.9 months (IQR = 7.6,20.9). Most patients were B-cell immunophenotype (74%), NCI-high risk (82%) and minimum residual disease (MRD) negative at the end of induction (56%). Bone marrow was a relapse site in 74% of patients; the rest had Isolated CNS disease (26%). All cases of isolated CNS relapse had normal baseline CNS assessment. Relapse treatment was undertaken for 27/34 (79%) patients, mostly with a regimen identical to that used at initial diagnosis. Majority (58%) achieved remission (CR); one patient was awaiting CR evaluation. The median duration of remission was 8.5 months (IQR = 6.4,15.4). One patient received stem-cell transplant and survives 3 years from relapse. Mortality during the first month of relapse therapy was 7/27 (26%). The median survival for treated patients was 5.5 versus 1.7 months for untreated patients. The overall one-year survival after relapse was 29.4%; 95% CI (13.4 - 47.3).

**Conclusions:** First-line ALL regimens were effective in achieving short term control of relapsed ALL, but associated with significant mortality. Patients treated for relapsed ALL had superior survival, with reduced blood product dependency, suggesting treatment efficacy. However, quality of life studies would inform overall treatment benefit.

EP251/#234 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### CHILDHOOD LEUKEMIA LONG-READ TRANSCRIPTOMICS BASED POINT OF CARE DIAGNOSIS: VALIDATION IN BIOBANKED BONE MARROW SAMPLES

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**Background and Aims:** Genomic testing for childhood leukemia is standard of care in high income countries (HIC), aiding in diagnosis, risk stratification, and prognosis enabling opportunities for targeted

treatment. Genomic testing in HIC often requires outside referral and is often unavailable in low-mid income countries (LMIC). Genomic testing, including gene fusions that characterize leukemia, can be identified with next-generation sequencing (NGS) and RNA expression analysis. **Aims:** To validate point of care (POC) RNA long-read sequencing (LRS) using Nanopore Promethion for genomic testing that identifies gene fusions in B-cell acute lymphoblastic leukemia (B-ALL). We hypothesize that RNA LRS can provide a fast and accurate POC method to detect genomic rearrangements and specific expression changes.

**Methods:** Our proof of principle study used 24 biobanked bone marrow samples from children with B-ALL. RNA was extracted and LRS completed using Oxford Nanopore Technologies (ONT) RNA sequencing. LRS results were compared to known genomic arrangements in the samples.

**Results:** We were able to consistently show that POC testing correlates with gold standard cytogenetic testing. LRS on 24 B-ALL samples correctly identified highly expressed fusion genes with high copy number (including ETV6-RUNX1, BCR-ABL1, KMT2A-AFF1 and TCF3-PBX1). One sample showed different fusion (in an assumed (1;19) and two fusion transcripts involving JAK2 were detected in BCR/ABL1 like leukemia. No actionable incidental findings were identified that were not already known.

**Conclusions:** Our study shows that RNA LRS can identify gene fusion and RNA expression in the bone marrow of patients with B-ALL for diagnosis, prognosis, risk stratification and treatment. This information is not consistently available in LMIC and in HIC requires costly send out with results often delayed. Testing in T-cell ALL and AML is currently ongoing. Our upcoming prospective study aims to overcome these barriers by attempting to create and prospectively validate a fast, accurate and low cost POC tool to diagnose childhood leukemia.

EP252/#1305 | **Poster Topic: AS05 SIOP Scientific Program/AS05.a Acute Lymphoblastic Leukaemia**

#### INCIDENCE OF INDUCTION TOXICITIES IN CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA IN GHANA

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**Background and Aims:** Due to limited supportive care, low- and middle-income countries must balance delivering intensive, curative chemotherapy with the risk of treatment-related morbidity and mortality (TRM). Our modified induction protocol for acute lymphoblastic leukaemia (ALL) incorporates anthracyclines fortnightly from Day 8, instead of weekly from Day 1 as in high income countries. The aim of this study was to describe induction toxicities and outcomes among children with ALL at Korle Bu Teaching Hospital (KBTH), Ghana.

**Methods:** Hospital-based cohort study of children aged 1 to 13 years newly diagnosed with ALL from August 2021 to January 2023. Toxicities were graded using the Common Terminology Criteria for Adverse Events, version 5.0.

**Results:** Of 31 patients, majority were male (58%). The median age was 5 years (IQR: 3-10 years). Fifteen (48.4%) presented with WBC  $\geq 100 \times 10^9/L$  and 22(71%) were NCI high-risk. Eleven patients (35.5%) who had LDH  $\geq 1000$  IU/L also had high-risk ALL. All 31 patients experienced at least one induction toxicity of any grade, and 29 (93.4%) had at least one severe (grade  $\geq 3$ ) toxicity. Severe toxicities were anaemia 23(79.3%), thrombocytopenia 22(75.9%), febrile neutropenia 19(65.5%), sepsis 7(24.1%), vomiting 6(20.7%), hypertension 6(20.7%), hyperglycaemia 4(13.8%), tumour lysis syndrome 4(13.8%) and stroke 3(10.3%). Tumour lysis syndrome was associated with WBC  $\geq 400 \times 10^9/L$  ( $p=0.00$ ). Stroke was significantly correlated with positive CNS status ( $p < 0.001$ ), LDH  $\geq 1000$ U/L ( $p=0.041$ ) and dexamethasone ( $p = 0.037$ ). Six (19.3%) deaths occurred between Induction days 11 and 27 (median: 19.5 days). Of the 25 patients who were alive at the end of induction, only 15(60%) were in morphologic remission.

**Conclusions:** Severe induction toxicities were common in our cohort, despite an adapted induction treatment regimen. Conversely, remission-induction rate was sub-optimal. There is need for more effective therapy and improved supportive care to minimize TRM and maximize cure.

EP253/#560 | **Poster Topic: AS05 SIOP Scientific Program/AS05.a Acute Lymphoblastic Leukaemia**

#### FACTORS ASSOCIATED WITH DIAGNOSIS DELAY IN PEDIATRIC LEUKEMIA: A SINGLE-CENTER RETROSPECTIVE STUDY

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**Background and Aims:** Factors affecting the diagnostic interval of pediatric leukemia are uncertain and complex. How delayed diagnosis and treatment induction affect patient survival is of concern among pediatric oncologists. Our study was performed to characterize the clinical factors associated with the diagnostic interval and to analyze whether delayed diagnosis affects the survival of patients with pediatric leukemia.

**Methods:** We retrospectively collected the data of patients with newly diagnosed pediatric leukemia at Okayama University Hospital from 2007 to 2022. The diagnosis delay was defined as the interval in days from the onset of symptoms to diagnosis.

**Results:** In total, 103 children with leukemia were eligible for analysis, and B-cell precursor acute lymphoblastic leukemia (ALL) was the



most frequent subtype ( $n = 64$ , 62%). The median diagnosis delay was 20 days. The patients' sex, age, initial white blood cell count, or initial platelet count had no association with diagnosis delay. Although not statistically significant, patients with low-risk ALL (hyperdiploid or *ETV6::RUNX1*) tended to have longer diagnosis delay than patients with other types of ALL (median of 25 and 18 days, respectively;  $p = 0.088$ ). Long diagnosis delay, which we defined as  $\geq 30$  days, was associated with neither 5-year event-free survival (70.1% in  $< 30$  days and 68.3% in  $\geq 30$  days,  $p = 0.986$ , log-rank test) nor overall survival (84.7% in  $< 30$  days and 89.4% in  $\geq 30$  days,  $p = 0.85$ , log-rank test).

**Conclusions:** Clinical factors such as sex, age, initial white blood cell count, or initial platelet count were not associated with diagnosis delay. Additionally, long diagnostic delay ( $\geq 30$  days) was not associated with survival of patients with childhood leukemia. As long as the leukemic biology of the patients is precisely classified, the diagnosis delay might have little adverse effect on their prognosis.

EP254/#1336 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
Acute Lymphoblastic Leukaemia

#### ACUTE RISE OF LEPTIN AFTER FIVE DAYS OF DEXAMETHASONE AND ITS ASSOCIATION WITH HUNGER, FAT MASS, SLEEP AND FATIGUE, IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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**Background and Aims:** Children with acute lymphoblastic leukemia (ALL) receive high doses dexamethasone during treatment, which induce acute side effects. The aims of the current study were to determine the influence of a five-day dexamethasone course on changes in leptin, fat mass, body mass index (BMI), hunger, sleep and fatigue and to explore the associations between these changes.

**Methods:** Pediatric ALL patients were included during maintenance treatment. Data was collected before (T1) and after (T2) a five-day dexamethasone course ( $6\text{mg/m}^2/\text{day}$ ). BMI, fat mass (bioelectrical impedance analysis) and leptin were assessed on both timepoints, as well as parent-reported questionnaires regarding hunger, fatigue and sleep problems. Changes after five days of dexamethasone (T2 versus T1) were assessed using paired tests. Correlation coefficients were

calculated to assess associations between these changes (Delta scores: T2-T1). Univariable regression analyses were used to explore possible contributing factors for high leptin on T1 (Z-score  $> 1.5$ ).

**Results:** We included 105 children with median age 5.4 years (range 3.0-18.8). Leptin and fat mass, as well as hunger scores, fatigue and sleep deteriorated significantly after five days of dexamethasone ( $p < 0.001$ ), in contrast to BMI ( $p = 0.12$ ). No significant correlations between delta leptin and delta fat mass, BMI, hunger, fatigue or sleep were found. Elevated leptin on T1 was associated with older age (odds ratio (OR) 1.51, 95%-confidence interval (95%-CI) 1.28-1.77), higher fat mass (OR 1.19, 95%-CI 1.07-1.33) and earlier maintenance week (OR 0.96, 95%-CI 0.92-0.99).

**Conclusions:** Five days of high dose dexamethasone treatment lead to direct and significant changes in leptin, hunger scores and fat mass, which may suggest a dexamethasone-induced state of acute leptin resistance. Since children with ALL are at increased risk for metabolic adverse events, it is important to understand the underlying mechanisms, and leptin resistance might play a role.

EP255/#1381 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
Acute Lymphoblastic Leukaemia

#### IN-PATIENT ODYSSEY IN THE LIFE OF 100 CONSECUTIVE CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA (ALL): A REAL-WORLD EXPERIENCE

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**Background and Aims:** In-patient hospitalizations during therapy of Acute Lymphoblastic Leukemia (ALL) are major determinants of long-term medical, financial and psycho-social outcomes. Available literature on factors affecting hospitalizations is scarce.

**Methods:** Retrospective cohort-analysis of children treated at a single tertiary cancer center was conducted. Data collected included demographics, disease characteristics, therapy-phase, length, and reason for hospital-admission. Analysis was done with Microsoft Excel, and R version 4.0.5.

**Results:** One-hundred newly-diagnosed, completely-treated, consecutive patients with ALL between 2013–2020 were included. The median age at diagnosis was 5 years (range 1-17) with a M:F ratio of 1.2:1 (55:45). Treatments were as per standard risk (SR) B-ALL in 51, high risk (HR) B-ALL in 37 and T-ALL in 12. The study-cohort required 605 admissions (median 6 admissions/patient, range 1-15, inpatient days 4852 (150.64 months), average 45.82 days/patient). Reasons for post-diagnosis admissions ( $n = 505, 2292$  days) were chemotherapy (204), febrile neutropenia (FN) (242) and other (59). The most common reasons for 'other' were gastrointestinal (19), neurological

(8), Infectious (6) and central-venous-access related (6). Of the FN admissions (n=242), 99(40.9%) were patients with SR-ALL, 104(42.9%) HR-ALL and 39(16.1%) T-ALL. Distribution of FN admissions in pre-maintenance and maintenance phase of treatment differed across the three risk-groups – SR (44 vs. 55), HR (58 vs. 46), and T-ALL (26 vs. 13)(p=0.0462). High-dose methotrexate comprised majority chemotherapy admissions (165/204,80.8%). FN admissions continued even in maintenance (114/242,47.1%). Median duration of chemotherapy admission was 3 days (range 2 – 6) and FN admission was 6 days (range 1 – 78). Distribution of length of hospitalization was statistically different across risk-groups, with SR patients requiring shorter admissions than HR or T-ALL (p<0.0001). Additionally, patients in the pre-maintenance phase required longer admissions, compared to those in maintenance phase (p<0.0001).

**Conclusions:** Children with ALL continue to spend significant days hospitalized due to complications of treatment, continuing even in maintenance. Our study provides a benchmark for interventions to improve upon causes for non-chemotherapy related admissions to meaningfully impact the quality-of-life and limit health-care burdens.

EP256/#420 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### CLINICAL OUTCOMES OF INFANT LEUKEMIA: EXPERIENCE FROM A SINGLE TERTIARY CENTER IN THAILAND

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**Background and Aims:** Treatment outcomes of childhood leukemia, both acute lymphoblastic leukemia (ALL) and acute myeloblastic leukemia (AML), have good response and greatly improved over time. However infant leukemia is associated with poor treatment outcomes due to distinctive clinical features. This study aimed to examine prognostic factors in infant ALL and AML aged under 2 years.

**Methods:** We retrospectively reviewed the medical records of patients aged under 2 years who were diagnosed with ALL and AML and treated at the Hematology Clinic of Songklanagarind Hospital between June 1979 and June 2021. The Kaplan Meier method was used to calculate the rates of event-free survival (EFS) and overall survival (OS). A univariate Cox proportional hazards regression model was used to identify clinical factors associated with poor EFS and OS. A p-value < 0.05 was considered statistically significant.

**Results:** Over the 42-year study period, there were 137 patients with acute leukemia aged under 2 years (12.9%), 70 were diagnosed with ALL and 67 were diagnosed with AML. The median age

of diagnosis in the ALL patients was 16 months. However, there were 20/70 (28.6%) ALL patients who were aged under 1 year. After induction therapy, 81.4% of children with ALL achieved remission. The 5-year EFS and 5-year OS rates were 41% and 46%, respectively. Among the AML patients, the median age of diagnosis was 15 months. There were 26/67 (38.8%) AML patients who were aged under 1 year. After induction therapy, 38.8% of patients with AML achieved remission. The 5-year EFS and 5-year OS rates were 9% and 10%, respectively. Patients with ALL who were younger than 1 year or whose initial WBC count was higher than 50,000/ $\mu$ L had worse outcomes. The relapse rate in ALL and AML was 40% and 41.8%, respectively.

**Conclusions:** Infant leukemia in children under 2 years of age was associated with poor outcomes.

EP257/#288 | Poster Topic: AS05 SIOP Scientific Program/AS05.a  
*Acute Lymphoblastic Leukaemia*

#### SURVIVAL ANALYSIS OF PEDIATRIC ACUTE LYMPHOCYTIC LEUKEMIA ACCORDING TO CHANGES IN RISK GROUP-BASED PROTOCOL: 20 YEARS OF EXPERIENCE

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**Background and Aims:** Recent treatment of acute lymphoblastic leukemia (ALL) is based on risk stratification and survival rates have reached over 70-80%. We investigated the survival rates and prognostic factors of patients with ALL.

**Methods:** This study analyzed patients who were diagnosed with ALL at the pediatrics department Samsung Medical Center (SMC) between 2000 and 2019. Patients were classified under the standard-risk (SR), High-risk (HR), and very HR (VHR) groups. During the study period, SMC protocol of HR group was changed twice. From 2000 to 2005, CCG-1882 protocol was used, from 2006 to 2014 Korean multicenter HR ALL-0601 protocol was used, and from 2015 to 2019 Korean multicenter HR ALL-1501 protocol was used.

**Results:** Of the 461 patients, the median age at diagnosis was 5.5 years old (range 0.1~26.5 yr) and those aged 15 years or older were 36 (7.8%). At cytogenetic test, Philadelphia chromosome in 24 patients, t(4;11) in 12 patients and hypodiploidy in 3 patients. And 123 patients had normal chromosome, 100 patients had hyperdiploidy. Complete remission was achieved in 437 patients (94.8%). The 10-year relapse free survival rate (RFS) was 77.2%, and the overall survival rate (OS) was 83.6% in total patients. The 10-year OS according to the SMC risk group was 95.5% in the SR group, 83.8% in the HR group, and

81.4% in the VHR group. The 5-year OS according to the treatment protocol of HR group was 79.9% in 1882 protocol, 83.0% in 0601 protocol, 96.2% in 1501 protocol treatment group. The prognosis was very poor with 60.9% of those aged 15 years and older. In addition, relapse occurred in 61 (13.2%) patients, and their 10-year OS after relapse was 33.7%.

**Conclusions:** Treatment outcome of ALL improved markedly. However, the survival rate of relapsed patients is still unsatisfactory. Need to characterize AYA patients, and relapsed patients.

EP258/#1597 | Poster Topic: AS05 SIOP Scientific Program/AS05.b  
*Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

### ACUTE PROMYELOCYTIC LEUKEMIA IN CHILDREN: A SINGLE CENTRE EXPERIENCE FROM PERÚ

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**Background and Aims:** Data on childhood acute promyelocytic leukemia (APL) from low-and middle-income countries is limited and early death (ED) remains one of the main causes of APL treatment failure. The aim of the study is to characterize the clinical features, treatment and outcome of children in a Peruvian National Cancer Center (INEN).

**Methods:** The retrospective study was conducted on patients ( $\leq 14$  years) with APL from 2,012 to 2,019. We analyzed clinical characteristics, risk group and survival. We used the Kaplan-Meier method for survival.

**Results:** The study included 52 patients with APL, its represents 26.6 % of acute myeloid leukemia cases in this cohort. Median age, 7.6 years [range, 1-13 years]. Male/Female relation was 0.93. The frequency of bcr-1, bcr-2 and bcr-3 was 58%, 6.5% and 35.5% respectively. FLT3-ITD mutation was detected in 1 patient. The patients were stratified into low-risk, intermediate-risk and high-risk groups according to baseline white blood cell counts ( $10 \times 10^9/L$ ) and platelets count ( $40 \times 10^9/L$ ). They were treated with all-trans-retinoic acid (ATRA)  $25 \text{ mg/m}^2$  and chemotherapy. Induction and three courses of consolidation were followed by maintenance for 2 years. The cumulative dose of daunorubicin equivalent anthracyclines were  $520 \text{ mg/m}^2$ ,  $620 \text{ mg/m}^2$  and  $600 \text{ mg/m}^2$ , respectively. Complete remission was obtained in 82.7% of patients; ED occurred in 8 (15.4%) patients and was mainly related to intracranial hemorrhage in the first week following diagnosis. Fourteen patients relapsed (26.9%), 7 of them are alive and leukemia-free (3 received arsenic trioxide and 4 received allogeneic HSCT). During the follow-up period (mean  $44 \pm 31.7$  months), the 3-year overall survival (OS) was 58.9% and the event-free survival (EFS) was 61.9%. No differences were found in OS and EFS between the three groups of risk and subtype of bcr.

**Conclusions:** The combination of ATRA and chemotherapy can improve the outcome of patients with APL, but the ED was relatively high in our study.

EP259/#165 | Poster Topic: AS05 SIOP Scientific Program/AS05.b  
*Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

### LONG-TERM OUTCOME OF CHILDHOOD ACUTE MYELOID LEUKEMIA: A 40-YEAR EXPERIENCE FROM A RESOURCE-LIMITED COUNTRY, SOUTHERN THAILAND

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**Background and Aims:** Although there have been advances in treating pediatric patients with acute myeloid leukemia (AML) in developed countries, treatment outcomes in low-to-middle-income countries remain poor. Studies on the survival results of AML in resource-limited nations are still scarce. The goal of this study was to investigate survival outcomes and risk factors for survival outcomes in children with AML who were treated at a tertiary center in Southern Thailand.

**Methods:** We analyzed the records of patients under the age of 18 from between 1979 and 2019 who with newly diagnosed AML. We divided the patients into 4 periods based on the chemotherapy protocol employed to treat them (period 1: 1979-1994, period 2: 1995-2005, period 3: 2006-2014, and period 4: 2015-2019). The 5-years event-free survival (EFS) and overall survival (OS) rates were calculated using the Kaplan Meier method. A Cox proportional hazards regression model was utilized to identify variables associated with EFS and OS.

**Results:** Throughout the 40-year period, 1,042 patients had acute leukemia diagnoses, with 316 of the cases (30.3%) having AML. Among the AML patients, there were 185 boys (58.5%) and 131 girls (41.5%), with a median age at initial diagnosis of 6.6 years. The 5-year EFS for periods 1, 2, 3, and 4 were 19.0%, 20.6%, 17.4%, and 39.4% ( $p = 0.29$ ), while the 5-year OS were 19.0%, 24.7%, 18.7%, and 41.3% ( $p = 0.15$ ), respectively. Age, white blood cell count and study period were significant predictors of survival outcomes. Overall survival of AML patients treated at our institution improved over the study period, rising from 19.0% in period 1 to 41.3% in period 4.

**Conclusions:** The treatment outcomes of childhood AML in this study showed improvement over time, although still inferior to those in developed countries.

EP260/#1596 | Poster Topic: AS05 SIOP Scientific Program/AS05.b  
*Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

### PEDIATRIC ACUTE MYELOID LEUKEMIA WITH FLT3-ITD MUTATION - RETROSPECTIVE ANALYSIS OF TREATMENT OUTCOME IN POLISH PEDIATRIC LEUKEMIA AND LYMPHOMA STUDY GROUP FROM 2005 TO 2022

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**Background and Aims:** The FMS-like tyrosine kinase 3 (FLT3) gene is mutated in 10-15% of pediatric acute myeloid leukemia (AML). FLT3-internal tandem duplication (ITD) mutations are associated with increased relapse risk and inferior outcomes. The aim of the study was analysis of patients with AML and FLT3-ITD treated from 2005 to 2022 in Poland.

**Methods:** Retrospective analysis of the nationwide pediatric AML database was performed. There were 577 patients registered from 2005 to 2022, excluding acute promyelocytic leukemia, myeloid leukemia in Down syndrome, MDS related AML and secondary AML. Among 497 children, FLT3-ITD was found in 54 patients (10.7%), 29 boys (53%) and 25 girls (47%), with median age 13.2 years (range 3-17.9). Coexisting mutation of WT1 was present in 13 of 35 patients with available results, NPM1 mutation was found in 5 of 23 children with available results. From 2005 to 2015 patients were treated with AML-BFM 2012 Interim protocol (30 children), from 2015-2019 with AML-BFM 2012 Registry (10 patients) and from 2019-2022 with AML-BFM 2019 recommendation (14 patients). Eleven patients (20%)

received FLT3 inhibitors. In 26 children (48%) stem cell transplantation (SCT) was performed.

**Results:** Probabilities of 5-year overall (OS), event-free (EFS) and disease-free (DFS) survival were lower in the FLT3-ITD positive patients compared to the children without mutation (0.51 vs 0.71,  $p=0.021$ ; 0.34 vs 0.59,  $p=0.0003$ ; 0.43 vs 0.70,  $p=0.001$  accordingly). Patients with coexisting WT1 mutation had lower probability of 5-year EFS (0.19 vs 0.69,  $p=0.003$ ). Coexisting NPM1 mutation was associated with higher 5-year OS (1.0 vs 0.25,  $p=0.011$ ). There was no difference in survival depending on the treatment protocol or use of FLT3 inhibitors. Probability of 5-years RFS was higher in patient who underwent SCT (0.61 vs 0.16,  $p=0.048$ ).

**Conclusions:** Use of SCT improved outcome in analyzed cohort. Treatment results in AML with coexisting FLT3-ITD and WT1 mutations are still unsatisfactory.

EP261/#364 | Poster Topic: AS05 SIOP Scientific Program/AS05.b  
*Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

#### GENETIC, EPIGENETIC, AND CLINICAL SIGNIFICANCE OF WILMS' TUMOR 1 (WT1) GENE IN PRIMARY ACUTE MYELOID LEUKEMIA AND ITS INFLUENCE ON PROGNOSIS

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**Background and Aims:** Acute myeloid leukemia is a genetically complex hematologic malignancy characterized by abnormal differentiation and clonal proliferation of myeloid progenitor cells in the bone marrow. Wilms tumor 1 (WT-1) gene is a critical regulator of malignant hematopoiesis, although underlying epigenetic alterations, and their clinical relevance have not been fully addressed in AML. In the present study, we aim to investigate the RNA expression, and methylation levels, of the WT-1 gene in AML cases.

**Methods:** Bone Marrow (BM) and Peripheral Blood (PB) samples were collected from 98 paediatric & adult AML cases (98 at diagnosis [day 0] and 89 after completion of induction chemotherapy [day 28]). WT-1 gene expression and promoter methylation status were assessed during both intervals (day-0 & day-28) by performing real-time polymerase chain reaction (RT-PCR) and methylation-specific polymerase chain reaction (MS-PCR).

**Results:** Of the 98 subjects studied, 63 were male (64.28%) and 23 were females (35.71%), out of these 85 (86.73%) cases showed overexpression of WT-1 gene at the time of diagnosis as compared with cases in complete remission (CR) remission or control samples ( $p<0.001$ ). Moreover, Robust hypermethylation of WT1 promoter was

observed in 74 (75.51%) AML cases at the time of diagnosis as compared with patients in complete remission (CR) remission or control samples ( $p = <0.001$ ). In all AML patients, WT-1 expression and methylation levels were inversely correlated with normal hematopoiesis and positively associated with age, high marrow blast counts, and adverse risk cytogenetic.

**Conclusions:** Overexpression and Hypermethylation of the WT-1 gene positively associates with the leukemic burden in most cases of AML. Thus, this gene can be considered a promising molecular marker for early diagnosis, and MRD detection, and a target for developing novel therapeutic approaches against AML.

EP262/#369 | Poster Topic: AS05 SIOP Scientific Program/AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes

### A PROSPECTIVE STUDY TO EVALUATE THE PROGNOSTIC IMPLICATIONS OF MMP-2 GENE IN ACUTE MYELOID LEUKEMIA

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**Background and Aims:** Acute myeloid leukemia (AML) is a complex hematologic malignancy characterized by the uncontrolled proliferation of immature myeloid cells in the bone marrow. Matrix metalloproteinase-2 (MMP-2) gene has been involved in tumor invasion and trafficking of normal hematopoietic cells. However, the molecular mechanism of MMP-2 and their molecular interaction in AML remains unknown. Therefore, this study aimed to characterize the molecular functions, clinical and prognostic value of MMP-2 gene in AML.

**Methods:** In this study, first, we investigated the expression level of the MMP-2 gene in AML ( $n=173$ ) and normal ( $n=70$ ) cases. Then, we did correlation analysis to find the potentially associated gene linked with the MMP-2 gene based on their expression levels using GEPIA2 database. Kaplan–Meier survival estimation was performed to evaluate the prognostic significance of MMP-2 using UALCAN platforms. In addition, we assess the DNA methylation status of MMP-2 gene using UCSC Xena browser and MEXPRESS database.

**Results:** In our analyses, MMP-2 mRNA was significantly overexpressed in AML ( $n=173$ ) cohorts as compared with normal cases ( $n=70$ ) and closely associated with poor overall survival ( $P <0.05$ ). Based on FAB classification higher MMP-2 expression was observed in M7 subtype, followed by M2 and M4. In correlation analysis MMP-2 gene was positively correlated with the WT-1 gene, followed by

CPA3, IGFBP2, FGFR1, RABL5, ATP1B1 genes with ( $PCC <0.65$ ) and negatively associated with SERPINB6 gene, followed by RGS10, IL12RB1, KIAA1949, VCL genes with ( $PCC >-0.5$ ) in our cohort. Furthermore, a lower methylation level of MMP-2 gene was observed in AML compared to normal cases, which were negatively associated with MMP-2 gene expression.

**Conclusions:** In this study, we found that MMP-2 plays a significant role in AML progression and may serve as a potential prognostic biomarker and therapeutic target for the effective management of AML.

EP263/#327 | Poster Topic: AS05 SIOP Scientific Program/AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes

### A STUDY OF CLINICAL PROFILE AND OUTCOMES OF PEDIATRIC PATIENTS WITH ACUTE MYELOID LEUKEMIA

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**Background and Aims:** Acute Myeloid Leukemia (AML) is characterized by clonal neoplastic proliferation of myeloid precursor cells in the bone marrow and arrest of their maturation. All patients under the age of 18 years are treated in Pediatric Oncology in our institute and they receive a standard induction therapy, the outcomes hence generated are assumed to be uniform and reflective of host factors. The study aims to describe the clinical, socio demographic profile and induction outcomes of pediatric patients with AML.

**Methods:** A retrospective analysis of patients upto 18 years of age presenting between 1st January 2017 to 31st December 2021 was done. Patients with diagnosis of de novo AML by flowcytometry were considered or with extra-medullary soft tissue mass, proven to be AML by immunohistochemistry. All the records of the patients are derived from the Pediatric Oncology database, and supplemented by the treatment files.

**Results:** Out of 56 patients analyzed, male-female ratio was 1.15. Median age was 7 years (Range: 0.2-18 years). WBC count at presentation ranged from 1,250/ $\mu$ l to 2,96,000/ $\mu$ l (median=29000/ $\mu$ l). 60% of patients were malnourished and majority belonged to lower socioeconomic strata. It was found that 93% of patients had fever at presentation followed by bleeding (61%), easy fatigability (53%), bone pain (46%), hepatosplenomegaly (39%), lymphadenopathy (14%). ELN risk categorization of patients were as follows: Favorable (52%), Intermediate (18%) High (28%), 1 patient couldn't be risk stratified. 47% patients achieved remission, 23% patients did not achieve remission, 16% died during induction and 14% abandoned treatment.

**Conclusions:** Demographic variables, nutritional status, WBC count, clinical presentations were not associated with outcomes of induction. Reason might be the presence of extensive support like accommodation in the hospital vicinity, free food and treatment and psychosocial

support that are available with the pediatric oncology unit. Risk categories were strongly associated with outcomes.

EP264/#1074 | Poster Topic: AS05 SIOP Scientific Program/AS05.b  
*Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

### GENOME-WIDE DNA METHYLATION ANALYSES OF CHILDHOOD MYELODYSPLASTIC NEOPLASM

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**Background and Aims:** Childhood myelodysplastic neoplasm (cMDS) comprises a heterogeneous group of rare clonal hematopoietic stem cell neoplasms. Its etiopathology is complex about 10-40% of patients progress to acute myeloid leukemia (AML). Knowledge about genetic and mainly epigenetic alterations in cMDS pathogenesis is still insufficient. Thus, the main objective of this study was to characterize the genome-wide DNA methylation profile in patients with cMDS.

**Methods:** The genome-wide methylation of cMDS and pediatric health donors (controls) profiles were performed by EPIC Methylation Bead-Chip. We also used data available from the "Gene Expression Omnibus" repository of 500 pediatric AML and 41 controls. WebGestalt, Gene ontology, and Kyoto Encyclopedia of Genes and Genomes pathways enrichment analyzes were performed to select differentially methylated regions in order to identify potential biomarkers associated with the evolution of cMDS to AML. The methylation profile data was validated by pyrosequencing for two genes: Wilm's Tumor gene (*WT1*) and tumor suppressor gene with significant homology to *TP53* (Tumor Protein P73- *TP73*) in 60 cMDS and 20 controls.

**Results:** Data analysis showed that there was a predominance of hypermethylated regions (2299) in relation to hypomethylated regions (1108), mainly in the transcription initiation regions and gene body. In this study, 25 pathways involved with carcinogenic mechanisms covering 387 genes were identified. The main pathways contemplated were focal adherence, calcium signaling, receptor tyrosine kinase pathway, hedgehog signage, Signaling Ras, and Map kinase signaling. cMDS patients in the initial phase had fewer methylation alterations than patients in the advanced phase and with cytogenetic alterations. These results were confirmed by the analyses of genes *WT1* and *TP73*.

**Conclusions:** Our findings suggest that there is an association between hypermethylation with the evolution of MDS and the poor outcome being promising biomarkers for prognosis and treatment choice.

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EP265/#404 | Poster Topic: AS05 SIOP Scientific Program/AS05.b  
*Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

### DOES PROPHYLACTIC IVIG REDUCE INFECTION RELATED MORTALITY IN CHILDREN TREATED FOR ACUTE MYELOID LEUKAEMIA

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**Background and Aims:** children with AML are at high risk for infectious complications because of prolonged severe neutropenia and profound immune system disruption brought on by the highly aggressive chemotherapy. Though profound neutropenia may be the foremost cause for infection related morbidity, hypogammaglobulinemia may contribute to this. We have been using IVIG prophylaxis in the immediate post chemotherapy period for children on treatment for AML from 2019. In this study, we compare our data with historical cohort.

**Methods:** 70 children diagnosed to have AML and opted for treatment January 2015 till December 2021 were included. Baseline characteristics, chemotherapy, complications during the cytopenia period and outcome till 4 weeks after the last dose of chemotherapy were retrieved from electronic medical records. All children received 2 courses each of ADE followed HIDAC. Prophylactic IVIG was given to all children from 2019 till 2021, at a dose of 400mg/kg, 24 hours after completion of each course of chemotherapy. This study was approved by the institutional review board (IRB min no 13512 dated 28-10-2020).

**Results:** 70 children with AML were treated during this period. Number of children analyzed following each course of chemotherapy and those who received IVIG were as follows; ADE1 70/34, ADE2- 48/28, HIDAC1-45/29, HIDAC2-42/28. 4/34 children who received IVIG died of infection following ADE1 compared to 13/36 who did not receive IVIG. ( $p=0.018$ ). Number of deaths following ADE2, HIDAC 1 and 2 in the IVIG group were 1 each and only one child died following HIDAC2 in the non-IVIG group. There was no difference in number of children in either group with culture positive infection, septic shock, needing PICU care between the groups.

**Conclusions:** Reduction in infection related mortality with prophylactic IVIG was observed only following the first course of chemotherapy in this group. Larger studies are required to validate this observation.

EP266/#803 | Poster Topic: AS05 SIOP Scientific Program/AS05.b  
*Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes*

### EVALUATION OF THE CYTOGENETIC RESPONSE WITH IMATINIB MESYLATE IN THE TREATMENT OF CHRONIC GRANULOCYTIC LEUKEMIA IN PEDIATRIC PATIENTS AFTER 6 YEARS OF FOLLOW-UP

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**Background and Aims:** Chronic granulocytic leukemia (CGL) is a rare pediatric malignancy. The potentially curative treatment was allogeneic bone marrow transplantation with 20% mortality and 17% probability of relapse. CGL results of a translocation between chromosome (9;22) forming a chimeric gene (BCR/ABL) which activates a tyrosine kinase blocked by Imatinib. Most clinical studies demonstrate its efficacy in adults due to its low incidence in pediatric population. To evaluate the clinical, hematological and cytogenetic remission of CGL and secondary toxicities in the pediatric population treated with Imatinib over 6 years.

**Methods:** A cohort of pediatric patients with LGC treated with Imatinib 400 - 800 mg every 24 hours who were not transplanted was analyzed for 6 years. Age, gender, clinical and hematological characteristics at admission and follow-up after the start of Imatinib were evaluated. Growth, neuroendocrine development and hematological toxicities were monitored. The early and major molecular response, development of resistance, OS and EFS were evaluated.

**Results:** Sixteen patients with LGC were included and 1 was excluded due to treatment abandonment. Of the total 60% were female and 40% were male with age range from 6 to 14 years with median of 13 years. Early molecular response occurred in 66% meanwhile major response in 86.6% of the patients, only 1 developed Imatinib resistance during follow-up. OS at 6 years was 95% and EFS was 86%. All patients presented growth arrest and adolescents delayed development of sexual characteristics. There was no evidence of hematological or non-hematological toxicity that required discontinuation of treatment.

**Conclusions:** Imatinib achieves complete cytogenetic and molecular remission in more than 80% of children with CGL. Toxicity is not severe and is well tolerated by all pediatric patients. The most important toxicity shown was growth arrest and delayed neuroendocrine development. Until now, there is no study that indicates when is the right moment to suspend the therapy in the pediatric population.

EP267/#884 | Poster Topic: AS05 SIOP Scientific Program/AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes

#### EARLY MORTALITY AND BLOOD PRODUCT UTILIZATION IN CHILDREN WITH ACUTE MYELOID LEUKEMIA IN LILONGWE, MALAWI: IN SUPPORT OF EARLY INTENSITY-ADAPTED PROTOCOLS

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**Background and Aims:** Survival of pediatric acute myeloid leukemia (AML) in sub-Saharan Africa is dismal, often <20%. Intensity-adapted protocols targeting treatment-related mortality in early therapy have been published but not widely adopted. The purpose of this study was to leverage seven years' experience treating AML in Lilongwe, Malawi evaluating patterns of mortality to determine if early intensity-adaptation may be appropriate in this resource-limited setting.

**Methods:** We conducted a retrospective cohort study of children age <18 years with *de novo* AML at Kamuzu Central Hospital between 2016-2022, excluding promyelocytic leukemia. Diagnoses were made by blast morphology +/- flow cytometry. Children were generally treated with two 10+3 inductions with cytarabine (100 mg/m<sup>2</sup>/BID) and doxorubicin (90 mg/m<sup>2</sup>/cycle) followed by two consolidation cycles with high-dose cytarabine (18 g/m<sup>2</sup>/cycle). Survival outcomes were described.

**Results:** We identified 53 patients. Thirty-six cases were confirmed by flow cytometry (67%). Two patients had trisomy 21. Two-year OS and EFS were 30% (95%CI, 20-47%) and 24% (95%CI, 14-39%), respectively. Median time to death from start of treatment was 25 days (interquartile range [IQR], 12-266). Twenty-one of 35 deaths (60%) occurred within 50 days of starting therapy (39% of cohort). Among patients with early death, the most common causes were hemorrhage (10, 48%) and infection (8, 38%). Both blood and platelet transfusion utilization was highest throughout Induction 1 versus later cycles (ANOVA p<0.001). Patients (n=20) who survived to receive high dose cytarabine in consolidation had a 2-year EFS of 56% (95% CI, 37-84). Nine patients (18%) relapsed a median of nine months from diagnosis (IQR, 7-10).

**Conclusions:** Childhood AML is curable in low-resource settings, but early treatment-related mortality is unacceptably high. Among patients surviving this critical phase, most were alive two years later. These data strongly support advocacy for increased blood product

capacity as well as implementing and evaluating intensity-adapted AML protocols targeting early mortality in low-resource settings.

EP268/#758 | Poster Topic: AS05 SIOP Scientific Program/AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes

#### VARIATION IN PLATELET LEVELS DURING TREATMENT FOR PEDIATRIC ACUTE MYELOID LEUKEMIA

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**Background and Aims:** Chemotherapy for acute myeloid leukemia (AML) results in prolonged neutropenia, increasing risk for infection. There remains a differential risk for infection despite similar chemotherapy and supportive care. This may result from variation in reduction of other cell lines, including platelets. Differences in platelet levels at baseline, nadir and recovery are described by treatment course and patient characteristics in a multicenter pediatric cohort.

**Methods:** A retrospective study of patients <21 years with newly diagnosed AML from 2011-2019 at one of XX hospitals in the Leukemia Electronic Abstraction of Records Network. Patient characteristics, treatment regimens, and laboratory results were extracted from the electronic record record four up to four chemotherapy courses. Platelet values at course entry, time from course entry to nadir, and time to recovery (>80,000 cells/uL) were summarized and compared across sex, age, race/ethnicity, and chemotherapy regimen using the Wilcoxon rank sum or Kruskal-Wallis tests.

**Results:** 208 patients contributed 19,601 platelet levels across 686 courses. Median age at diagnosis was 9.2 years (interquartile range, 2.4-14.6). Median platelet levels declined shortly after chemotherapy initiation and did not recover for at least 21 days in all courses. Median platelet values at course entry, time to nadir, and time to recovery were similar across sex and race/ethnicity within each course. Time to platelet nadir differed by chemotherapy regimen in induction I and by age category in intensification I. Time to recovery differed by age group within all courses.

**Conclusions:** The trajectory of platelet levels was similar in each course, although decline and recovery did vary by certain patient characteristics. Variation in platelet trajectories may represent an opportunity to further understand differential risk of infection in children with AML.

EP269/#1762 | Poster Topic: AS05 SIOP Scientific Program/AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes

#### GEMTUZUMAB OZOGAMICIN FOR RELAPSED OR PRIMARY REFRACTORY ACUTE MYELOID LEUKEMIA IN CHILDREN - EXPERIENCE OF THE POLISH PEDIATRIC LEUKEMIA AND LYMPHOMA STUDY GROUP (PPLLSG)

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**Background and Aims:** Gemtuzumab ozogamicin (GO), one of the first targeted drugs used in oncology, consists of an anti-CD33 monoclonal antibody bound to a derivative of cytotoxic calicheamicin. After the drug was withdrawn in 2010 due to a significantly increased rate of early deaths, GO regained approval in 2017 for the treatment of adults and children with acute myeloid leukemia (AML) refractory or relapsed (r/r) and de novo AML. The aim of the study is to analyze retrospectively the effects of treatment and the toxicity profile of GO in children with primary refractory or relapsed AML.

**Methods:** From January 2008 to December 2022, 35 children were treated with GO in the Polish Paediatric Leukemia and Lymphoma Study Group (PPLLSG) centres (18 girls and 17 boys, mean age 6.3 years). Primary refractory disease was the indication for GO use in 13 children, the first early AML relapse in 15 children, the first late in 5, and the second early in 2 children. Thirteen children had poor risk genetics at the time of diagnosis leukemia.

**Results:** Most of the children (72%) had more than 5% bone marrow leukemic blasts (0.1-100%; median 22%) before the start of GO therapy. Most of the patients (30/35) received 1 administration of GO in combination with chemotherapy (IDA-FLA, DOXO-FLA, FLA, FLAG). Of the 35 patients, 18 (52%) achieved complete remission, 8 presented with progression, and 6 with relapse. GO therapy was followed by haematopoietic stem cell transplantation in 19 children. Twenty-one children eventually died from disease progression, VOD, COVID, CMV. Fourteen patients (40%) live in the first or subsequent remission of the disease. Hematological toxicities and VOD were reported during GO therapy.

**Conclusions:** The use of GO in severely pretreated children with previous failure of failure of AML treatment is a possible and effective fusion therapy to SCT, with an acceptable toxicity profile.



EP270/#1569 | Poster Topic: AS05 SIOP Scientific Program/AS05.b  
Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes

### GERMLINE MUTATIONS IN DDX41 IN A CHILDHOOD CANCER COHORT: PREVALENCE AND CASE REPORT

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**Background and Aims:** Germline mutations in *DDX41* (*gmDDX41*) predispose to myeloid malignancies and possibly to other cancers. Carriers typically develop cancer after the fourth decade of life. This study aims to establish the frequency of *gmDDX41* in pediatric oncology patients.

**Methods:** Germline exome sequencing was performed between 2014 and 2022 in children diagnosed with cancer in Québec, Canada, as part of oncogenomic research projects. *DDX41* variants were interpreted according to ACMG guidelines to identify pathogenic (P) or likely pathogenic (LP) variants.

**Results:** 376 patients, diagnosed with 386 cancers (207 [53.6%] solid tumors and 179 [46.4%] hematological malignancies), were included. One (1/376, 0.3%) germline *DDX41* LP variant was identified, NM\_016222.4:c.305\_306del (p.Lys102Argfs\*32), previously reported in 5 adults diagnosed with acute myeloid leukemia (AML). The affected individual is a 7-month-old girl diagnosed with AML (1/42 AML). She had no family history of cancer but was also diagnosed with mosaic Down Syndrome (T21). The germline origin of *DDX41* variant, maternally inherited, was confirmed in gDNA from fibroblasts. Bone marrow aspiration revealed myeloblasts with maturation and flow cytometry was consistent with a myeloid phenotype. Somatic mutations were identified in *GATA1* and *STAG2*, but not in *DDX41*. The patient completed treatment according AAML0431 protocol and remains leukemia-free 1.5 years after end of therapy. While the incidence of AML is markedly increased in T21 patients, a combination of risk factors could have contributed to AML development. Only one other case of childhood cancer with *gmDDX41* at compound heterozygous state was reported in a 5-year-old diagnosed with blastic plasmacytoid dendritic cell neoplasm.

**Conclusions:** Although *gmDDX41* are rare in pediatric oncology, we report its occurrence in an infant with mosaic T21 who developed AML. Additional studies are needed to determine the frequency of *gmDDX41* in pediatric AML patients, and whether additional risk factors are required.

EP271/#286 | Poster Topic: AS05 SIOP Scientific Program/AS05.b  
Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes

### PRELIMINARY INVESTIGATION ON THE USE OF LOW DOSE CHEMOTHERAPY WITH G-CSF AS INDUCTION THERAPY IN PEDIATRIC AML TREATED IN A TERTIARY HOSPITAL IN THE PHILIPPINES

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**Background and Aims:** Treatment outcomes for children with AML has improved substantially with the use of intensified induction chemotherapy and improved supportive care, however, intensive induction therapy is associated with life-threatening complications. In LMICs, challenges brought about by the pandemic necessitated the use of a less intensive induction regimen. This study aimed to determine the effectiveness and tolerability of low dose chemotherapy/G-CSF as induction chemotherapy among children with de novo AML treated at the Philippine Children's Medical Center from July 2021 to 2022

**Methods:** This study prospectively enrolled newly diagnosed AML patients. A regimen containing doxorubicin plus low dose cytarabine and G-CSF was given as 2 courses of induction therapy. The rate of remission and adverse events were reported.

**Results:** Twenty one (21) patients were diagnosed with AML during the study period. Eighteen (18) fulfilled the inclusion criteria. After induction course I, 55% (10/18) patients achieved remission and 7 of 15 (46.7%) patients who received the second induction course attained sustained remission. Grade 3-4 thrombocytopenia and myelosuppression were reported in all patients who received the first induction course. There were three (3) toxic deaths, two from neutropenic sepsis and one from intracranial bleeding. The cohort of non-responders were older (11.6 years vs 9.7 years) and had higher initial WBC count ( $59.6 \times 10^9/L$  vs  $30.9 \times 10^9/L$ ). Over-all remission rate after 2 courses of LDC/G-CSF was 38.9% (7/18). None of the patients in this study abandoned treatment.

**Conclusions:** In this preliminary study, LDC/G-CSF regimen induced remission in AML patients with lower initial WBC count. However, this needs to be validated in future studies with a bigger sample population.

EP272/#1607 | Poster Topic: AS05 SIOP Scientific Program/AS05.b  
Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes

### OUTCOMES OF CHILDREN AND ADOLESCENTS WITH ACUTE PROMYELOCTIC LEUKEMIA TREATED WITH ALL-TRANS RETINOIC ACID AND ARSENIC TRIOXIDE

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**Background and Aims:** Acute promyelocytic leukemia (APML) represents about 7% - 12% of childhood acute myeloid leukemia (AML). Use of all-trans retinoic acid (ATRA) and arsenic trioxide (ATO) has allowed reducing or avoiding use of other chemotherapeutic agents for children with APML. There is limited data of children treated with ATRA and ATO from low-middle income countries (LMIC). We conducted this retrospective analysis to look for outcomes of children and adolescents treated with ATRA, ATO ( $\pm$  chemotherapy).

**Methods:** Children and adolescent (aged  $\leq 18$  years) diagnosed as APML between 1st January 2016 and 31st December 2021 were included. Two-year event free survival (EFS), and overall survival (OS) were calculated.

**Results:** Out of total 298 cases of AML, 71 (23.8%) were diagnosed with APML and 62 received treatment with ATRA, ATO ( $\pm$  chemotherapy). Median age was 12 years (IQR 9 - 15 years). There was a minimal male preponderance (Male:female ratio 1.2:1). High-risk disease (total leukocyte counts  $\geq 10,000/\text{cumm}$ ) was seen in 38 (61%) children. Eleven children with low-risk disease received induction and consolidation with ATRA and ATO without maintenance treatment. Thirteen low-risk and 38 high-risk children received induction and consolidation with ATRA, Daunorubicin and ATO followed by maintenance treatment with 6 MP, methotrexate and ATRA. Total 35 (56.5%) children died, 34 during induction and one after relapse. Two year EFS and OS for all children was 41.1% and 43.1%, respectively. Two-year EFS and OS for children who survived  $> 15$  days was 91.8% and 96.4%, respectively. Two-year EFS of children with low-risk and high-risk disease was 62.5% and 28%, respectively ( $p=0.006$ ) and two-year OS was 62.5% and 31.1%, respectively ( $p=0.02$ ).

**Conclusions:** Good survival was seen with ATRA-ATO based treatment in children who achieved induction remission. Early induction mortality is still major factor contributing to lower survival in LMIC. Children with high-risk disease had dismal outcome.

EP273/#720 | Poster Topic: AS05 SIOP Scientific Program/AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes

#### PEDIATRIC ACUTE MYELOID LEUKEMIA: EXPERIENCE FROM A TERTIARY CARE CENTRE IN INDIA

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**Background and Aims:** Treatment of pediatric acute myeloid leukemia (AML) in developing countries is challenging due to socio-economic constraints. There is a scarcity of published data on the demographics and outcomes of children with AML in India. We analysed the characteristics and outcome of pediatric AML patients treated at our centre.

**Methods:** Retrospective data of pediatric AML treated at our centre between January 2010 and February 2023 was collected. Patients treated between January 2010 and June 2014 were taken as Group 1 and the rest as group 2. Acute promyelocytic Leukaemia patients were excluded.

**Results:** A total of 133 patients was evaluable. The median age was 11.5 years (range 0.5 to 24 years); male: female ratio 1.1:1. Group 1 ( $n=43$ ) received chemotherapy as per AML MRC 10 protocol. Karyotyping and/or PCR for t (8;21), inv 16 and t (15;17) were done for risk stratification. Twenty-eight (65.11%) patients attained complete remission (CR). Two patients underwent AHST in CR2. With a median follow-up of 14 months (range 1 - 149) overall and event-free survival was 30.23% and 27.9% respectively. Nine (20.9%) had relapsed disease. Group 2 ( $n= 90$ ) patients were risk stratified with karyotyping and molecular mutation (NPM, FLT3, CEBPA) analysis. Since October 2020 next generation sequencing was also done. Post-induction Good-risks patients were treated with 3 cycles of chemotherapy (HIDAC); Intermediate-risk patients were treated with either Chemo or AHST; Poor-risk patients were treated with AHST. Seventy-seven (85.55%) patients attained CR. Relapse occurred in 23 patients. AHST was done in 26 patients in CR1 and 22 in CR2. The overall and event-free survival was 48.88% and 43.33% respectively with a median duration follow-up of 16.5 months (range 1- 103). Induction mortality due to sepsis or refractory disease was 14.2% for the entire cohort.

**Conclusions:** With better risk stratification and the use of AHST, survival outcome has increased in our cohort.

EP274/#663 | Poster Topic: AS05 SIOP Scientific Program/AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes

#### EMP1 IN PEDIATRIC ACUTE MYELOID LEUKEMIA: TO TARGET OR NOT TO TARGET?

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**Background and Aims:** Although the survival of pediatric acute myeloid leukemia (pedAML) patients has considerably improved in the last decades, the relapse rate known to be associated with residual leukemic stem cells (LSC) remains high. New therapeutic options targeting the LSC while avoiding short-term and long-term toxicity, are warranted. We have previously shown *EMP1* is significantly over-expressed in LSC compared to hematopoietic stem cell fractions. In addition, *EMP1* was documented as part of the 17-gene stemness score (LSC17) predicting relapse and a 6-membrane protein gene (6-MPG) score predicting the prognosis of cytogenetically normal AML. In both signatures, high *EMP1* expression correlated with worse overall survival. Altogether these data suggest that *EMP1* may be a promising immunotherapeutic target in pedAML.

**Methods:** The mRNA and protein expression of *EMP1* were evaluated in commercially-available hematological cell lines and pedAML samples using RT-qPCR, Western blot, and flow cytometry. Expression in normal blood cells and tissues was evaluated by flow cytometry and immunohistochemistry. Using the R2 and TARGET databases, association analyses of *EMP1* expression with clinical and molecular characteristics were performed, as well as gene set enrichment analyses.

**Results:** In silico analyses showed variable mRNA expression of *EMP1* in multiple AML datasets and a significant correlation between high *EMP1* transcript levels and the presence of *inv(16)*. RT-qPCR confirmed the broad expression of *EMP1* in various AML cell lines (n=9). By Western blot expression of *EMP1* was found in multiple hematological cell lines, including AML. Flow cytometry showed overexpression of *EMP1* in 66% of the evaluated pedAML samples (n=6/9), but also showed expression in normal blood cells. Importantly, immunohistochemistry revealed *EMP1* expression in multiple normal tissues.

**Conclusions:** Although *EMP1* presents as an interesting membrane-associated target widely expressed in pedAML, its abundant expression in normal blood cells and tissues will impede it from further exploration as an immunotherapeutic target.

EP275/#821 | Poster Topic: AS05 SIOP Scientific Program/AS05.c  
*Lymphomas*

#### SUCCESSFUL INAUGURATION OF THE PEDIATRIC PTLD COLLABORATIVE (PPC) PROVIDES AN EXCELLENT PLATFORM FOR PTLD REGISTRY AND PROSPECTIVE STUDIES

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**Background and Aims:** Motivated by challenging cases and unanswered management questions in rare subtypes of monomorphic post solid organ transplant lymphoproliferative disorders (PTLD), we formed a collaborative to further study post solid organ transplant Burkitt lymphoma (PSOT-BL) and Epstein-Barr virus-negative monomorphic PTLD (EBV[-]M-PTLD).

**Methods:** Forty-three institutions in US, UK, Germany and Canada were invited to participate in the collaborative

**Results:** Of 43 institutions invited 28 responded. Lack of time and or administrative support were the most frequent barriers among responders. Two successful studies were completed between 2020 and 2022: PSOT-BL and EBV[-]M-PTLD in 14 and 11 centers respectively. Results of these 2 studies were published and found that a wide variety of regimens were used. It was not possible to determine the rationale of the choice of various treatment regimens, highlighting the uncertainties regarding optimal treatment and lack of guidelines. Because of the small number in patients' subgroups, statistical analysis was limited to determination of EFS, and OS did not allow subgroup or multivariate analysis, highlighting the limitations of analyzing data from small subgroups of patients. The collaborative was successful in data collection, robust participation in writing and editing abstracts [N=2] and

manuscripts [N=2]. Limitations encountered included: 1) Regulatory, lengthy and time-consuming administrative process to finalize data sharing agreements and IRB approval, 2) Small number of patients, making it difficult to justify time in getting regulatory approval, 3) Lack of funding for data management and statistical support, 3) Retrospective data collection resulting in some missing data. Areas of unmet need were lack of prospective data in uncommon types of PTLD resulting in uncertainties regarding the best treatment and prognostic factors

**Conclusions:** Successful collaboration across 15 pediatric transplant centers was feasible and provided an excellent platform for future prospective work. Wider participation and funding support to develop a PTLD registry and prospective data collection are next steps.

EP276/#1128 | Poster Topic: AS05 SIOP Scientific Program/AS05.c Lymphomas

#### THE CHARACTERISTICS OF HODGKIN LYMPHOMA PATIENTS REGISTERED IN THE FRENCH AFRICAN PEDIATRIC ONCOLOGY GROUP (GFAOP) HOSPITAL BASED REGISTRY

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**Background and Aims:** Hodgkin's Lymphoma (HL) is a curable cancer with 90% OS in high-income county. The first HL GFAOP study using data from 2006 to 2012 from 6 Pediatric Oncology Units shows OS at 82%. Here we describe the characteristics of children diagnosed with HL attending GFAOP pediatric oncology units and attempt to look at outcome for this group and hopefully identify progress and different pathways for improvement.

**Methods:** Using the GFAOP Hospital Based Cancer Registry (2017-2021) we extracted data from 15 GFAOP units, 13 from Sub-Sahara countries and 2 from North Africa, for children <18 years with a suspicion of a HL. Histological reports confirmed diagnosis, and stage was allocated according to Anne Arbor Classification. Follow up information was collected at 12 months post diagnosis and extended to 36 months from 2019.

**Results:** Two hundred and five patients were identified with a suspicion of HL following clinical examination, 198 of whom had their diagnosis confirmed and 183 were treated (92%). The sex ratio was 4:1 in favor

of boys. A total of 50% of all patients were from Dakar (20%), Rabat (20%) and Antananarivo (11%). Of the 180 patients treated, stage was unknown for 38 (21%), 15 were Stage I (6.6%), 49 Stage II (27.2%), 56 Stage III (31.1%) and 21 Stage IV (11.6%). Follow-up information was available for 90% of staged and treated patients: 65 patients were in complete remission with a median follow-up of 37 months (29-76), 1 patient in remission after relapse, 14 died. Nine patients abandoned and 2 patients were lost to follow up following treatment.

**Conclusions:** This study provided a baseline assessment prior to the implementation of the new Hodgkin Lymphoma therapeutic recommendations for the GFAOP. It identifies difficulties in services to manage diagnosis and correctly stage these children.

EP277/#796 | Poster Topic: AS05 SIOP Scientific Program/AS05.c Lymphomas

#### DEVELOPMENT OF THE ADAPATED RESOURCE AND IMPLEMENTATION APPLICATION (ARIA) ADAPATED MANGEMENT GUIDELINE (AMG) FOR HODGKIN LYMPHOMA (HL): A REPORT FROM THE ARIA GUIDELINES PROJECT

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**Background and Aims:** HL is a World Health Organization (WHO) Global Initiative for Childhood Cancer index cancer. The standard of care for HL is well known, but safe adaptations for settings with limited access to chemotherapy, radiation, supportive care, and advanced imaging are lacking. The ARIA HL AMG was developed to address knowledge gaps in the established evidence-base and facilitate adaptations of therapy for contexts with limited resources.

**Methods:** Using various collaborative networks, we empaneled a multidisciplinary mix of pediatric hematologists-oncologists, radiation oncologists, surgeons, and nurses. The panel was designed with an intentionally diverse mix of WHO regional and World Bank income level representation. Panel members reviewed three drafts of the AMG with comments/feedback integrated into the source document after each round. Where evidence was identified as lacking, the panel also completed a three-round modified-Delphi consensus method. As consensus was achieved, the AMG was sent to a panel of two external expert reviewers.

**Results:** Forty panel members from 12 pediatric oncology consortiums or international societies participated in the ARIA HL panel. A total of 632 comments were received after rounds 1, 2 and 3 of the AMG structured review process. All comments were centrally reviewed, and the AMG was iteratively revised. When areas of disagreement among the comments were identified, small content-specialized groups from within the panel were formed to discuss alternative language or recommendations. In addition, all 10 Delphi statements reach consensus and were integrated into the AMG: four after the first round, five after the second and one after a third round.

**Conclusions:** The ARIA HL AMG is the first guideline to provide comprehensive management guidance to support healthcare providers regardless of resource settings. The AMG is now freely available on [ariaguide.org](http://ariaguide.org), a web-based dissemination resource designed to support rapid adoption of the guidelines worldwide.

EP278/#1054 | Poster Topic: AS05 SIOP Scientific Program/AS05.c  
*Lymphomas*

#### OUTCOME OF RELAPSE IN CHILDREN AND ADOLESCENTS WITH BURKITT LYMPHOMA: EXPERIENCE OF THE PEDIATRIC HEMATOLOGY AND ONCOLOGY CENTER IN RABAT (MOROCCO)

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**Background and Aims:** Relapses after successful and intensive front-line treatment of B Non Hodgkin lymphoma (B-NHL) are rare. Survival of children/adolescents with relapsed B-NHL remains poor after intensive initial treatment. The Rabat center is supported by the Groupe Franco-Africain d'Oncologie Pédiatrique (GFAOP) and uses the therapeutic protocols of this group. **Objectives:** to describe relapsed Burkitt lymphoma (BL) in children/adolescents treated with the GFA/LB 2005 protocol in the pediatric hematology and oncology center of the children's hospital of Rabat (Morocco).

**Methods:** We retrospectively reviewed relapsed Burkitt lymphoma between August 2009 and September 2021.

**Results:** A total of 13 cases out of 170 BL relapsed (7%). The average age was seven years and 10 months (2 years 7 months - 15 years) with a sex ratio of 3.33. Ten patients were classified as treatment group B initially (77%) and three were treated as group C initially, Rituximab was not used in initial treatment. The main initial location was abdominal alone or associated with other locations. The median time to relapse after complete remission was two months (range 1.5 months to 12

months). The most common site of relapse was the central nervous system, the site of relapse was isolated in 54% of cases and multiple in 46%. All patients received reinduction chemotherapy, 46% received Rituximab and 5 patients HD chemotherapy with autologous HSCT. The response rate to first-line salvage chemotherapy was 38%, one patient in our series had a 2<sup>nd</sup> neuromeningeal relapse occurring eight months after his 2<sup>nd</sup> CR, this patient was put on 3<sup>rd</sup> CR after high dose chemotherapy followed by HSCT. Six patients were still alive (46%). The main cause of death in our series after salvage treatment was disease progression (71%).

**Conclusions:** Therapeutic guidelines at relapse in BL were to obtain a second complete remission and to consolidate the remission with HD chemotherapy followed by HSCT.

EP279/#409 | Poster Topic: AS05 SIOP Scientific Program/AS05.c  
*Lymphomas*

#### OUTCOMES AND TREATMENT RELATED TOXICITIES IN CHILDREN WITH HODGKIN LYMPHOMA ON OEPA (VINCRIStINE, ETOPOSIDE, PREDNISONE, DOXORUBICIN) – A LOW AND MIDDLE-INCOME COUNTRY (LMIC) EXPERIENCE

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**Background and Aims:** Hodgkin Lymphoma (HL) has excellent survival rates with different treatment regimens, thus chemotherapy selection requires careful consideration of treatment-related toxicities. There is limited data on the safety profile and outcomes of patients with HL on OEPA (vincristine, etoposide, prednisone, doxorubicin) based protocols from low and middle-income countries (LMICs). This study was designed to evaluate the outcomes of pediatric patients with HL treated on OEPA at a tertiary care center in Pakistan.

**Methods:** All pediatric patients with HL treated on EuroNet PHL-C1 based protocol at Aga Khan University Hospital between March 2015- November 2019 were retrospectively included. Toxicities were defined as febrile neutropenia (FN), gastroenteritis (GE), oral mucositis (OM), and neuropathy. Imaging was performed after two cycles of OEPA to assess treatment response.

**Results:** We identified 20 patients with HL treated on OEPA. Male:female ratio was 1:1 and median age 12 (IQR 6.5-14) years. The majority (n=16 80%) had advanced stage III/IV. During OEPA-1, 16 (80%) patients had treatment toxicities, including 10 (50%) with GE and 9 (45%) with FN. Nine (45%) needed admission for a median 4 (IQR 3-7) days. One patient had treatment-related death after OEPA-1. During OEPA-2, 13 (65%) patients had treatment toxicities, 6 (35%) with FN, 2 (10%) with OM, and 2 (10%) with neuropathy. Of these, 7 (35%) needed admission for a median 3.5 (IQR 3-5) days. After OEPA-2, 11 (55%) patients had complete metabolic response on PET CT and 2 had

adequate response on CT-contrast. Six (30%) patients received radiotherapy treatment. The overall survival was 95% at median 48 (IQR 36-60) months and event-free survival was 85% at median 24 (IQR 18-42) months.

**Conclusions:** Our data indicates that OEPA-based regimens tend to cause significant toxicities requiring hospital admission. Given a LMIC context, other regimens with less toxicity profiles should be preferred.

EP280/#1324 | **Poster Topic: AS05 SIOP Scientific Program/AS05.c Lymphomas**

### A UNIQUE DISEASE: A 20 YEAR RETROSPECTIVE STUDY OF NLPHL AT A TERTIARY CARE HOSPITAL IN PAKISTAN

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**Background and Aims:** There is a paucity of published literature on pediatric nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL), a rare subtype of Hodgkin lymphoma, especially from low-middle income countries (LMIC). This study evaluates the clinical characteristics and outcomes of NLPHL patients of a tertiary hospital in an LMIC.

**Methods:** A retrospective study was conducted by Indus Hospital and Health Network (IHNN), Karachi to determine the outcomes of pediatric patients diagnosed with NLPHL between 2002 and 2022.

**Results:** A total of 17 patients, ranging from 2-15 years with a mean age of  $8.9 \pm 4.4$  years, were registered of which 13 (76.5%) were male. Stage 2 was the most frequently seen ( $n=11$ , 64.7%). B-symptoms were present in 8 patients (47.1%). Bone marrow involvement was seen in 2 patients, with 1 having extra-nodal involvement as well. Bulky disease was not seen in any of the cases. Treatment was initiated by 14 patients (82.4%) of which 7 (50%) received standalone chemotherapy, 3 (21.4%) underwent node resection alone, and 4 (28.6%) received both. Radiation was not given to any patient. Complete remission without relapse was achieved by 8 (57.1%) while relapse was reported in 4 patients (28.6%) who then received 2nd line treatment and are still alive. Median follow-up time was 36 months (range 9-84 months). Disease related death occurred in 1 patient and transformation to diffuse large B-cell lymphoma (DLBCL) was seen in 1 case.

**Conclusions:** Due to the low incidence of NLPHL, there is limited data available internationally and hence no standard management protocol has yet been established. At present, varying regimens have been used based on the setting and availability of resources. NLPHL is known for its indolent course and overall excellent prognosis hence, larger scale, prospective research is needed to decide an optimal, standardized therapy regimen for this disease.

EP281/#244 | **Poster Topic: AS05 SIOP Scientific Program/AS05.c Lymphomas**

### CHILDHOOD HODGKIN LYMPHOMA IN SUB-SAHARAN AFRICA: A SYSTEMATIC REVIEW AND META-ANALYSIS ON THE EFFECTIVENESS OF THE USE OF CHEMOTHERAPY ALONE

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**Background and Aims:** Childhood Hodgkin lymphoma (HL) is a highly curable cancer. Although combined chemotherapy and radiotherapy is the standard treatment for HL, many countries in Sub-Saharan Africa (SSA) have little or no access to radiotherapy and use chemotherapy alone to treat childhood HL. Children with HL have a high survival rate in developed countries; this has yet to be established in SSA. Our aim was to assess the effectiveness of the use of chemotherapy alone in children with HL in SSA.

**Methods:** We searched Medline, Cinahl, Cochrane Central, and Embase, and a pre-print server (AfricArxiv), for records from January 2000 to December 2022. The identified evidence was screened and extracted by two independent reviewers. Eligibility criteria included interventional and observational studies that evaluated the survival outcomes of children with Hodgkin lymphoma between 0 and 18 years of age in SSA. The preferred reporting items for systematic reviews and meta-analyses (PRISMA) were followed, and the GRADE tool was used to assess the quality of the included studies.

**Results:** The initial searches yielded 318 results. Following the application of the eligibility criteria, six studies were included in the review. All the included studies were observational with relatively small sample sizes (6-106). Three of these studies were included in the meta-analysis of overall survival and mortality. The most common clinical presentation and histological type of HL noted were lymphadenopathy (> 70%) and nodular sclerosing subtype, respectively, and about 80% of the patients presented with advanced disease. The pooled estimates for overall survival, mortality, and treatment-related deaths following treatment with chemotherapy only were 67.8% (95% CI: 42.1-88.8%), 30.8% (95% CI: 12.9-52.3%), and 8.2% (95% CI: 1.4-19.7%), respectively, using the random effects model.

**Conclusions:** Chemotherapy alone may be adequate for the treatment of childhood HL in SSA. Adequately powered or multi-centric studies and evidence extending to developing countries are highly recommended.

EP282/#890 | **Poster Topic: AS05 SIOP Scientific Program/AS05.c Lymphomas**

### CHARACTERISTICS OF RELAPSED HODGKIN LYMPHOMA IN PEDIATRIC PATIENTS; A 10 YEAR RETROSPECTIVE STUDY OF AN LMIC

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**Background and Aims:** With conventional standard treatment modalities, children and adolescents with Hodgkin lymphoma (HL) have long-term overall survival rates of over 90%. However, primary refractory disease may occur in 5-10% of HL patients, while relapse occurs in 5-10% of patients with early stage disease and up to 30% in advanced stage. This study evaluated patient characteristics of HL relapse and their response to second line treatment of standalone chemotherapy or in combination with radiotherapy. Immunotherapy and autologous stem cell transplantation (ASCT) were not available in our setting.

**Methods:** A retrospective study was conducted between 2013 and 2022 by the Department of Pediatric Oncology of Indus Hospital & Health Network, to determine outcomes of patients with Hodgkin Lymphoma relapse.

**Results:** A total 742 patients were diagnosed with Hodgkin Lymphoma at IHHN. Of these, 48 (6.5%) patients presented with relapse and 35 (4.7%) with refractory disease after initial chemotherapy. In HL relapse patients, 57% were stage IV at initial diagnosis with most common pathology being nodular sclerosis constituting 42.9% of patients. The most common age group was 6-10 years, 45.8%. B symptoms were experienced by 25 (52%) patients. A time to relapse of >12 months following diagnosis was seen in 69% and 3-12 months was seen in 31%. After receiving second line treatment which constituted of either EPIC or gemcitabine/vinorelbine cycles, complete remission was achieved by 34 (70.8%) patients, partial remission was seen in 5 (10.4%), disease progression in 5 (10.4%), 3 (6.3%) patients left during treatment, and 1 (2.1%) was treatment-related mortality. Re-radiation in second line treatment was only required for 2 patients. Second relapse was seen in 11 (28.2%) of 39 complete and partial remission patients.

**Conclusions:** Major limitations in the treatment of HL relapse exist in low-resource settings. Dedicated efforts are required to provide facilities for immunotherapy and ASCT free of cost in LMICs.

EP283/#66 | Poster Topic: AS05 SIOP Scientific Program/AS05.c  
*Lymphomas*

#### EPIDEMIOLOGICAL, CLINICAL CHARACTERIZATION AND OUTCOME OF BURKITT LYMPHOMA IN CAMEROON; A TEN YEAR REVIEW SHOWS DECREASING INCIDENCE

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**Background and Aims:** Burkitt Lymphoma (BL) is the most common childhood cancer in areas where malaria is holo-endemic where it constitutes half of all childhood cancer diagnoses and up to 90% of lymphomas. Though a curable cancer which responds very well to chemotherapy alone, it still causes a lot of morbidity and mortality in these areas. The study aimed to determine the incidence and trends of BL and to describe the clinical and epidemiological characteristics as well as the outcome of children treated for BL in Cameroon from 2007 to 2016.

**Methods:** We retrospectively reviewed 1042 medical records of children diagnosed with BL in the four major pediatric cancer treatment centres in Cameroon from 2007 to 2016.

**Results:** Males constituted 59% and 58% of the participants were between 4 to 9 years. Almost 90% (797/915) of the patients came from 4 out of 10 regions. About 70% presented more than one month after symptom onset. Majority had advanced disease-stages III and IV accounting for 65.3% and 16% respectively. The commonest tumour location sites were abdomen (71.8%) and Jaw (43.6%). The overall Age Standardized Incidence Rate for BL was 5.9/100000 and the annual incidence dropped steadily from 1.7/100000 in 2007 to 0.5/100000 in 2016. We had 976/1042 (93.7%) initiated on treatment, 35/1042 (3.4%) died without initiation and 26/1042 (2.3%) direct palliative care. For the patients initiated on treatment, 56.8% (554/976) completed treatment, 34.3% (335/976) died, 8.2 % (80/976) abandoned treatment, 41/976 (4.2%) had refractory disease and 197/976 (20.2%) relapsed with 78.5% of the relapse occurring within 6 months from diagnosis. For the patients that completed treatment, 377/554 (68%) declared cured, 48/554(8.7%) died and 57/554(10.3%) lost to follow up.

**Conclusions:** BL incidence in Cameroon dropped over time from 2007 to 2016. Poor outcome due to advanced disease stage at presentation due to delayed presentation.

EP284/#1150 | Poster Topic: AS05 SIOP Scientific Program/AS05.c  
*Lymphomas*

#### PARTIAL EVALUATION OF THE AVERAGE DIRECT MEDICAL COSTS OF BURKITT'S LYMPHOMA TREATMENT AND ECONOMIC ANALYSIS FROM FAMILIES' PERSPECTIVE IN BOBO-DIOULASSO (BURKINA FASO)

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**Background and Aims:** Burkitt's lymphoma is the most frequent childhood cancer in Bobo-Dioulasso. This cancer is also a good illustration of the curability of childhood cancers. However, management remains a challenge in a context of limited resources. The objective of this study was to partially evaluate the average direct medical costs of treating Burkitt's lymphoma and to compare these costs with the average income of the concerned families.

**Methods:** It was an economic analysis. The standard patient method was used, based on the stage of the disease frequently

encountered, the age of preference and the average normal weight for the selected age. The latest therapeutic recommendations of the Groupe Franco-Africain d'Oncologie Pédiatrique were used. The availability of drugs and their prices were assessed in pharmacies in Bobo-Dioulasso. The average income of 30 families of children with cancer was also assessed.

**Results:** Anticancer drugs were scarce in pharmacies with only 2/62 pharmacies having the majority of anticancer drugs. The average medical cost of treatment for Burkitt's lymphoma was 815 dollars. There was considerable heterogeneity in prices from one pharmacy to another. The majority of families of hospitalized children had a low socio-economic level, with an average annual income of less than 825 dollars for all families.

**Conclusions:** Although partial, the evaluation of these costs makes it possible to establish their inadequacy with the incomes of the families. The management of Burkitt's lymphoma may be less expensive in Africa than in the West, but in the absence of adequate social security, it remains out of reach for the majority of families in the context of poverty. The implementation of a policy of subsidizing the cost of treatment is more than necessary.

EP285/#1703 | Poster Topic: AS05 SIOP Scientific Program/AS05.c  
*Lymphomas*

#### WHOLE BODY MRI VERSUS PET CT IN STAGING AND FOLLOWING CHILDREN AND ADOLESCENTS WITH DIAGNOSED LYMPHOMA: CROSS SECTIONAL DIAGNOSTIC PERFORMANCE STUDY

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**Background and Aims:** Lymphoma is a frequent malignancy in childhood and is diagnosed through clinical and histopathological evaluation. Computed tomography 18 F FDG (PET CT) is the imaging method of choice for staging, but its frequent use and consequent exposure to radiation poses a potential risk of side effects (qualitative and quantitative), especially in children. Whole-body diffusion-weighted imaging (WBMRI) is an ionizing radiation-free imaging method that can be used to screen for neoplasm-related lesions such as lymphoma. The aim of this study is to compare the diagnostic performance of WBMRI and PET CT in detecting lesions in children with lymphoma.

**Methods:** Patients younger than 19 years old, diagnosed with lymphoma, staged and treated in the Hospital de Clínicas de Porto Alegre between October/2017 and January/2022, were scanned both on PET CT and WBMRI. The interval of time between both methods did not exceed 14 days, and the course of treatment should be the same.

**Results:** Fifteen patients were included (1 female and 14 males), with a total of 482 lesions detected, with three histopathological types: Hodgkin (8); Burkitt (6); T-cell lymphoblastic (1). According to this partial analysis, a mean value of 12.93 lesions described in PET CT and 19.20 lesions in WBMRI (SE of 4.59 and 6.76; SD of 17.80 and 26.20, respectively). The related samples Wilcoxon rank test was  $p \leq 0.05$  by (SE of 11.23). Positive correlation was found as demonstrated by the Spearman test (0.02 - significant over 0.01) and in the evaluation of the Bland-Altman plot (different from 0).

**Conclusions:** The analysis suggests that WBMRI can detect lesions in children and adolescents with lymphoma with a significant positive correlation with PET CT (the standard method) and is a free-ionizing radiation method.

EP286/#913 | Poster Topic: AS05 SIOP Scientific Program/AS05.c  
*Lymphomas*

#### CLINICOPATHOLOGIC PROFILE AND TREATMENT OUTCOMES OF CHILDREN WITH NON-HODGKIN LYMPHOMA IN ETHIOPIA

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**Background and Aims:** Non-Hodgkin's lymphoma (NHL) is one of the commonest childhood malignancies in Ethiopia. In high-income countries, five-year event-free survival (EFS) for localized NHL (stage I and II) is 95% to 100% and more than 80% for advanced-stage disease (stages III & IV). In this study, the clinical characteristics and treatment outcomes of children with NHL treated at Tikur Anbessa Specialized Hospital in Ethiopia were assessed.

**Methods:** A retrospective review of patients with histologically proven NHL treated between 2014-2019. was undertaken. Immunophenotype and genetic tests were not available. A modified ALLCL protocol was used to treat all NHL except lymphoblastic lymphoma. Kaplan Meier estimates were used to calculate five-year EFS and overall survival (OS).

**Results:** One hundred forty-nine children were included in the study. 44.3% of the cases were between five and ten years of age, the remaining 32.2% and 23.5% were between one to five and 10 to 15 years old, respectively. 70.5% of cases were male, 67% had advanced disease (stage III and IV). The commonest manifestation was abdominal swelling (55%) and the commonest subtype was Burkitt's lymphoma (53%), Low hemoglobin levels, high LDH, and older age were



significantly associated with advanced disease. Treatment-related mortality accounted for 59% of the total deaths. The five-year EFS and OS rates were 63% and 67%, respectively.

**Conclusions:** Five-year EFS and OS for childhood NHL at Tikur Anbesa Specialised Hospital were lower than that reported in both middle and high-income countries but were high compared to most sub-Saharan reports (less than 50%). Treatment-related mortality was high, suggesting that improvement in supportive care is essential in order to improve outcomes.

EP287/#1346 | Poster Topic: AS05 SIOP Scientific Program/AS05.c  
*Lymphomas*

#### CLINICAL FEATURES AND TREATMENT OUTCOMES OF HODGKIN LYMPHOMA: A RETROSPECTIVE REVIEW IN A PEDIATRIC ONCOLOGY UNIT OF TERTIARY HOSPITAL IN UGANDA

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**Background and Aims:** Hodgkin lymphoma (HL) is a highly curable cancer with an estimated annual incidence of 80,000 cases worldwide. Its treatment is remarkable, with 5-year survival rates exceeding 90% for patients with early-stage disease. The aim of the study was to describe the clinical characteristics, treatment, and survival outcomes of pediatric patients with HL in a resource-limited tertiary facility.

**Methods:** A retrospective review was undertaken on all pediatric patients treated for Hodgkin's lymphoma at the Pediatric Oncology Unit of Mulago National Referral Hospital in Kampala, Uganda between 2019 and 2022. Collecting and analyzing data pertaining to demographic and clinical characteristics, treatment, and survival outcomes, was done.

**Results:** The study included 31 patients who had been diagnosed with HL. The median age at diagnosis was 9 years ((IQR), 6.5). Three-quarters of the patients (70%) were male, and mostly with stage 3 and 4 disease (67%). The most common histological sub-type was mixed cellularity (42%), followed by Nodular sclerosing (27%) and others (23%). The majority (61%) of patients received chemotherapy on schedule; however, 24% missed some and 3% received all chemotherapy but not on schedule. Only 39% of patients got radio-therapy. The treatment regimen was a combination of doxorubicin, bleomycin, vincristine, etoposide, prednisone, cyclophosphamide (ABVE-PC) treatment regimen was the most common (82%). Following treatment, 48% of

patients achieved complete response. The 2-year overall survival (OS) was 54% with a median follow-up time of 8.5 ((IQR), 11.7) months. The 2-year OS advanced-stage disease was 47% compared to 70% for early-stage disease, ( $P < 0.001$ ).

**Conclusions:** This study shows a 48% complete response for Hodgkin's lymphoma. It also provides insight into the clinical presentation and treatment outcomes among pediatric patients in a low resource setting tertiary hospital. A longitudinal study should be carried out to identify factors responsible for this poor response rate to treatment of Hodgkin's lymphoma.

EP288/#1461 | Poster Topic: AS05 SIOP Scientific Program/AS05.c  
*Lymphomas*

#### UNDERSTANDING THE CAUSES OF DEATH FOR CHILDREN DIAGNOSED WITH BURKITT LYMPHOMA AT REGIONAL CANCER REFERRAL HOSPITAL IN TANZANIA

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**Background and Aims:** Cure rates for Burkitt lymphoma (BL) is >90% in high income settings, but survival remains below 50% in many low- and middle income countries. The aim of this work is to analyze causes and phase of treatment associated with BL patient death at a large cancer referral centre in Tanzania. These breakpoints will guide chemotherapy intensification efforts to improve outcomes.

**Methods:** Retrospective patient data was abstracted from the Bugando Medical Centre (BMC) childhood cancer database for all patients diagnosed with BL and treated per the Tanzanian National Treatment protocol from 2016-2022. Extracted data included demographics, site/stage of disease, treatment received and outcomes. Categories of cause of death included treatment related toxicity (including tumor lysis), disease progression on therapy, relapsed disease, non-cancer cause, and unknown cause after abandoning therapy.

**Results:** A total of 121 patients were diagnosed but outcome data was available for 98 patients and included in this analysis. A total of 52% ( $n=43$ ) had stage III or IV disease at presentation. The 1-year overall survival rate was 58%, and 36% of patients abandoned care. Among patients who died, 9.8% ( $n=5$ ) occurred before treatment initiation, 19.6% ( $n=10$ ) died from treatment associated toxicity, 23.5% ( $n=12$ ) died from disease progression while on therapy and 21.6% ( $n=11$ ) died from disease recurrence after completing therapy.

**Conclusions:** We continue to report a high mortality rate for patients treated with Burkitt Lymphoma. This may be due to high proportion

of patients with advanced stage, and the high treatment abandonment rate. A total of 45% of patient death was due to progressive or relapsed disease indicating the importance of intensifying chemotherapy, however, 29.4% were in-hospital deaths before initiation or while on treatment. Therefore, additional supportive care guidelines and patient monitoring are necessary to balance any treatment intensification in the future.

EP289/#1216 | Poster Topic: AS05 SIOP Scientific Program/AS05.c  
*Lymphomas*

#### EPSTEIN - BARR VIRUS - POSITIVE DIFFUSE LARGE B-CELL LYMPHOMA IN PAEDIATRIC AGE GROUP - A CASE SERIES

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**Background and Aims:** Epstein - Barr virus (EBV) - positive diffuse large B-cell lymphoma (EBV+DLBCL), not otherwise specified (NOS) is a B cell neoplasm in immunocompetent individuals. It was previously designated as EBV+DLBCL of the elderly as it was first described above age of 60 years. Subsequently cases were described in younger individuals who showed better treatment outcomes and survival.

**Methods:** We retrospectively reviewed clinico-pathological details of 11 cases of EBV+DLBCL, NOS diagnosed at our institute in the paediatric age group (<18 years) between 2012 and 2022.

**Results:** The median age at diagnosis was 15 years. Male to female ratio was 1.7:1. Clinical and imaging details were available for 8 cases. There was no documented predisposing immunodeficiency. Six cases presented with nodal disease, and 2 cases were extranodal (bone and soft tissue). Eight cases presented in advanced stage (Stage III/IV). Serum EBV DNA result was available for a single case (positive). Histologically, all the cases showed variable number of mono/bi/multinucleated Hodgkin/Reed-Sternberg cells. Ten out of 11 cases were polymorphic resembling classical Hodgkin lymphoma (cHL) (microenvironment of small lymphocytes, plasma cells, and histiocytes) and one was monomorphic type. Immunohistochemistry revealed diffuse expression of pan-B cell markers (CD20/PAX5/CD79a) and EBV-LMP1 in the neoplastic cells in all cases. CD30 showed variable expression in 9 cases. CD15 was positive in a single case. Median survival was 34 months and one patient died of disease.

**Conclusions:** Recognition of EBV+ DLBCL in paediatric population from cHL carries dramatic implications in management and prognosis.

EP290/#1656 | Poster Topic: AS05 SIOP Scientific Program/AS05.c  
*Lymphomas*

#### CYTOLOGY: UNIQUE RELEVANCE FOR NON-HODGKIN LYMPHOMA DIAGNOSIS IN LOW- AND MIDDLE-INCOME COUNTRIES

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**Background and Aims:** Cytology is an established diagnostic modality for Non-Hodgkin Lymphoma (NHL). NHL constitutes a significant portion of common childhood malignancies in Sub-Saharan Africa. Traditionally, diagnosis is achieved by histology from a tissue biopsy specimen. Cytology offers an alternative liquidized specimen through fine needle aspiration (FNAC) of tumour or serous effusions. Concerns about the accuracy of cytology resulting in specimen re-sampling and poor long term tissue storage potential, have discouraged routine use of this method. In Low- and Middle-Income Countries, skilled practitioners and supplies to perform biopsy are often in short supply, resulting in delayed diagnosis or no biopsy at all. FNAC provides an alternative low skill set procedure option for tissue diagnosis. Here-in, we reviewed the efficacy and cost effectiveness of in the diagnosis of NHL at our centre, between February 2019 and January 2023.

**Methods:** We performed a retrospective chart review of all children diagnosed with NHL. We collected data on the method of diagnosis, the turnaround time, dollar cost of pathological diagnosis. Correlations were measured for cases where multiple diagnostic methods were used. Diagnostic accuracy was also assessed for those cases with collateral cytogenetic evaluation.

**Results:** One hundred thirty-two children were diagnosed with NHL. Of these, 31 (23.4%) were diagnosed using biopsy alone, 84(63.6%) were diagnosed with FNAC only and 17 (12.9%) with both FNAC and biopsy of which 10 had correlation. Viable cytogenetics were performed for 21 children who had FNAC. The average turnaround time for FNAC was 4 hours (morphology) and 24 hours (flowcytometry) versus 12 days for tissue biopsy. The average cost for FNAC with flowcytometry was \$62.1 versus \$637 for histology and immunohistochemistry.

**Conclusions:** Cytology (FNAC) is an efficient, cost-effective and accurate form of diagnosis of NHL in LMIC.

EP291/#415 | Poster Topic: AS05 SIOP Scientific Program/AS05.c  
*Lymphomas*

#### FEASIBILITY OF A NEW RISK STRATIFICATION SYSTEM IN PEDIATRIC ANAPLASTIC LARGE CELL LYMPHOMA: RESULT OF A PROSPECTIVE OPEN-LABEL MULTIPLE-INSTITUTION STUDY

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**Background and Aims:** The risk stratification of pediatric anaplastic large cell lymphoma (ALCL) has not been unified. In this study, new risk factors were included to establish a new risk stratification system for ALCL, and its feasibility in clinical practice was explored.

**Methods:** On the basis of the non-Hodgkin's lymphoma Berlin-Frankfurt-Munster 95 (NHL-BFM-95) protocol, patients with minimal disseminated disease (MDD), high-risk tumor site (multiple bone, skin, liver, and lung involvement), and small cell/lymphohistiocytic (SC/LH) pathological subtype were enrolled in risk stratification. Patients were treated with a modified NHL-BFM-95 protocol, combined with maintenance therapy using an anaplastic lymphoma kinase inhibitor or vinblastine in selective patients.

**Results:** A total of 136 patients were enrolled in this study between February 2015 and January 2022 from 17 institutions in South China. The median age was 8.8 years. There were 10, 91, 35 patients with stages II, III and IV. There were 9, 49 and 78 patients in R1, R2 and R3 group. The rate of objective response to first-line chemotherapy was 94.9%. The 3-year event-free survival (EFS) and overall survival of the entire cohort were 77.7% and 92.3%, respectively. The 3-year EFS rates of R1, R2, and R3 patients were 100%, 89.5%, and 67.9%, respectively.

The prognosis of patients with MDD (+), stage IV cancer, pathological subtype of SC/LH, and high-risk tumor sites was poor, and the 3-year EFS rates were 45.3%, 65.7%, 55.7%, and 67.9%, respectively. At the end of follow-up, one of the 5 patients who received maintenance therapy with VLB relapsed, and seven patients receiving ALK inhibitor maintenance therapy did not experience relapse.

**Conclusions:** This study established a new risk stratification system to improve the individualized treatment of pediatric ALCL that is convenient and feasible in clinical practice. Among high-risk group, patients with SC/LH lymphoma and MDD (+) at diagnosis still need to receive better treatment.

EP292/#679 | Poster Topic: AS05 SIOP Scientific Program/AS05.4 Stem Cell Transplantation

#### HSCT IN RARE ONCOLOGICAL AND HEMATOLOGICAL DISEASES IN CHILDREN: EXPERIENCE OF THE NATIONAL MEDICAL RESEARCH CENTER OF ONCOLOGY NAMED AFTER N.N. BLOKHIN

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**Background and Aims: Background.** One of the key stages in the treatment of children with malignant and benign neoplasms is hematopoietic stem cell transplantation (HSCT). Rare non-malignant diseases in some cases belong to the group of so-called precancerous pathology, which makes the topic relevant for specialists working with malignant neoplasms (MNT) in children. **Aims.** To present the experience of HSCT in children with rare oncological and hematological diseases in children in the N.N. Blokhin NMRCO.

**Methods:** At the N.N. Blokhin NMRCO for the period 2019-2022 HSCT was performed in 31 patients with rare oncological and hematological diseases: retinoblastoma (RB)n=5, germ cell tumor (GCT)n=9, Fanconi anemia (AF)n=3, Wilms' tumor (WT)n=9, dyskeratosis congenita (CD)n=3 and pleura -pulmonary blastoma (PPB)n=1, sialoblastoma (SB)n=1. Patients underwent autologous (auto-HSCT) and allogeneic (allo-HSCT) transplantations. M:W=17:14. Median age 47 months (25-192). All patients underwent pharmacological conditioning-children with AF and VD (allo-HSCT) using Busulfan, Fludarabine, ATG and

Cyclophosphamide. Children with RB, SB and GCT (auto-HSCT) with the inclusion of Etoposide, Thiotepa, Carboplatin and Cyclophosphamide, a patient with PPB (auto-HSCT)-Treosulfan and Melphalan, patient with WT (auto-HSCT)-Melphalan. The source of cells in auto-HSCT is peripheral blood (PB), in allo-HSCT: bone marrow (BM) from a sibling-5, PSC from an unrelated donor-1.

**Results:** The patients successfully underwent HSCT. In the early stages after HSCT, complications were noted: toxicoderma of 1-2 degrees, oropharyngeal mucositis of 1-2 degrees, neutropenic enterocolitis of 1-2 degrees. These complications were stopped on the background of standard therapy. Signs of acute GVHD stage 1 were observed in 2 patients after allo-HSCT. Restoration of leukopoiesis with auto-HSCT was recorded on average on the 12th day, and with allo-HSCT, on the 19th day. No significant toxicity was recorded. One death was recorded in a child with RB after 7 months. due to relapse. Median follow-up -16 months (1-31 months).

**Conclusions:** HSCT in children with rare oncological/hematological diseases is a therapy option with acceptable results. Each patient with a rare oncological and hematological disease requires an individual approach to management during HSCT and subsequent follow-up.

EP293/#1856 | **Poster Topic: AS05 SIOP Scientific Program/AS05.d Stem Cell Transplantation**

#### OUTCOMES OF SECOND ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR PATIENTS WITH RELAPSED OR GRAFT FAILURE IN PEDIATRICS

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**Background and Aims: Background:** Hematopoietic Cell Transplantation (HCT) is a curative treatment modality for patients with acute leukemia, however, between 30-35% will have post-transplant relapse and 3.8 to 5% graft failure. A second transplant is a potentially curative option, limited by the comorbidities of the first transplant. The 2-year survival rate is 29%. **Objective:** Describe the outcomes of patients who received a second allogeneic transplant, complications, and overall survival (OS) and event-free survival (EFS).

**Methods:** Descriptive, retrospective, longitudinal study in a cohort of 4 patients diagnosed with Acute Lymphoblastic Leukemia (ALL) and Acute Myeloid Leukemia (AML) who underwent an HCT2 from 2020

to 2023 at Hospital Infantil Teletón de Oncología. Statistical analysis with Kaplan-Meier method.

**Results:** Cohort of 4 patients, 3 men, median age of 15 years (range, 9-17), diagnoses ALL (n=3), AML (n=1). In HCT1 myeloablative conditioning 100%, Donor types were haploidentical (n=3) and Matched unrelated donor (MUD) (n=1). Two patients had post-transplant relapse, the median remission duration after HCT1 was +455 days, 2 patients had graft failure. In TCHP2 the median time between transplants was 13.4 months (range 1.4-24.4) Busulfan/cyclophosphamide conditioning (n=3) and anti-thymocyte globulin (n=1), bone marrow source (n=2), peripheral blood (n=2), MUD 10/10 (n=2), haploidentical (n=2) graft-versus-host disease (GVHD) 100%, skin (n=3), refractory gastrointestinal (n=2), hepatic (n=1), sinusoidal obstruction syndrome (SOS) (n=3). The median follow-up of surviving patients after HCT2 was 12 months (range, 9-14). The most common cause of death was SOS (n=2), the rates of OS, EFS were 50%. Comorbidities in survivors hypothyroidism, chronic gastrointestinal GVHD, megaloblastic anemia, osteoporosis.

**Conclusions:** A second HCT is feasible in selected patients with relapsed or graft failure after HCT1. The survival benefit was identified in patients with longer days between transplants, as well as the use of MUD 10/10. Main limitation of the work the number of patients.

EP294/#386 | **Poster Topic: AS05 SIOP Scientific Program/AS05.d Stem Cell Transplantation**

#### FAMILY DECISION MAKING AND EXPERIENCES OF GASTROSTOMY VERSUS NASOGASTRIC TUBE FEEDING DURING ALLOGENEIC BONE MARROW TRANSPLANT

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**Background and Aims:** Children undergoing bone marrow transplant (BMT) often become unable to eat and drink putting them at risk of malnutrition. Additionally, they must take many medicines throughout BMT. Tube feeding becomes required by almost all children to meet these demands, with parents in charge of their use. Two tubes are typically used: nasogastric (NGT) or gastrostomy. At the UK centre where this study took place, families are offered choice of these tubes. This qualitative study explored why families chose either tube and their experiences of tube feeding.

**Methods:** Recruitment took place over 18 months during pre-admission consultations with the BMT team. Parents participated in semi-structured interviews, children participated in creative methods using scrapbooks and unstructured interviews. Participants were interviewed twice: on admission, to explore why they chose a gastrostomy or NGT; and 1-2 months post-discharge, to discuss their experiences of tube feeding. Interviews were thematically analysed.

**Results:** Sixteen parents and six children with NGT, 17 parents and three children with a gastrostomy, were interviewed. Parents experienced choice as a spectrum of freedom, some having complete autonomy, others being told which tube to have by clinicians. Parents undertook a delicate balancing act, weighing up pros and cons of each tube alongside factors specific to their child, such as age and activity, with cosmetic differences and consideration of lay advice and prior experiences. To children both tubes were an asset, particularly to administer medications, and comfort was a primary reason for wanting a gastrostomy over NGT.

**Conclusions:** Clinical teams can help parents navigate this complex decision-making process, weigh up their options and make a truly informed choice through collaborative discussions and provision of balanced information. Ensuring the child's voice is heard through research is paramount to providing optimal healthcare but is often difficult in practice. Building rapport was key to making the children's interviews work.

EP295/#652 | Poster Topic: AS05 SIOP Scientific Program/AS05.d Stem Cell Transplantation

#### HAPLOIDENTICAL HSCT USING AB T CELL-DEPLETED GRAFT IN PEDIATRIC PATIENTS WITH ACUTE LEUKEMIA

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**Background and Aims:** Over the last years, the use of HLA haploidentical HSCT (haplo-HSCT) from family members has been increasingly used in patients with hematologic malignancies and non-malignant disease diseases. We investigated the outcomes of ex vivo  $\alpha\beta$  T-cell depleted allogeneic hematopoietic stem cell transplantation (HSCT) from haploidentical family donor (HFD) in children and adolescents with acute leukemia (AL).

**Methods:** Forty-three pediatric patients with AL in CR1 or CR2 underwent their first HSCT from HFD (haplo-HSCT) between May 2012 and May 2022 at Asan Medical Center Children's Hospital. Conditioning regimen consisted of fludarabine-cyclophosphamide-ATG and low dose total body irradiation (TBI) of 6 Gy for AML (N=22) and 8 Gy for ALL (N=21). 30 patients received HSCT in CR1 and 13 in CR2. Donors were father in 16, mother in 18 and sibling in 9.

**Results:** All 43 patients achieved sustained neutrophil engraftment at a median of 10 days (range, 9-13). CI of acute GVHD grade 2-4 and 3-4 were 28% and 9%, respectively. Three patients developed moder-

ate/severe chronic GVHD requiring systemic steroid treatment. Two patients died of non-relapse causes with TRM of 5.4%. Nine patients relapsed at a median of 5.6 months (range, 3.1-11.4) with relapse rates of 21% (ALL 24% and AML 19%). At a median follow up of 45 months (range, 9-131), 3-y leukemia-free survival (LFS) was  $74\% \pm 6.7\%$  (ALL 71% and AML 77%,  $P > .05$ ). LFS was not statistically different according to phase of disease (CR1 77%, CR2 68%), donor relationship (father 88%, mother 61%, sibling 78%), and donor haplotype (B 78%, A 70%).

**Conclusions:** Our study demonstrated that haplo-HSCT using  $\alpha\beta$  T-cell depleted graft is an effective transplant option for pediatric patients with acute leukemia who lack a suitable related or unrelated donor.

EP296/#402 | Poster Topic: AS05 SIOP Scientific Program/AS05.d Stem Cell Transplantation

#### TRANSPLANTATION OUTCOME OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKEMIA WITH EXTREME HYPERLEUKOCYTOSIS AT DIAGNOSIS IN YEUNGNAM REGION OF KOREA: MULTICENTER RETROSPECTIVE STUDY

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**Background and Aims:** Acute lymphoblastic leukemia (ALL) with extreme hyperleukocytosis is associated with early mortality from leukostasis and also has a high relapse rate. To improve the clinical outcome in these patients, allogeneic hematopoietic stem cell transplantation (HSCT) is indicated in first complete remission (CR1).

**Methods:** From January 2005 to December 2017, 38 of 535 (7.1%) ALL patients who had an initial white blood cell (WBC) count of  $>200 \times 10^9/L$  at Yeungnam region of Korea were reviewed retrospectively. We compared the treatment outcome of allogeneic HSCT and intensive chemotherapy in patients with extreme hyperleukocytosis.

**Results:** The median age of patients with extreme hyperleukocytosis was 7.1 years (range, 0.1-17.6 years), and the median initial WBC count was  $360 \times 10^9/L$  (range, 201-929  $\times 10^9/L$ ). Eleven patients (28.9%) had 1 or more early complications during induction therapy included respiratory and neurological symptoms. Early death during remission induction therapy occurred in 4 patients (10.5%) with intracranial hemorrhage, pulmonary hemorrhage and sepsis. Six patients (15.7%) did not achieve CR. After induction chemotherapy, 16 patients in CR1 received an allogeneic HSCT from HLA matched related and unrelated donors and 18 patients were still treated with intensive chemotherapy

only. Relapse occurred in 10 patients (29.4%) of the extreme hyperleukocytosis. The estimated 5-yr event-free survival rate (EFS) and overall survival (OS) were  $57.1 \pm 8.1\%$ ,  $69.3 \pm 7.8\%$  respectively. The patients who received an allogeneic HSCT in CR1 had a longer OS and EFS from the end of induction than those treated with intensive chemotherapy only, but did not show statistically significant difference (EFS;  $74.5 \pm 11.0\%$  vs.  $55.6 \pm 11.7\%$ ;  $p=0.35$ , OS;  $80.8 \pm 10.0\%$  vs.  $74.6 \pm 11.1\%$ ;  $p=0.62$ ). The 3-year cumulative incidences of relapse in patients who received an allogeneic HSCT in CR1 was lower than those treated with intensive chemotherapy but there was not statistically significant. ( $20.2 \pm 10.5\%$  vs  $41.2 \pm 11.9\%$ ;  $p=0.27$ )

**Conclusions:** The pediatric ALL with extreme hyperleukocytosis may benefit from allogeneic HSCT in CR1.

EP297/#1199 | Poster Topic: AS05 SIOP Scientific Program/AS05.d  
Stem Cell Transplantation

### TACROLIMUS INDUCED TYPE IV RENAL TUBULAR ACIDOSIS IN A PEDIATRIC HSCT PATIENT

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**Background and Aims:** Calcineurin inhibitors (CNI) are vital immunosuppressive agents used in hematopoietic and solid organ transplants. Although nephrotoxicity is well documented, type IV Renal Tubular Acidosis (RTA) is a rare complication. We report the first pediatric case of type IV RTA induced by Tacrolimus in a Hematopoietic Stem Cell Transplant (HSCT) patient.

**Methods:** 6 year old female child, underwent an allogeneic matched sibling donor HSCT for Thalassemia Major and was on a sustained release tacrolimus preparation. 8 months post-HSCT, she presented with severe hyperkalemia of 6.23 mmol/L (3.5-5.1), chloride 112 (98-106) and creatinine 0.5 (0.29-0.47). Venous blood gas showed metabolic acidosis with a pH of 7.1. Urine electrolytes showed potassium 6 mmol/L (10-40), chloride 198 mmol/L (50-130) and sodium 191 mmol/L (20-120) with normal urine anion gap. Persistent acidosis, hyperkalemia and hyperchloremia, with normal creatinine led us to suspect a type IV RTA. Calcium gluconate was started with an insulin dextrose drip and salbutamol nebulisation. Bicarbonate supplementation with potassium binders was given.

**Results:** As she had suboptimal response to the interventions, 0.1 mg fludrocortisone was started daily. Post 1st dose of fludrocortisone, renal parameters improved to normal range with serum potassium 4.14 mmol/L, chloride 106 mmol/L, and bicarbonate 19.9 mmol/L. Venous blood gas showed a pH 7.34, pCO<sub>2</sub> 37.2, and pO<sub>2</sub> 46.4. She was discharged on Fludrocortisone, K binders and bicarbonate tablets.

**Conclusions:** CNI reduce Na<sup>+</sup>/K<sup>+</sup>/ATPase and Na<sup>+</sup>/K<sup>+</sup>/2Cl<sup>-</sup> activity causing Type IV RTA. Causative drugs usually are trimethoprim, potassium sparing diuretics and angiotensin inhibitors. CNIs also downregulate the mineralocorticoid receptors causing hypo aldosterone states by increased resistance or reduction in serum aldosterone levels. Impaired urinary potassium excretion causes hyperkalemia and normal anion gap metabolic acidosis. It is imperative to keep type IV RTA as a differential in pediatric HSCT patients on CNIs as it can lead to fatal hyperkalemia if not diagnosed. They are asymptomatic with normal urine output and creatinine with no correlation to CNI levels.

EP298/#303 | Poster Topic: AS05 SIOP Scientific Program/AS05.d  
Stem Cell Transplantation

### UPFRONT HAPLOIDENTICAL HSCT IN PEDIATRIC APLASTIC ANEMIA: OUR CENTRE EXPERIENCE IN LAST 1 YEAR

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**Background and Aims:** Aplastic anaemia (AA) leads to severe pancytopenia requiring multiple blood product transfusions which if not treated, the children succumb to life threatening infections. Past studies have compared treatment with immunosuppression (IS) and Matched Sibling Donor (MSD) Hematopoietic stem cell transplant (HSCT), with HSCT being the only curative option. Herein, we share our centre experience of Haploidentical HSCT as upfront curative therapy for 6 pediatric AA patients in the last 1 year.

**Methods:** Mean age for the 6 patients was 9.1 years, with 4 presenting with severe AA, 2 with very severe disease. Mean time from diagnosis to HSCT was 82.8 days. Causes included Fanconi's anemia, PNH positivity and 1 with a genetic mutation with uncertain significance. One patient amongst the 6 had acquired AA post hepatitis B infection. All underwent a Haploidentical HSCT due to lack of MSD or 10/10 MUD. They were conditioned with rabbit ATG (5 mg/kg/day X 3 days on day -9 to -7), Cyclophosphamide (14.5 mg/kg/day on day -6 and -5), Fludarabine (30 mg/m<sup>2</sup>/day X 5 days on -6 to -2) and total body irradiation 400cGy on day -1. Bone marrow harvest (BMH) was done for 5 patients, and one was BMH plus PBSC due to inadequate counts. Average CD34 dose was  $5.61 \times 10^6$ /kg. WBC engraftment was 16.4 and platelet was 25.2 days. GVHD prophylaxis included PtCy, calcineurin inhibitors and ATG during conditioning.

**Results:** The overall survival was 66.7%, with 2 TRMs (Acute pulmonary hemorrhage and sepsis secondary to early graft failure). CMV viremia was seen in 33% and one developed steroid responsive acute upper GI gut GVHD. 4/6 patients are doing well post HSCT with full donor chimerism.

**Conclusions:** MSD and MUD HSCT are not always a possibility, and for AA, we must aim to provide a cure to all with a Haploidentical HSCT.

EP299/#1258 | Poster Topic: AS05 SIOP Scientific Program/AS05.d  
Stem Cell Transplantation

### SUCCESSFUL HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANT FOR PYRUVATE KINASE DEFICIENCY

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**Background and Aims:** Pyruvate kinase deficiency (PK deficiency) is a rare genetic disorder which arises due to mutations in PKLR gene resulting in haemolytic anemia. Although symptoms can be initially managed with blood transfusions, iron chelators and splenectomy, a Hematopoietic Stem Cell Transplant (HSCT) and/or gene therapy are the only curative options available. We describe a successful haploidentical stem cell transplant for a case of PK deficiency.

**Methods:** Our patient presented with history of pathological jaundice in the first 24 hours of life, requiring multiple exchange transfusions. On further evaluation for prolonged jaundice, genetic work up showed homozygous mutation in PKLR gene, c.1529G>A (p.Arg 510Gln) with autosomal recessive inheritance, confirming the diagnosis of PK deficiency. Transfusion frequency gradually increased to once every 15-20 days. He had a cholecystectomy performed for recurrent gallstones. At the age of 13, he was referred to our centre for consideration of HSCT. With no fully matched donors in the family and unrelated donor search being unfruitful, we opted to proceed for a haploidentical HSCT with his elder sibling who had a heterozygous mutant of the same gene, which we felt would not be a contraindication for him to be the donor.

**Results:** He received 2 cycles of pre-transplant immunosuppression with Dexamethasone, Fludarabine and Cyclophosphamide, given daily for 5 days. He was conditioned with ATG, Thiotepa, Fludarabine, Cyclophosphamide and TBI. Bone marrow harvest product of 6.4 X 10<sup>6</sup>/Kg was infused. GVHD prophylaxis was with PtCy and Cyclosporine. Engraftment kinetics were 100% by day 25.

**Conclusions:** At 10 months post-transplant, child is clinically well with a stable haemoglobin and intact graft function with no jaundice or further requirement of any blood products. PKD patients can be successfully treated with haploidentical HSCT being an option for all and should be considered at a younger age to avoid disease complications and better success rates.

EP300/#1058 | Poster Topic: AS05 SIOP Scientific Program/AS05.d  
Stem Cell Transplantation

### HEMATOPOIETIC STEM CELL TRANSPLANTATION AS AN EFFECTIVE TOOL FOR TREATMENT FOR THE PATIENT WITH X-LINKED SEVERE COMBINED IMMUNODEFICIENCY AND PERSISTENT SARS-COV-2

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**Background and Aims:** X-linked severe combined immunodeficiency (X-SCID) is a fatal disorder if not treated with hematopoietic stem cell transplantation (HSCT) or gene therapy. X-SCID combined with persistent SARS-CoV-2 (460 days), secondary aplasia and sepsis is a challenge with HSCT as the only option to save a child's life.

**Methods:** A 2-year-old male patient with X-SCID (mutation IL2RC was genetically confirmed) was treated at the Belarusian Research Center for Pediatric Oncology, Hematology and Immunology, where he underwent allogeneic haploidentical related bone marrow HSCT.

**Results:** HLA-typing was complicated by maternal microchimerism of blood and some other tissues (genetically confirmed). SARS-CoV-2 was unsuccessfully treated with intravenous immunoglobulin and remdesivir. The patient received natural killer (NK) cell therapy (four infusions, mother-donor) to eliminate the virus and prepare for HSCT. Despite the optimistic results of the studies, after treatment, the patient suffered from secondary aplasia retained a systemic inflammatory response and two episodes of sepsis caused by *Klebsiella pneumoniae* and *Acinetobacter baumannii* (multidrugresistant). To treat an uncontrolled, potentially life-threatening bloodstream infection, the patient received a combination of antibiotic therapy and regular transfusions of donor granulocytes (twenty-two infusions). Despite the limited literature on the effectiveness of HSCT in SARS-CoV-2, the decision was made to proceed with the procedure. The patient received the mother's bone marrow stem cells, and 100% donor chimerism was achieved on day +14. On day +17, laboratory confirmation of the elimination of the SARS-CoV-2 virus was received.

**Conclusions:** In the early post-transplant period, the patient has a gradual recovery of hematopoiesis and resolution of the infectious process, which confirms the effectiveness of HSCT for the treatment of SCID

and SARS-CoV-2 infection. The weak severity of acute «graft-versus-host disease» can be explained by maternal microchimerism.

EP301/#1087 | Poster Topic: AS05 SIOP Scientific Program/AS05.d  
Stem Cell Transplantation

#### DEVELOPMENT OF A NEW LOGISTICS SOLUTION FOR THE DELIVERY OF STEM CELLS TO THE REPUBLIC OF BELARUS IN 2020-2022

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**Background and Aims:** The performance of allogeneic unrelated hematopoietic stem cell transplants (HSCT) in the Republic of Belarus in 2020 was jeopardized due to the global COVID-19 pandemic and following the unprecedented tightening of security, coupled with the restriction of transport links because more than 80% of all transplants were delivered from Germany and Poland. To ensure the possibility of further performance of HSCT in children and adults, it became necessary to develop a radically new way to solve this problem.

**Methods:** To resolve the issue, the donor search coordinators of the Belarusian Research Center for Pediatric Oncology, Hematology, and Immunology and the Minsk Scientific and Practical Center for Surgery, Transplantology, and Hematology collaborated with the DKMS registry, OnTime and time:matters delivery companies with the support of Ministry of Health and State Border Service during 2020-2022.

**Results:** In 2020, with the involvement of courier services and with the support of the Ministry of Health, it was possible to carry out seven deliveries of transplants from Germany and Poland for both clinics. And already in 2021, the country faced air traffic restrictions. The solution was the development of transit routes through third countries (Turkey, Azerbaijan) subject to mandatory observance of time limits of 72 hours, as well as ground delivery through customs checkpoints with Lithuania and Poland. In parallel with this, the issue of making international payments was also resolved with the involvement of intermediary banks. Thus, twenty-eight transplants were delivered in 2021 and twenty-three more in 2022, corresponding to the pre-pandemic transplant activity level in the Republic.

**Conclusions:** Both existing and any new challenges directly or indirectly affect the process of transplant delivery to the Republic of Belarus. However, joint efforts at all levels of the logistics chain can solve these issues most effectively.

EP302/#1652 | Poster Topic: AS05 SIOP Scientific Program/AS05.d  
Stem Cell Transplantation

#### DOES THE CHOICE OF DONOR GENDER AFFECT SURVIVAL IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTS – RESULTS FROM A TERTIARY CARE CENTRE IN INDIA?

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**Background and Aims:** Studies have suggested that the gender of the donor may affect outcomes in haploidentical HSCTs, with the mother being a better donor in Haploidentical T cell deplete transplants and the father in T cell-replete transplants.

**Methods:** We did a retrospective analysis of the haploidentical pediatric transplants at our centre from 15<sup>th</sup> August 2018 to 31<sup>st</sup> December 2022 to see if gender affected transplant-related mortality and overall survival at one year.

**Results:** 42 haploidentical HSCTs were done for both malignant and non-malignant indications. All children had negative donor-specific antibodies for Class I & II prior to transplant. Thirty-two children had male donors (30 fathers, two brothers) (Cohort A), while ten children had female donors (9 mothers, one sister) (Cohort B). In 9 children, there was a donor-recipient mismatch -5 had female donors for male recipients, and 4 had male donors for female recipients). 27 transplants were T cell replete, with 21 having male donors. Of the 15 TCR alpha beta-depleted CD45RA-depleted transplants, 11 had male donors. 2 patients with a female donor and sex mismatch had primary graft failure. In contrast, no patient with a male donor in a female recipient suffered from primary graft failure. The transplant-related mortality at Day 100 (TRM) in Cohort A was 15% (5/33). TRM in Cohort B was 20% (2/10). One patient died before 100 days in each gender-mismatched group. Twenty-nine children underwent HSCT more than one year ago. In this group, 23 had male donors, and 6 had female donors. 13 (56%) in Cohort A survive at > 1-year post-transplant (10 T cell replete, 3 T cell-depleted). 2(33%) children in Cohort B survive at >1 year post transplant (1 each in T cell replete and T cell deplete group).

**Conclusions:** Though our numbers are small, male donors appear better in haploidentical transplants, both T cell replete and TCR alpha-beta depleted CD45RA depleted transplants.

EP303/#532 | Poster Topic: AS05 SIOP Scientific Program/AS05.d  
Stem Cell Transplantation

#### OUTPATIENT ADMINISTRATION OF BLINATUMOMAB: HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR REFRACTORY ACUTE LYMPHOBLASTIC LEUKEMIA IN A PEDIATRIC ONCOLOGIC CENTER IN MEXICO



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**Background and Aims:** Acute Lymphoblastic Leukemia (ALL) is the most common pediatric cancer and the most common subtype of pediatric leukemia, the high toxicity and relapse of many patients require the development of novel therapeutic approach. New therapeutic approaches such as targeted immunotherapy in combination with Hematopoietic Stem Cell Transplantation (HSCT) must be taken in count to revolutionize the management of numerous ALL subtypes, improve treatment outcomes and maintaining low toxicity without losing the effectiveness of the treatment. We evaluated a novel therapeutic approach in Mexico, the outpatient administration of blinatumomab infusion in patients with relapsed/refractory acute lymphoblastic leukemia (R/R ALL).

**Methods:** Cohort study To evaluate use of Blinatumomab and HSCT as treatment in ambulatory patients with RR/ALL in terms of overall survival and disease-free survival at Hospital Infantil Teleton de Oncologia (HITO).

**Results:** Blinatumomab was administered for R/R ALL prior to HSCT in 9 patients. The mean age was 10.1 years (SD  $\pm$ 4.84). 66% women (n= 5) and 44% men (n=4). In the evaluation prior to the administration of Blinatumomab, 66% of the patients presented positive MRD (N=5) and 44% of the negative cases (N=4). The number of cycles of Blinatumomab received to achieve complete remission and MRD negative: 4 patients received 1 cycle (44%), 3 patients received 3 cycles (33%), and 2 patients received 2 cycles (22.2%). 56% of the cases achieved remission. Of these, 12% achieved a first complete remission with one blinatumomab cycle, 88% required a second or third cycle to achieve it. Complications: 33% of the patients presented Cytokine Release Syndrome (n=3), moderate was the most frequent grade 22% (n=2) and 11% mild (n=1). 2 were admitted to UTIP. Four patients died (44.4%).

**Conclusions:** Ambulatory administration of Blinatumomab is safe in Low and Middle Income country no differences in mortality or infections was observed compared with other studies in High income countries

EP304/#307 | Poster Topic: AS05 SIOP Scientific Program/AS05.d Stem Cell Transplantation

## FROM BENCH TO BEDSIDE: STANDARDIZED AND VALIDATED MINIMAL RESIDUAL DISEASE AT STEM CELL TRANSPLANTATION PROGRAM. CLINICAL IMPACT IN A LOW INCOME COUNTRY

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**Background and Aims:** Acute leukemias have an incidence of 75.3 per million people per year and represent 50.8% of childhood cancers in Mexico, relapse rate is 15-20%, Evaluation of Minimal Residual Disease (MRD) is performed in different times: on day 15, end of induction and Pre transplant. There are different techniques: Flow cytometry (FC)/PCR/ Next generation sequencing. In México FC is performed in almost all centers, only this center has an external validation (Boston Children Hospital). Technique had been performed in addition to having it validated. Overall concordance for ALL/ AML was 0.56 (Cohen's k index). A marked improvement in agreement was observed after standardization of antibody panels and analytical strategy. This paper was designed in order to evaluate concordance of remission using MRD by FC in patients referral to this center from different center across México.

**Methods:** Cohort study: Using the result in order to establish three groups 1.- No concordance positive: MRD <0.01% (negative) referral center and >0.01% (positive) in our center 2.- No concordance negative: MRD >0.01% (negative) referral center and <0.01% (positive) in our center 3.- Concordance: both negative

**Results:** N=130 patients 1.- No concordance positive: 30 patients were referral with MRD by FC from different center in Mexico as negative but positive in our center, no Stem cell transplantation was performed until achieved remission. 10/20 achieved remission and SCT was performed later. 2.- No concordance negative: 10 patients were positive from referral center/ negative in this center 3.- Concordance 90 cases were concordant

**Conclusions:** MRD by Fc is a excellent option to evaluate remission before SCT and Predictive value for this MRD has been demonstrated before Using a validated and standardized FC is so important in order to select candidate to SCT and get better results in pos SCT time

EP305/#566 | Poster Topic: AS05 SIOP Scientific Program/AS05.d  
Stem Cell Transplantation

**PROPHYLACTIC RITUXIMAB REDUCES INCIDENCE OF EBV-DNA-EMIA AND EBV-PTLD IN CHILDREN, BUT OCCURRENCE AND THERAPY OF EBV-PTLD DECREASES SURVIVAL AND INCREASES THE RISK OF RELAPSE**

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**Background and Aims:** Children after allogeneic hematopoietic cell transplantation (allo-HCT) are at risk of development of Epstein-Barr virus (EBV) infection: EBV-DNA-emia and PTLD (post-transplant lymphoproliferative disorder). One of rarely used anti-EBV strategies is prophylaxis with rituximab. The objective of the study was to analyze the incidence of EBV-DNA-emia and EBV-PTLD in patients after allo-HCT with respect to use of prophylaxis, and to analyze impact of EBV-associated complications on transplant outcomes.

**Methods:** A total number of 276 patients (105 girls and 171 boys) aged <18 years on the day of the first diagnosis, who underwent allo-HCT between 2007-2019 in single center, were included into the study. Donors: MFD-24.3%, alternative-75.7%. Over the study period, three subsequent strategies of EBV management were implemented of monitoring and pre-emptive therapy (PET): (A) no prophylaxis, PET when DNA-emia  $>10^4$  copy/mL; (B) prophylaxis, PET  $>10^4$  copy/mL; (C) prophylaxis, PET  $>10^5$  copy/mL.

**Results:** The overall incidence of EBV-DNA-emia and EBV-PTLD was 28.6% (n=79) and 8.7% (n=24), respectively. The incidence of EBV-DNA-emia was 35%/12%/21% (p=0.014) in respective strategies, and EBV-PTLD 12%/0%/4% (p=0.025). In multivariate analysis, rituximab prophylaxis (HR=0.35; p<0.0001) and T-cell depletion (HR=16; p<0.0001) were significant for occurrence of EBV-DNA-emia; while rituximab prophylaxis (HR=0.20; p=0.0025) for EBV-PTLD. The efficacy of rituximab prophylaxis was 79.5%; preemptive therapy 88.4%; EBV-PTLD therapy 70.9%. Patients with EBV-PTLD had dismal 5y overall survival (33±10% vs 65±4%; p=0.0010), and higher incidence of relapses (71±15% vs 29±4%; p=0.0137), with OR=2.6 (95%CI=1.1-6.4; p=0.0332). In the analysis of the risk factors for death in patients after allo-HCT, four unfavorable prognostic factors were determined: diagnosis of malignant disease, disease progression, presence of EBV-PTLD and the presence of invasive pulmonary aspergillosis after HCT.

**Conclusions:** Prophylactic administration of rituximab reduced the number of EBV-associated complications (EBV-DNA-emia and EBV-PTLD). However, occurrence and therapy of PTLD contributed to increased relapse rate and lower overall survival.

EP306/#474 | Poster Topic: AS05 SIOP Scientific Program/AS05.d  
Stem Cell Transplantation

**BARRIERS AND FACILITATORS TO IMPLEMENTATION OF STANDARD OPERATING PROCEDURES BY A VIETNAMESE NATIONAL PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT AND CELLULAR THERAPY CONSORTIUM**

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**Background and Aims:** To promote quality care in hematopoietic stem cell transplantation (HSCT), the Foundation for the Accreditation of Cellular Therapy (FACT) requires use of evidence-based standard operating procedures (SOPs) for accreditation in HSCT. Survival rates are improved at accredited centers. There is a paucity of literature outlining best practices for implementing SOPs in resource-limited settings. The Vietnamese Pediatric Hematopoietic Stem Cell Transplant and Cellular Therapies Consortium consists of all 14 hospitals treating children with blood diseases and cancer in Vietnam. Across hospitals, use of SOPs for clinical procedures is variable and none have FACT accreditation. This study examines barriers and facilitators to implementing SOPs for pediatric HSCT in five consortium hospitals with established programs and three initiating HSCT within a year.

**Methods:** We conducted semi-structured interviews with nine physicians and six nurses from consortium hospitals. The Consolidated Framework for Implementation Research (CFIR) informed the discussion guide and validated approach to rapid qualitative analysis. Verbatim transcripts were summarized using a CFIR-informed template and data were consolidated into matrices to identify shared themes.

**Results:** Barriers and facilitators associated with implementation processes, health system factors, SOP characteristics, and inner and outer setting dynamics, were shared regardless of HSCT experience. Implementation barriers included (1) lack of coordinated approach to developing and distributing SOPs, (2) SOP length and complexity, (3) limited provider time, (4) variability in access to medications, and (5) inconsistent audits of SOPs. Implementation facilitators included (1) adaptability of SOPs across hospitals, (2) existing hospital-based

mechanisms for SOP approval, (3) utility of SOPs in training providers, (4) checklists supporting SOP use, and (5) shared understanding that SOPs improve quality and safety of care.

**Conclusions:** While providers identified barriers to SOP use, they conveyed widespread support among consortium sites for overcoming these challenges. Results can be leveraged to develop national strategies for implementing SOPs for pediatric HSCT in Vietnam.

EP307/#1798 | Poster Topic: AS05 SIOP Scientific Program/AS05.d Stem Cell Transplantation

### EXTRACORPOREAL PHOTOPHERESIS FOR ACUTE AND CHRONIC GVHD IN PEDIATRIC HCTS RECIPIENTS: INSIGHTS FROM KING HUSSEIN CANCER CENTER

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**Background and Aims:** Extracorporeal photopheresis (ECP) is an effective therapy for GVHD in children who do not respond adequately to systemic corticosteroids or develop adverse effects.

**Methods:** This retrospective study aimed to evaluate the safety and efficacy of ECP in children with acute and chronic GVHD who underwent hematopoietic stem cell transplantation (HCT) at King Hussein Cancer Center in Jordan from 2017 to 2023.

**Results:** Fifteen patients with acute GVHD underwent ECP, and 25 patients with chronic GVHD underwent ECP. The primary indications for HSCT were malignant diseases (67%), with leukemia and lymphoma being the most common diagnoses. Most patients received mycophenolate mofetil and calcineurin inhibitors as primary treatment, and 57% of patients were on second-line therapy for acute GVHD during ECP. The median number of ECP cycles was 3 for acute GVHD and 22 for chronic GVHD, with the best response observed at a median of 0.5 months and after a median of 5 ECP cycles for acute GVHD and a median of 4 ECP cycles for chronic GVHD. Complete resolution of acute GVHD occurred in 60% of patients, and complete resolution of chronic GVHD was observed in 18% of patients, while partial response was observed in 82% of patients. ECP was discontinued at a median of 75.5 days, primarily due to complete resolution of GVHD. At a median follow-up of 2.1 years, 70% of patients with acute GVHD and 68% of patients with chronic GVHD were alive.

**Conclusions:** In conclusion, ECP is an effective treatment option for inducing response in most pediatric patients with acute and chronic GVHD post-HSCT, allowing for the discontinuation of steroid therapy.

EP308/#619 | Poster Topic: AS05 SIOP Scientific Program/AS05.d Stem Cell Transplantation

### RELAPSED ACUTE LYMPHOBLASTIC LEUKAEMIA AFTER ALLOGENEIC STEM CELL TRANSPLANTATION: A THERAPEUTIC DILEMMA IN COUNTRIES WITH HARD ACCESS TO CELLULAR THERAPY

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**Background and Aims:** In Brazil, treating pediatric acute lymphoblastic leukaemia (ALL) relapses post allogeneic hematopoietic stem cell transplantation (allo-HSCT) represents a challenge. The approval for CAR-T cells (Tisagenlecleucel) use in Brazil (ANVISA, 2022) shows promise in improving the overall survival of patients with refractory/relapsed B-cell ALL who are up to 25 years old.

**Methods:** Report of a patient with B-cell ALL treated with Tisagenlecleucel following a relapse 1 year post allo-HSCT.

**Results:** A 16 year-old boy with B-cell ALL underwent HSCT in september/2021 with a haploidentical donor. Graft source was bone marrow (BM). Neutrophil engraftment and 100% donor cells chimerism were achieved. Myeloablative conditioning was cyclophosphamide (CY) and total body irradiation. Graft versus host disease (GVHD) prophylaxis was post-transplant CY, mycophenolate mofetil and cyclosporin. His transplant course was complicated by cytomegalovirus infection, BK polyomavirus-associated grade III hemorrhagic cystitis, sepsis due to *Candida parapsilosis* and grade IV skin GVHD which all resolved 6 months post transplant. In October/2022, the patient presented with a combined BM and central nervous system (CNS) CD19 positive relapse and was referred to tisagenlecleucel. His marrow showed 11.8% of blasts and CNS 96.2%. Apheresis was performed 2 months prior to infusion.  $148 \times 10^6/\text{kg}$  CD3+ cells were harvested, with a final product of  $3.26 \times 10^6/\text{kg}$  CAR T-cells. While awaiting Tisagenlecleucel production, he received low doses of methotrexate, vincristine and dexamethasone as bridging chemotherapy. Prior to cell therapy his BM showed 0.0032% MRD and CSF was negative. As lymphodepletion, the patient received fludarabine and CY. Patient had grade I cytokine release syndrome on day+3 and no neurotoxicity. Molecular remission was achieved on Day+25. Follow-up: thrombocytopenia (Day+17) and neutropenia (Day+25), resolved by Day+56; B-cell aplasia in peripheral blood samples measured by flow cytometry on Day+23.

**Conclusions:** Approval of tisagenlecleucel use in Brazil has expanded treatment options and shows promise in improving the overall survival of patients with refractory/relapsed B-cell ALL. Cost remains a challenge.

EP309/#438 | Poster Topic: AS05 SIOP Scientific Program/AS05.e  
*Neuroblastoma*

**IN VITRO RADIOSENSITIVITY SCREEN OF TH-MYCN  
TRANSGENIC MOUSE MODELS OF HIGH-RISK  
NEUROBLASTOMA FOR INVESTIGATING THE EFFECT OF  
RADIOTHERAPY ON CAR-T CELL EFFICACY IN SOLID TUMOUR**

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**Background and Aims:** The success of adoptive cell therapy such as CAR-T cells in haematological malignancies has yet to be seen with solid tumour, such as neuroblastoma, where high-risk disease has low survival rates. This is because CAR-T cells are unable to traffic into and persist within an immunosuppressive tumour microenvironment (TME). The immune-mediated effects of radiotherapy may counteract these barriers and promote CAR-T cell efficacy in solid tumour. The immune-mediated effects of radiotherapy are dependent on immunogenic cell death (ICD), a regulated form of cell death that implicates key danger-associated molecular patterns (DAMPs), including extracellular ATP, HMGB1 and calreticulin, that amplify the immune response via their downstream immune-mediated effects. In neuroblastoma, the widely used TH-MYCN transgenic mouse models for high-risk neuroblastoma are a good candidate to investigate this combination therapy in vivo. However, radiosensitivity needs to be ascertained to determine the optimal single dose of radiation to use in conjunction with CAR-T cells.

**Methods:** We have screened five TH-MYCN transgenic mouse models in vitro measuring extracellular ATP and ecto-calreticulin in response to a range of single radiation doses over 72- and 48-hours post-treatment, respectively.

**Results:** Our findings suggest that these models vary in radiosensitivity with some showing little upregulation of extracellular ATP and ecto-calreticulin, but visually showing a potential cytostatic effect with recovery in proliferation at later time points post-treatment.

**Conclusions:** This data provides a comprehensive look at the radiosensitivity of these models, of which the effect on CAR-T cell efficacy will be determined in further in vitro and in vivo experiments.

EP310/#719 | Poster Topic: AS05 SIOP Scientific Program/AS05.e  
*Neuroblastoma*

**WTAP FACILITATES THE PROGRESSION OF NEUROBLASTOMA  
VIA M6A-YTHDC2-DEPENDENT EPIGENETIC OVEREXPRESSION  
OF KHK**

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**Background and Aims:** To reveal the changes of m6A methylation level in neuroblastoma and its correlation with clinical manifestations, and to focus on further exploring the potential biological functions and specific molecular mechanisms of m6A methylation modification in the occurrence and development of neuroblastoma.

**Methods:** We first study on the expression and clinical correlation of WTAP in neuroblastoma. Then explore the biological function of WTAP in regulating the occurrence and development of neuroblastoma. Last we study the molecular mechanism of WTAP in neuroblastoma.

**Results:** The overall level of mRNA m6A methylation was significantly decreased due to the low expression of WTAP, a "writer" of methyltransferase in NB patients. Functionally, WTAP inhibited the proliferation capability and tumor metastasis of NB cells in vitro and in vivo. Mechanistically, KHK was the downstream target of WTAP-mediated m6A modification. In addition, WTAP-regulated m6A modification inhibited the decay of KHK mRNA in a YTHDC2-dependent manner, thereby increasing the level of KHK, activating the non-canonical NF- $\kappa$ B pathway and promoting the initiation and development of NB.

**Conclusions:** From a therapeutic perspective, our study suggested that high intake of fructose may should be restricted in NB patients and the WTAP-KHK-YTHDC2 axis could be a potential target for NB progression.

EP311/#1295 | Poster Topic: AS05 SIOP Scientific Program/AS05.e  
*Neuroblastoma*

**TREATMENT OF HIGH-RISK NEUROBLASTOMA IN MOROCCO  
ACCORDING TO HR-NBL-MA 2010 PROTOCOL: A REPORT  
FROM PEDIATRIC HEMATOLOGY AND ONCOLOGY CENTER OF  
RABAT**

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**Background and Aims:** The treatment of high-risk neuroblastoma (NBL/HR) is one of the most difficult challenges in pediatric oncology.

The prognosis of these patients has improved over the past twenty years thanks to the strengthening of induction chemotherapy and immunotherapy. The aim of this study is to report the experience of the management of HR neuroblastoma treated with HR-NBL 2020 protocol.

**Methods:** This work is a retrospective study of 52 cases of high-risk neuroblastoma treated in the Pediatric Hematology and Oncology Center at the Children Hospital in Rabat over a period of 8 years (from January 2015 to December 2022). All our patients were treated according to the HR-NBL-MA 2010 protocol (induction chemotherapy, surgery, consolidation by high-dose chemotherapy followed by autologous HCST, radiotherapy and retinoic acid).

**Results:** The median age at diagnosis was 40 months and the sex ratio was 1.7. Abdominal sites were the most common primary tumor localization (86%). Metastases are mainly settled in the medullar and bone areas (80%). We investigated the MYCN status in 13 patients and amplification was seen in 8 cases. All our patients were treated according to the HR-NBL-MA 2010, by induction chemotherapy (5 HR cures, followed by surgery (94% of cases) and postoperative chemotherapy (70% of cases). Intensification with high-dose chemotherapy (Busulfan/melphalan), followed by an autologous CSH was performed on average 9 months after the start of treatment. The treatment was continued with radiotherapy (71%), and maintenance treatment (61%), no patient was put on immunotherapy with Anti GD2. During follow-up, 22 (42%) are currently alive, including 17 in complete remission and 5 in relapse. 30 (58%) died, 25 from their disease and 5 from treatment-related complications.

**Conclusions:** The treatment protocol for high-risk neuroblastoma (HR-NBL-MA 2010) is feasible in Morocco. It has provided us with a learning curve for the management of these patients formerly under palliative treatment.

EP312/#440 | Poster Topic: AS05 SIOP Scientific Program/AS05.e Neuroblastoma

#### DINUTUXIMAB/ DINUTUXIMAB BETA IN CHILDREN WITH HIGH RISK NEUROBLASTOMA: A SINGLE CENTER EXPERIENCE IN ARGENTINA

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**Background and Aims:** Anti-GD2 antibody is standard of care for patients with high-risk neuroblastoma (HRNB) since 2010 worldwide, but is not available in Argentina. First patient could be treated in Argentina at Hospital de Niños Ricardo Gutierrez on 2017 by importing the drug. Thereafter 19 patients received antiGD2 as maintenance therapy or due to relapsed/refractory disease. The aim is to describe feasibility and related toxicities.

**Methods:** Retrospective review of medical records of patients with HRNB treated with immunotherapy at Hospital de Niños Ricardo

Gutierrez (2017–2023). From 2017 to 2018 dinutuximab (cho14.18) was administered at 17.5mg/m<sup>2</sup> per 5 days (10 hours infusion). Thereafter Dinutuximab beta was implemented initially at short term infusion (20mg/m<sup>2</sup>/day over 5 days) and then long term infusion (10mg/m<sup>2</sup>/day over 10 days continuous infusion).

**Results:** Thirty two patients were admitted with HRNB (2017–2022). Median age: 36months (r:19–168); 12 male, 7 female. Anti GD2 result feasible in 19 patients (15 maintenance, 4 relapsed/refractory disease). Thirteen could not be treated with immunotherapy (9/32 died for progression during induction and in 4/32 drug was not available). Fifteen received dinutuximab beta as maintenance:7/15 completed 5cycles (4/7alive in CR at 3, 35, 48 y 60months; 3 relapsed and died), 3/15 relapsed and died before completing 5cycles, 3/15 are ongoing treatment, 1/15 suspended by parents decision and 1/15 suspended for toxicity (paralytic midriasis). Four received immunotherapy as salvage treatment (3p died without response,1p alive with disease) Over 65 dinutuximab cycles, toxicities included: fever 15p, mild-to-moderate pain 6p, hematological abnormalities 3p, rash 2p, capillary-leak syndrome 1p, nausea/vomiting/anorexia 1p, paralytic midriasis 1p. Most events occurred during first treatment cycle and decreased in frequency and intensity in subsequent cycles. Patients with LTI had better pain management.

**Conclusions:** Despite lack of availability in Argentina, treatment with dinutuximab beta was feasible with manageable toxicities with supportive care. LTI was better tolerated. Follow-up of this cohort will be carried out to report survival data.

EP313/#1374 | Poster Topic: AS05 SIOP Scientific Program/AS05.e Neuroblastoma

#### NEW TREATMENTS, NEW CHALLENGES: NEPHROTOXICITY ASSOCIATED WITH NAXITAMAB IN HIGH-RISK NEUROBLASTOMA PATIENTS

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**Background and Aims:** Anti-GD2-based immunotherapy has improved the prognosis of patients with high-risk (HR) neuroblastoma. Naxitamab is a humanized monoclonal anti-GD2 antibody approved for refractory/relapsed HR-neuroblastoma limited to bone and/or bone marrow. The most frequent adverse effects (AE) of naxitamab are infusion-related such as pain, tachycardia, and fever. Hypertension (HT) is common, however less is known about this and other renal toxicities. We aim to describe the renal toxicity profile associated with naxitamab in patients with HR-neuroblastoma.

**Methods:** Retrospective descriptive study including 244 patients treated with naxitamab (either monotherapy or associated with chemotherapy) from June 2017 to December 2022 in whom renal

involvement and/or HT was detected. We used the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 to evaluate the severity of the AE.

**Results:** Mean age of the cohort was 8 years (41% female -101- and 59% male -143-). 26.6% presented some grade of nephrotoxicity: HT (11.9%), acute renal damage (ARD 10.2%) and proteinuria (5.3%), developing all during the first 3 cycles. All of them were mild (Grades 1 and 2) except one patient with ARD grade 3 and two patients with HT grade 3. Six patients with HT had an Ambulatory Blood Pressure Monitoring (ABPM) showing 2 nocturnal-HT, 2 diurnal-HT without specific-pattern, and 2 dysautonomic-patterns. All cases with ARD were tubular except two patients who presented acute tubule-interstitial nephritis. Among patients with proteinuria (none nephrotic range): 38% were tubular, 38% glomerular and 23% mixed. Two patients presented ARD + HT and three a combination of HT + ARD + proteinuria. Two of them had previous chronic renal damage (CKD stage 2 and 3).

**Conclusions:** Arterial hypertension and tubular acute damage are the most frequent renal toxicities. Short-and long-term follow-up including ABPM, and early markers of renal damage, could lead to a more efficient understanding and management of these side effects.

EP314/#942 | Poster Topic: AS05 SIOP Scientific Program/AS05.e Neuroblastoma

#### IMPROVING THE OUTCOME OF NEUROBLASTOMA IN A LOW-MIDDLE INCOME COUNTRY: STILL A LONG WAY TO GO

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**Background and Aims:** Neuroblastoma is the most common extra-cranial solid tumor in children. Advanced disease is frequent at presentation. Treatment of high risk disease is challenging, requiring multimodality treatment. Previous studies from India have noted higher proportion of advanced disease, high rate of progression/poor response and relapse. Aim of the present study was to analyze any change in clinical profile and outcome of neuroblastoma over two decades.

**Methods:** Data was divided into two time periods (2003-2012 and 2013-2022) for comparison. Diagnosis was established by biopsy, immunohistochemistry and bone marrow examination. MIBG scan and MYCN amplification were not available. PET scan was available in later years. Staging was done as per INSS. Treatment included chemotherapy (OPEC initially, rapid COJEC later) followed by surgical resection/debulking and radiotherapy. Autologous stem cell transplant was available in last 3 years.

**Results:** Case records of 45 patients (20 and 25 in each decade) were analyzed. Mean age was  $42.5 \pm 20.8$  months (range 13 months-8 years). Male to female ratio was 3.5:1. In the first decade, all patients (100%) had stage 4 disease with bone marrow involvement in 60% of them.

Half of them had complete/good partial response to chemotherapy and underwent surgical resection/debulking followed by radiotherapy. Remaining had partial response/progressive disease. Only 2 patients had OS of  $26.0 \pm 7.2$  months. In the second decade also, all patients presented with stage 4 disease. Half of them had bone marrow involvement. They received OPEC initially and rapid COJEC in last five years of study. Fourteen of 25 patients had complete/ good partial response of which 4 patients underwent autologous stem cell transplant. Two of them relapsed. Four patients had OS of  $30.4 \pm 6.6$  months.

**Conclusions:** There is an urgent need to create awareness and diagnose the patients early. In spite of newer therapeutic modalities being available, the outcome remains dismal due to patients presenting with advanced disease.

EP315/#328 | Poster Topic: AS05 SIOP Scientific Program/AS05.e Neuroblastoma

#### ROLE OF INTRATUMORAL CD11B+CD49B+NATURAL KILLER (NK) CELLS IN MURINE NEUROBLASTOMA AFTER CO-ADMINISTRATION OF ANTI-PD-1/PD-L1 ANTIBODIES

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**Background and Aims:** Induction of immune cells infiltrations into the tumor microenvironment is an important step in the anti-tumor immunotherapy. In our previous study, we reported that co-administration of anti-PD-1/PD-L1 antibodies inhibited neuroblastoma growth and promoted intratumor infiltration of CD3<sup>+</sup>CD11b<sup>+</sup>CD49b<sup>+</sup> NK cells (Inoue et al. SIOP 2022). Here, we investigated the role of these intratumoral NK cells.

**Methods:** Mouse Neuro-2a neuroblastoma cells were subcutaneously inoculated into A/J mice, and anti-PD-1/ PD-L1 monoclonal antibodies (mAbs; 200 mg/mouse) were intraperitoneally co-administered into mice 5 times (on day 7,8,9,12 and 14 after tumor cell inoculation). Expression of PD-1, PD-L1, NKG2D and CD69 molecules on the NK cells by flow cytometry. Naïve A/J mice were intraperitoneally injected with anti-asialo GM1 antibodies (AAGM1) 3 times (on day 0,7 and 10) to deplete NK cells (the absence of CD3<sup>+</sup>CD11b<sup>+</sup>CD49b<sup>+</sup> cells in the spleen was confirmed by flow cytometry). Finally, tumor inoculated A/J mice were injected with AAGM1 (on day 2, 9, 12) and anti-PD-1/ PD-L1 mAbs (on day 7, 8, 9, 12, 14), and the tumor weights were measured to assess the anti-tumor effect.

**Results:** PD-1 was not expressed on the surface of tumor cells. PD-L1 was expressed on tumor-infiltrating NK cells in the isotype-treated mice group, but its expression was decreased in the anti-PD-/PD-L1 mAbs-treated group (isotype vs mAb:  $6.86 \pm 2.21$  vs  $1.71 \pm 2.24$  %;  $p=0.0396$ ). NKG2D and CD69 expression was observed, but there

were no statistically significant differences between groups. When mice depleted of NK cells with AAGM1, suppression of tumor growth by co-administration of anti-PD-1/PD-L1 mAbs was abrogated.

**Conclusions:** Infiltration of CD11b<sup>+</sup>CD49b<sup>+</sup> NK cells with reduced PD-L1 expression into the tumor microenvironment could be recruited for the anti-tumor immune response induced by immune checkpoint inhibitors in neuroblastoma.

EP316/#1185 | Poster Topic: AS05 SIOP Scientific Program/AS05.e Neuroblastoma

### PROFILING OF EXOSOMAL SMALL NUCLEOLAR RNA PRODUCED BY NEUROBLASTOMA CELL LINE CELLS SK-N-SH AND IMR32

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**Background and Aims:** Small nucleolar RNA (snoRNA) is a class of non-coding RNA. It binds to its essential proteins to form functional small nucleolar ribonucleoproteins and stabilizes other non-coding RNAs through post-transcriptional processing such as methylation and pseudouridylation. snoRNAs are known to be involved in cell proliferation, cell migration, and cell survival in cancer by regulating signaling pathways. Exosome is a type of extracellular vesicle produced by cells that carry various molecular constituents including RNA. They mediate intercellular communication and influence various aspects of cell biology by transmitting their contents. We aimed to profile snoRNAs generated in neuroblastoma cell line cells and those secreted into the exosomes to identify the snoRNAs potentially important for intercellular communication.

**Methods:** Two neuroblastoma cell lines, SK-N-SH and IMR32, were cultured in 10 mL DMEM/10% FBS with or without exosome depletion in 10 cm dishes. Cells and culture media were collected at 80% confluence. Total RNA including miRNA was extracted from the cells as well as exosomes purified from the culture media by resin. Small RNA-seq was performed on the obtained RNA and the results were processed using the GeneGlobe provided by QIAGEN. The data were analyzed to identify differentially expressed snoRNAs.

**Results:** A comparison of media with or without FBS did not find any snoRNAs apparently derived from FBS. In SK-N-SH cells, a total of 19 snoRNAs were upregulated and 42 snoRNAs were downregulated with greater than two times differences when compared to IMR32 cells. In SK-N-SH exosomes, two snoRNAs were upregulated and 63 snoRNAs were downregulated with greater than two times differences when compared to IMR32 exosomes. Comparing the cells with the corresponding exosomes, SNORD3A, SNORD3C, and SNORD33 were consistently increased in the exosomes.

**Conclusions:** We profiled differentially expressed snoRNAs in two different neuroblastoma cell lines and exosomes. Their expression levels seemed to reflect the characteristics of the cells.

EP317/#457 | Poster Topic: AS05 SIOP Scientific Program/AS05.e Neuroblastoma

### PERSONALIZED THERAPY OF PATIENTS WITH NEUROBLASTOMA: THE EXPERIENCE OF DMITRY ROGACHEV NATIONAL MEDICAL RESEARCH CENTER OF PEDIATRIC HEMATOLOGY, ONCOLOGY AND IMMUNOLOGY

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**Background and Aims:** Patients with high-risk neuroblastoma (HRNB) and relapsed disease have an extremely unfavorable prognosis and need therapy intensification. Targeted therapies are considered. Aim: to study the experience of personalized therapy (PT) in patients with NB.

**Methods:** Since 2018, 155 patients with a diagnosis of HRNB or relapse/progression regardless of the risk group, have been searched for mutations using targeted high-performance sequencing of QIASeq (Qiagen, Germany) with 56 genes, including *ALK*. The *ALK* amplification was determined by MLPA and FISH. PT was prescribed based on the literature data of the various drugs effectiveness at the time. The results of PT were evaluated to 19.12.2022.

**Results:** Markers of sensitivity to molecular-directed therapy were detected (above the IIC level by AMP/ASCO/CAP) in 16% (25/155): 17 - *ALK* mutations, 3 - *ALK* amplification, 3 - aberrations in the tyrosine kinase family genes (*MAP2K1*, *BRAF*, *PDGFRA*), 2 - high TMB (>10 mutations per Mb, determined using the QIAGEN TMB panel). 16 patients were prescribed therapy: 13 - *iALK* (1 - alectinib, 3 - lorlatinib, 4 - crizotinib, 5 - ceritinib), 2 - pembrolizumab, 1 - imatinib. The median duration of PT was 4.4 months (0.2-42.6). PT was prescribed in addition to the conventional therapy (in 5 cases - in the 1st line, 11 - subsequent lines). Grade 3-4 toxicity was observed in 3 cases (hepatic - 2, gastrointestinal and neurological - 1). Currently, 8 patients continue PT, 7 terminated therapy because of disease progression in 6 (2 - rapid progression) and toxicity in 1.

**Conclusions:** The most common target for therapy in NB is *ALK* aberrations. *iALK* are well tolerated and can be effectively used with various therapy regimens, including chemotherapy. Other targets were detected less frequently than *ALK*. To assess the efficiency of their blockade the collection of larger number of patients are needed.

EP318/#660 | Poster Topic: *AS05 SIOP Scientific Program/AS05.e Neuroblastoma*

### INPOG-NB-18-01: RETROSPECTIVE SURVEY OF “REAL WORLD” OUTCOMES OF PEDIATRIC NEUROBLASTOMA IN INDIA

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**Background and Aims:** Neuroblastoma (NB) is the commonest solid tumor in young children, but single institution studies from India show a low incidence with predominantly advanced disease. We conducted a retrospective multi-institution survey to determine the “real world” occurrence, management and outcome of pediatric NB in India.

**Methods:** Thirteen institutions across India participated with Institutional Ethics Committee approval, the study was registered with Clinical Trials Registry India. Retrospective data was submitted online using a custom-designed Google Form, on children with NB <15 yrs age diagnosed from 1-6-2016 to 31-8-2021

**Results:** Patients with NB (n=277) had median age 2.36 yrs (Range=0-14.9 years), M:F ratio 1.4:1 diagnosed with Ultrasound (n=144), CT (n=163), PET-CT (n=147), MRI (n=36) and MIBG (n=32). Pathology (INPC) was favorable in 89 (32.1%), unfavorable in 161 (58.2%), and unknown in 27 (9.7%). MYCN-amplification was present in 53, absent in 142 and unknown in 82. Urine VMA was tested in 72. Tumor location was adrenal/upper abdomen (n=175, 63.2%), Pelvic/lower-abdomen (n=51, 18.4%), Cervical/thoracic (n=42, 15.2%) Brain/skull/orbit (n=8, 2.9%) and Unknown (n=1, 0.3%). INRG staging was M (n=146, 52.7%), L1 (n=38, 13.7%), L2 (n=80, 28.9%), MS (n=13, 4.7%). Opsoclonus-myoclonus occurred in 11/277 (4%), and spinal cord compression in 13/277 (4.2%) Patients had primary resection in 50 (gross total resection=40, sub-total resection=10), biopsy in 190, with “second-look” surgery in 43; 228 received chemotherapy, and 67 radiation. 47 underwent BMT, only 3 immunotherapy. 3-year overall survival for L1, L2, M and MS respectively was 91.2% (81.6-100%), 66.0% (54.4%-77.7%), 24.7% (16.7%-32.6%) and 75% (50.5% - 99.5%), with

corresponding 3-year event free survival 85.2% (73.4-97.2%), 51.8% (40.3%-63.3%), 23.6% (16.0%-31.3%) and 38.9% (14.7%-67.7%).

**Conclusions:** NB staging and biology in India parallels high income countries, but gender bias and diagnostic variation is seen (e.g. PET-CT is widely used but MIBG rarely). While low-risk NB has good outcomes, high-risk NB remains suboptimal, with low utilization of BMT/immunotherapy.

EP319/#427 | Poster Topic: *AS05 SIOP Scientific Program/AS05.e Neuroblastoma*

### EVALUATION OF ADVERSE EVENTS IN PATIENTS WITH RELAPSED REFRACTORY NEUROBLASTOMA RECEIVING DINUTUXIMAB BETA PLUS CONVENTIONAL CHEMOTHERAPY

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**Background and Aims:** Neuroblastoma is the most common extracranial solid tumor of childhood. Relapse refractory disease is seen in more than 50% of the cases, especially in the high-risk group. Herein, we proposed to investigate the adverse events of the combination of immunotherapy with chemotherapy in relapsed refractory neuroblastoma patients.

**Methods:** This study was managed at the Institute of Oncology, Department of Pediatric Oncology center between January 2020-December 2022. Adverse events that developed during treatment of dinutuximab beta (DB) concurrently with chemotherapy were documented.

**Results:** The M/F ratio:1(16/16) and the median age at diagnosis was 39 months (13-105 months). 19 patients received treatment according to TPOG 2009 protocol, and the remaining 13 patients according to TPOG 2020 protocol. The median relapse refractory time was 12 months (3-58 months). The most frequently chemotherapy given with DB was Irinotecan-Temozolamide. The other main chemotherapy courses were ICE (ifosfamide-carboplatin-etoposide), TVD (topotecan-vincristine-doxorubicin), temozolomide-topotecan, ifosfamide-etoposide-carboplatin, oxaliplatin-vincristine-cyclophosphamide. The median number of DB courses administered were 9(1-18) and the total number of courses applied in our center were 290. The most common adverse events detected were leukopenia (81%), anemia (79%), thrombocytopenia (77%), fever (78%), elevated liver function tests (54%), allergic rash (28%), pain (35%), eosinophilia (13.8%), tachycardia (38%), diarrhea-vomiting (40.3%), hypertension (18%). Capillary leak syndrome was seen in only 2 cases for a total of 3 cycles and could be controlled without the need for intensive care unit administration after discontinuing the drug with symptomatic treatment. No neurological complications were observed.

**Conclusions:** Neutropenia, thrombocytopenia, and anemia were the most common and expected side effects because we applied



immunotherapy and chemotherapy together in our patients with relapsed refractory neuroblastoma. During the treatment, erythrocyte and thrombocyte suspension supports were given. Fever and elevation in liver tests are the other most common adverse events, and while it was more common in the first cycles of the same patient, its frequency decreased in subsequent cycles. In conclusion, adverse effects seen in patients with relapsed refractory neuroblastoma who received chemotherapy and immunotherapy together were at the expected frequency and no serious adverse events were observed.

EP320/#747 | Poster Topic: AS05 SIOP Scientific Program/AS05.e  
*Neuroblastoma*

### MATH-1 PROTEIN EXPRESSION LEVELS IN NEUROBLASTOMA MAY BE A PREDICTIVE FACTOR FOR RISK STRATIFICATION

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**Background and Aims:** Neuroblastoma is remarkable for its broad spectrum of clinical behavior, varying from spontaneous regression to progressive disease. This diversity in behavior correlates closely with defined clinical and biological features and combinations of prognostic variables are used for risk-group assignment. MATH-1 (Atoh1) is a basic helix-loop-helix transcription factor that is highly expressed in proliferating progenitors of specialized neuroepithelium in the developing dorsal hindbrain. MATH-1 plays a role in the differentiation of subsets of neural cells by activating E box-dependent transcription. In this study, we aimed to investigate the MATH-1 expression levels among neuroblastoma patients and to determine if MATH-1 expression in tumor tissue could be a prognostic biomarker for neuroblastoma.

**Methods:** Histological tumor sections of 56 cases of varying stages and risk groups of neuroblastoma were studied. MATH-1 protein expression levels were evaluated by immunohistochemical staining on paraffin sections of neuroblastoma patient tissue samples. All sections were independently and blindly studied for protein expression under microscopic examination. Tissue samples were categorized due to protein expression levels as positive ( $\geq 5\%$ ) and negative ( $< 5\%$ ). The chi-Square test was applied to detect the significance of protein expressions between risk groups and disease stages.

**Results:** 60% of the patients were categorized as low-risk and 40% were intermediate to high-risk. 33% of the tumor tissues of low-risk patients were positively stained for MATH-1 whereas only 10 % of the tumors from intermediate-to-high-risk patients showed significant staining. This difference between the ratios of MATH-1 positive cases in the low and intermediate-to-high-risk patient groups was statistically significant ( $p < 0.05$ ).

**Conclusions:** Results of this study can propose that MATH-1 expression in neuroblastoma can be a useful biomarker for risk stratification.

However, further studies are required to clearly identify other factors effective in the relation between MATH-1 expression and neuroblastoma risk stratification.

EP321/#984 | Poster Topic: AS05 SIOP Scientific Program/AS05.e  
*Neuroblastoma*

### TOLERABILITY AND SAFETY OF EFLORNITHINE (DFMO) IN HIGH-RISK NEUROBLASTOMA (HRNB) PATIENTS TREATED WITH DFMO MAINTENANCE THERAPY

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**Background and Aims:** The polyamine and ornithine decarboxylase inhibitor DFMO has been studied as a chemopreventative agent in several cancers including neuroblastoma. It has been employed as a maintenance therapy for HRNB patients in remission in Beat Childhood Cancer Research Consortium Trials.

**Methods:** Complete case safety data from two open-label prospective, pediatric Phase II studies (NMTRC003B and NMTRC014) of HNRB

patients in remission after upfront or relapse treatment who were treated with DFMO ( $750 \pm 250 \text{ mg/m}^2$  BID for up to 2 years with a 5-year follow-up) were pooled for evaluation of DFMO tolerability/safety. Adverse events (AEs) were graded according to the Common Terminology Criteria for Adverse Events.

**Results:** 311 subjects ( $n=52$  on NMTRC003B and  $n=259$  on NMTRC014) with a mean DFMO exposure of 1.5 years, were included in the analysis. DFMO was well-tolerated with 4.8% ( $n=15$ ) discontinuing treatment due to AEs; 10.6% ( $n=33$ ) requiring temporary dose interruptions; and 4.8% ( $n=15$ ) requiring dose reductions. Hypoacusis was the most common reason for dose modification (interruption or reduction). Thirty-five subjects (11.3%) experienced hypoacusis with 12 (3.9%) requiring dose modification; the hypoacusis resolved in the majority 67% (8/12) upon temporary interruption of DFMO and resuming treatment at a lower or original dose. Four patients (1.3%) discontinued treatment due to hearing loss. The other most common AEs were elevations in liver functions, vomiting, diarrhea, anemia, and neutropenia. Most AEs occurred within the first 6 months of treatment and resolved with continued treatment and/or dose adjustment. Serious adverse events (SAEs) occurred in 16.7% ( $n=52$ ) of patients with the most common being dehydration, vomiting, pneumonia, and hypoglycemia. The majority (88%) of these SAEs were unrelated to DFMO. No AEs resulted in death.

**Conclusions:** DFMO was well-tolerated with few discontinuations overall. Hypoacusis was managed by DFMO interruption and/or dose reduction. The DFMO tolerability/safety profile supports its use as long-term maintenance treatment for HRNB

EP322/#659 | Poster Topic: AS05 SIOP Scientific Program/AS05.e Neuroblastoma

#### RISK FACTORS IN HIGH RISK NEUROBLASTOMA PATIENTS OVER 5 YEARS: RESULTS FROM THE HR-NBL1/SIOPEN TRIAL

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**Background and Aims:** Association of age >5years with worse outcomes in high-risk neuroblastoma patients was previously shown. Here we investigate risk factors and outcomes in this population.

**Methods:** Patients with INSS stages 2,3,4 or 4S with MNA, or INSS stage4 without MNA aged  $\geq 12$  months at diagnosis up to 20 years were eligible in HR-NBL1/SIOPEN trial (recruitment 2002-2022). Several randomisations (R1,R2,R3,R4) showed use of BUMEL high dose treatment and use of Dinutuximab beta (DB) resulted in superior outcomes. Within age groups >5y at diagnosis 683 patients (59% male) were observed (median age: 6.8y (range,5-20.7) and 57% were recruited after 2009 (median follow up 7.8y).

**Results:** Treatments received were: Rapid Cojec in 607pts (89%); BUMEL in 370pts (CEM 45 pts) and in maintenance DB in 152pts (23%) whilst 128 had 13-cis RA only. Predominant primary tumour site was abdominal (85%), 24% had MycN amplification (MNA), and 90% had >1 metastatic compartment (MC) involved. The 5-year event-free (5y-EFS) and overall survival (5y-OS) were  $0.27 \pm 0.02$  and  $0.42 \pm 0.02$ . Localised MNA disease (23/607pts) had a 5y-EFS of  $0.55 \pm 0.11$ , 129 with MNA+ stage4 had a 5y-EFS of  $0.37 \pm 0.04$  and MNA- Stage 4  $0.26 \pm 0.02$  ( $p=0.013$ ). Age groups of 5-10y (548pts), 10-14y (74pts)

and >14y (61pts) had 5y-EFS of  $0.27\pm 0.02$ ,  $0.29\pm 0.06$  and  $0.20\pm 0.05$ , respectively. Prior 2009 (291pts) 5y-EFS was  $0.16\pm 0.0$ , but after 2009(391pts)  $0.35\pm 0.03$  ( $p=0.000$ ). Involvement of only 1 MC resulted in 5y-EFS of  $0.44\pm 0.06$ , but >1 MC in  $0.24\pm 0.02$  ( $p=0.002$ ). LDH>2UN above normal had a 5y-EFS of  $0.23\pm 0.02$ , but with <2UN  $0.30\pm 0.03$  ( $p=0.008$ ). All patients receiving DB had a 5y-EFS of  $0.50\pm 0.04$ , whereas those with 13-cis RA only  $0.27\pm 0.04$  ( $p=0.000$ ). These results were comparable in stage 4. Cox-Regression for EFS found adverse independent prognostic impact for stage4  $p=0.048$ (HR 2.0), age >14y  $p=0.004$ (HR 1.7), LDH>2UN  $p=0.002$ (HR 1.4) and the period  $\leq 2009$   $p<.0001$ (HR1.8).

**Conclusions:** Known risk factors were confirmed. Biological profiles are key future research objectives in these patients.

EP323/#653 | **Poster Topic: AS05 SIOP Scientific Program/AS05.e Neuroblastoma**

### 3D NEUROBLASTOMA TUMOR-SPHERE MODELS FOR DRUG SCREENING AND CELL MIGRATION ASSESSMENT

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**Background and Aims:** Three-dimensional sphere culture recapitulates the cellular characteristics of solid tumors and has become the popular choice in cancer research. With the advancement of high-throughput microscopy and proper optimization of cell-based assays, we have established a robust and novel screening platform for neuroblastoma disease modeling. This study evaluated two specific aspects: 1) comparison of drug resistance pattern between 3D and 2D cells; and 2) assessment of cancer cell migration capacity in a 3D sphere spreading assay.

**Methods:** First, the drug inhibitory effects (IC50 and IC90 values) were compared between monolayer culture and 3D neuroblastoma spheres. Second, to utilize high-content imaging while avoiding phototoxicity, we developed a stain-free, bright-field based sphere spreading assay. The assessments of cell migration from thousands of images were done automatically by a novel, script-based image processing pipeline.

**Results:** With the same cell number, 3D spheres were more resistant to chemotherapeutic drugs including Vincristine, Paclitaxel and Etoposide than 2D culture, and the differences were significant and could reach the higher end of inhibitory concentration. Next, as the spheres grew in size— which might reach up to  $1000\mu\text{m}$  and became static for over 2 weeks—reduced oxygen tension was detected by the hypoxia fluorescent probe and much higher doses of chemotherapy were required to achieve the same cytotoxic effect. For the migration assessment, the bright-field sphere spreading assay allowed direct measurement of cell migration in the 3D model, and helped to

identify the relevant signaling pathways that control neuroblastoma cell migration.

**Conclusions:** The present study has demonstrated both the potential and limits of the 3D sphere model in drug discovery. The extension of the current understanding and techniques to patient-derived organoids will provide an excellent platform for translational research and help bridge the gap between in vitro and in vivo models.

EP324/#319 | **Poster Topic: AS05 SIOP Scientific Program/AS05.e Neuroblastoma**

### LNCRNA DANCER PROMOTES ABL2-MEDIATED METASTASIS VIA DECOYING OF MIR-125-5P IN NEUROBLASTOMA

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**Background and Aims:** Neuroblastoma is one of the most common extracranial solid tumors in childhood that is already developed malignant metastatic in 73% of patients at the time of diagnosis. Neuroblastoma is characterized by early-onset age and a high frequency of metastasis. Although improvements in clinical treatment methods, such as surgery, radiotherapy, chemotherapy and immunotherapy, the prognosis and mortality rate of patients with high-risk neuroblastoma are still far from satisfactory. Over the past decades, numerous studies on primary neuroblastoma have identified significant factors that contribute to prognosis and tumor progression, such as age, MYCN amplification, 11q deletion, and heterogeneous. However, metastasis which is the leading death cause of this cancer has remained poorly understood. Therefore, a better understanding of neuroblastoma metastatic mechanisms will be essential for improving the prognosis and treatment of children with neuroblastoma.

**Methods:** Based on our previous high-throughput transcriptomic data analysis, we identified that a higher expression of differentiation antagonizing nonprotein coding RNA (DANCER) was detected in children with stage 4 high-risk neuroblastoma and was associated with poorer prognoses.

**Results:** Further experiments revealed that DANCER could positively regulate the expression of tyrosine-protein kinase ABL2 by competitively sponging miR-125a-5p, which subsequently stabilizes actin cytoskeleton to mediate pseudopodia formation and promotes the metastasis ability of neuroblastoma cells. It has been reported that ABL2 and cortactin interact with each other to stabilize the actin filament and affect the cofilin pathway. Furthermore, we confirmed that up-regulated DANCER expression significantly promoted the interaction between ABL2 and cortactin, thus activating the SSH1-cofilin pathway. Moreover, regulating the expression of miR-125a-5p significantly reversed the function of DANCER in neuroblastoma.

**Conclusions:** Our study suggests DANCER as an oncogenic lncRNA that promotes neuroblastoma progression via the DANCER/ miR-125a-5p

/ABL2 axis, which may serve as a novel prognostic biomarker and therapeutic target for neuroblastoma.

EP325/#828 | Poster Topic: *AS05 SIOP Scientific Program/AS05.e Neuroblastoma*

#### ANALYSIS OF CLINICAL DIAGNOSIS AND TREATMENT CHARACTERISTICS OF NEUROBLASTOMA WITHOUT AN APPARENT PRIMARY SITE

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**Background and Aims:** To analyze the clinical features of neuroblastoma (NB) children without an apparent primary site, and to summarize the clinical diagnosis and treatment experience.

**Methods:** A retrospective analysis was conducted on 11 cases of NB children without an apparent primary site in the Department of Surgery, Children's Hospital of Fudan University from June 2012 to February 2020.

**Results:** Among the 11 cases, there were 4 males and 7 females. The median age of onset was 18.5 (11.8, 27.3) months. The first symptoms were fever (4 cases), abdominal distension (2 cases), lower extremity pain (2 cases), fatigue (1 case), skin yellow stain (1 case), body surface mass (1 case), and orbital bruising (1 case). The metastases were multiple bone metastases with bone marrow metastases (7 cases), liver metastases (3 cases), and dorsal muscle metastases (1 case). The levels of NSE, LDH and 24-hour urinary VMA were increased in 81.8%, 88.9% and 71.4% of patients. There were 9 cases in stage IV and 2 cases in stage IVs. All 3 children who did not receive cancer-related treatment died, 1 of the children treated died. The overall 5-year cumulative survival rate was 62.3%, and the 5-year cumulative survival rate of children receiving tumor-related treatment was 85.7%.

**Conclusions:** Early diagnosis of neuroblastoma without an apparent primary site is difficult. Diagnosis relies on histopathological biopsy of metastatic lesions or bone marrow aspiration. After standardized and effective tumor-related treatment, children can mostly obtain a better prognosis.

EP326/#841 | Poster Topic: *AS05 SIOP Scientific Program/AS05.e Neuroblastoma*

#### FACTORS OF RECURRENCE IN STAGE IV NEUROBLASTOMA

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**Background and Aims:** The microenvironment of metastases, such as bone marrow, and lung, may lead to tumor recurrence. However, it is unknown if the microenvironment of metastases of neuroblastoma is associated with tumor recurrence. We analyzed the factors of recurrence in patients with stage IV neuroblastoma through a retrospective study.

**Methods:** A total of 57 patients with stage IV neuroblastoma in Shanghai Children's Hospital from April 2014 to April 2022, were included in this study. Kaplan–Meier method and multivariate Cox regression model were used to assessing the factors, especially for different metastases, that may have an impact on tumor recurrence.

**Results:** Of the 57 patients with stage IV neuroblastoma, 38 were boys and 19 were girls, the median age was 39 months (range:6-120). The mean follow-up time was 30 months (range: 7-90). The recurrence rate was 35%(20/57). The most common metastatic site was bone marrow in 39 cases (68%), which was also the most common recurrence site (11/33, 33%), followed by bone metastases in 39 cases (68%), distant lymph node metastases in 15 cases (26%), liver metastases in 8 cases (14%), intracranial metastases in 5 cases (9%), and other metastases in 18 cases (32%). In univariate analysis, five-year recurrence-free survival (RFS) was associated with serum LDH (P=0.001), Serum NSE (P =0.003), MYCN amplification (P =0.000), bone marrow metastasis (P =0.049), and the number of metastatic sites (>4, P =0.017). Cox analysis showed that MYCN amplification was an independent risk factor for recurrence in children with stage IV neuroblastoma (HR=1.69, 95%CI=1.02-2.80, P=0.04).

**Conclusions:** MYCN gene is an independent risk factor for recurrence in children with stage IV neuroblastoma. The microenvironment of bone marrow needs further study to explore its effect on recurrence in patients with stage IV neuroblastoma.

EP327/#321 | Poster Topic: *AS05 SIOP Scientific Program/AS05.e Neuroblastoma*

#### DUAL HDAC AND PI3K INHIBITOR CUDC-907 INHIBITS TUMOR GROWTH AND STEM-LIKE PROPERTIES VIA SUPPRESSING PTX3/CD44 IN NEUROBLASTOMA

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**Background and Aims:** Neuroblastoma (NB) is one of the common solid tumors in childhood and threatens the lives of children. Patients with advanced or recurrent NB have a poor prognosis. CUDC-907, as a novel dual-target inhibitor of histone deacetylase (HDAC) and phosphatidylinositol-3-kinase (PI3K), has been proved to play an anti-tumor role in several tumors. However, whether CUDC-907 has anti-tumor effect in NB is still unclear.

**Methods:** We investigated the effect of CUDC-907 on the proliferation, migration, apoptosis, and stem-like properties in NB cells.

Xenograft mouse models were used to determine antitumor activity of CUDC-907 *in vivo*. Molecular and biochemical methods were employed to define the underlying mechanisms of anti-neuroblastoma activity of CUDC-907.

**Results:** We demonstrated that CUDC-907 inhibits proliferation, migration and promotes apoptosis of NB cells. Additionally, CUDC-907 down-regulates the expression level of MYCN, as well as PI3K/AKT and MAPK/ERK pathways. Furthermore, CUDC-907 decreased cancer stem-like cell properties of NB cells, reduced their sphere forming ability *in vitro* and tumorigenicity *in vivo*. CD44 is one of the most frequently used markers for cancer stem cells. Our findings illustrated that CUDC-907 inhibits cancer stem-like cell properties of human NB cell line SK-N-BE (2) via inhibition of CD44 and its ligand PTX3.

**Conclusions:** These findings indicate that CUDC-907 might be developed into a possible therapeutic approach for NB patients.

EP328/#859 | Poster Topic: AS05 SIOP Scientific Program/AS05.e  
*Neuroblastoma*

#### CHANGES IN IMAGE-DEFINED RISK FACTORS AND THE PRIMARY TUMOR VOLUME OF NEUROBLASTOMA DURING NEOADJUVANT CHEMOTHERAPY

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**Background and Aims:** Image-defined risk factors (IDRFs) are associated with clinical stage in neuroblastoma. This study aims to explore changes in IDRFs and the primary tumor volume during neoadjuvant chemotherapy in patients with neuroblastoma.

**Methods:** We retrospectively reviewed the clinical data of 53 patients with neuroblastoma meeting our inclusion criteria at our hospital from April 2014 to April 2020. The number of IDRFs and the primary tumor volume at diagnosis and during neoadjuvant chemotherapy were determined. The mean follow-up time was 29 (range: 4–72) months.

**Results:** There were a total of 148 IDRFs, among which “vascular encasement” IDRFs (68, 45.9%) and “renal pedicle contact” IDRFs (32, 21.6%) were the most common. After 2 courses of neoadjuvant chemotherapy, the number of “two body compartments”, “intraspinal tumor extension” and “trachea-compressing” IDRFs decreased significantly ( $P=0.001$ ). The number of IDRFs decreased significantly with four courses of neoadjuvant chemotherapy, especially in “intraspinal tumor extension” IDRFs ( $P=0.034$ ). After two, four, six, and eight courses of neoadjuvant chemotherapy, primary tumor volumes were reduced by 54%, 69%, 63%, and 44%, respectively. Those results were

consistent with high-risk group patients. After four courses of neoadjuvant chemotherapy, volume reduction of the primary tumor was related to MYCN amplification ( $P=0.044$ ) and pathology ( $P=0.032$ ). The number of courses of neoadjuvant chemotherapy, reduction in the primary tumor volume, or reduction in the number of IDRFs had no impact on the five-year event-free survival (EFS), which was associated with the risk group ( $P=0.029$ ).

**Conclusions:** The number of IDRFs decreased significantly with four courses of neoadjuvant chemotherapy. A reduction in the number of IDRFs and the primary tumor volume did not affect the five-year EFS of patients with neuroblastoma.

EP329/#896 | Poster Topic: AS05 SIOP Scientific Program/AS05.e  
*Neuroblastoma*

#### EFFECT OF RNA N6-METHYLADENOSINE READER IGF2BP3 ON INVASION AND APOPTOSIS OF NEUROBLASTOMA CELLS

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**Background and Aims:** To investigate the effects of RNA m6A methylation reader IGF2BP3 gene on the invasion and apoptosis of neuroblastoma (NB) cells.

**Methods:** The expression level of IGF2BP3 in NB cell lines was detected by fluorescence quantitative PCR and Western blot. SK-N-BE (2) cells were selected to transfect siRNA targeting IGF2BP3 gene, and IMR-32 cells were selected to transfect IGF2BP3 eukaryotic expression plasmid. Transwell test was used to detect the change of cell invasion ability after changing the expression of IGF2BP3 and Flow cytometry was used to detect the effect of changing the expression of IGF2BP3 on the level of apoptosis; the changes of invasion-related molecules were detected after IGF2BP3 expression was altered.

**Results:** SK-N-BE (2) cells with the highest expression level of IGF2BP3 had the strongest invasiveness, and IMR-32 cells with the lowest expression level of IGF2BP3 had the weakest invasiveness. After transfection of siRNA targeting IGF2BP3 gene into SK-N-BE (2) cells, the invasiveness of cells decreased and the level of apoptosis increased; After transfection of IGF2BP3 eukaryotic expression plasmid into IMR-32 cells, the cell invasiveness was increased and the level of apoptosis was decreased, the differences were statistically significant; Changes in IGF2BP3 expression can regulate the expression of invasion-related molecules.

**Conclusions:** The down-regulation of IGF2BP3 expression in NB cells can inhibit the invasion of NB cells and promote cell apoptosis, IGF2BP3 can be attempted as a potential target for blocking NB progression. The down-regulation of IGF2BP3 expression in NB cells can inhibit the invasion of NB cells and promote cell apoptosis, IGF2BP3 can be attempted as a potential target for blocking NB progression.

EP330/#1663 | Poster Topic: AS05 SIOP Scientific Program/AS05.e  
Neuroblastoma

### URINARY CATECHOLAMINE METABOLITES AS MARKER FOR RELAPSE IN HIGH-RISK NEUROBLASTOMA

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**Background and Aims:** Urinary catecholamine metabolites are useful diagnostic and prognostic biomarkers for neuroblastoma. Currently, catecholamines are not included in response criteria for therapy. It is unclear whether urinary catecholamines are useful markers for neuroblastoma relapse.

**Methods:** Urinary catecholamine status was determined at diagnosis, end of induction, complete remission (CR) and relapse in 153 high-risk neuroblastoma patients that were treated according to the NBL2009 protocol. The catecholamine metabolites homovanillic acid, vanillylmandelic acid, dopamine, 3-methoxytyramine, norepinephrine, epinephrine, normetanephrine and metanephrine were measured. Catecholamine status was defined as positive if at least one metabolite was above the reference value. CR was defined as SIOPEN score <1 on MIBG scan and a negative bone marrow biopsy.

**Results:** At diagnosis, 150 of 153 patients had a positive catecholamine status (98%), compared with 77 of 97 at end of induction (79%), 54 of 86 at CR (63%), and 29 of 48 at relapse (60%). Catecholamine status at diagnosis and at end of induction was not associated with relapse-free survival or overall survival (OS) in the overall high-risk cohort. However, in patients with MYCN-amplified tumors, positive catecholamine status at end of induction was associated with reduced relapse-free survival (median survival 26.3 months versus 31.2, 58.7, and 46.6 months for patients with MYCN-amplified tumors with negative catecholamine status and with MYCN-non amplified patients,  $P=0.04$ ). At CR, patients with positive catecholamine status had a median relapse-free survival of 23.8 months versus 36.3 months for patients with negative catecholamine status, regardless of MYCN status. Moreover, positive catecholamine status was associated with lower relapse-free survival (hazard ratio for relapse 3.4,  $P<0.05$ ) and lower OS (hazard ratio for death 3.5,  $P=0.02$ ).

**Conclusions:** Positive urinary catecholamine status at time of CR predicted poor relapse-free survival and OS. Remarkably, the percentage of catecholamine negative urine was higher at relapse than at initial diagnosis, suggesting differences in tumor biology.

EP331/#1060 | Poster Topic: AS05 SIOP Scientific Program/AS05.e  
Neuroblastoma

### EFFICACY OF NAXITMAB IN REFRACTORY HIGH-RISK NEUROBLASTOMA

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**Background and Aims:** High-risk neuroblastoma (HR-NB) has a poor prognosis when there is residual disease post-induction in bone (~64%) or bone marrow (BM) (~28%). Naxitamab is a humanized GD2-binding monoclonal antibody administered with granulocyte-macrophage colony-stimulating factor (GM-CSF) in patients with refractory/relapsed (R/R) HR-NB in bone and/or BM. We report pre-specified interim analysis of Trial 201 in patients with refractory disease (data cut-off 31-dec-2021).

**Methods:** Ongoing Trial 201 (phase II, NCT03363373) evaluates naxitamab+GM-CSF in patients with R/R HR-NB with residual disease in bone/BM. Soft tissue and actively progressing disease were addressed prior to enrollment. Naxitamab was infused at 3mg/kg/dose (~90mg/m<sup>2</sup>/dose) intravenously on Days 1/3/5 with GM-CSF administered subcutaneously on Days -4 to 5 (monthly cycles). Response was evaluated by independent review using INRC criteria.

**Results:** In 26 patients with refractory disease, the overall response rate was 58% [95%CI:37-77] with 46% complete response (CR). Median number of cycles to first overall response were 2 (range:2-7) and to CR were 2 (range:2-8). Median duration of response (mDoR) was not estimable (NE) [95%CI:25-NE weeks] as 13/15 patients had ongoing responses at last independent review. Median follow-up for DoR was 6.1 months. Compartmental responses were 69% [95%CI:48-86] (CR=50%) in refractory bone disease (n=26) and 92% [95%CI:62-100] in refractory BM disease (n=12). Estimated 1-year PFS was 52% [95%CI:25-73] and 1-year OS was 96% [95%CI:75-99]. The frequency of Grade 3+ and serious related adverse events was lower for patients with refractory vs. relapsed disease, i.e. including severe

hypotension (51% vs. 68%), increased ALT (0% vs. 14%), and hypoxia (3% vs. 16%).

**Conclusions:** Naxitamab+GM-CSF cleared residual bone/BM disease in nearly half of HR-NB patients refractory to induction therapy with meaningful mDoR and encouraging 1-year PFS and OS. **Acknowledgements:** This study was funded by Y-mAbs Therapeutics, Inc.

EP332/#1609 | Poster Topic: AS05 SIOP Scientific Program/AS05.e Neuroblastoma

### NAXITAMAB EFFICACY AND SAFETY IN PATIENTS TREATED WITH AND WITHOUT STEROID PREMEDICATION

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**Background and Aims:** Naxitamab is a humanized GD2-binding monoclonal antibody used in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF) to treat patients with refractory/relapsed (R/R) high-risk neuroblastoma (HR-NB) with residual disease in bone and/or bone marrow (BM). To reduce adverse events (AEs) with naxitamab, corticosteroid premedication on cycle 1 day 1 (C1D1) became required during ongoing Trial 201.

**Methods:** Trial 201 (phase II, NCT03363373) evaluates naxitamab+GM-CSF in patients with R/R HR-NB with residual disease in bone/BM without soft tissue or actively progressing disease. Naxitamab was administered (intravenously) at 3mg/kg/dose (~90mg/kg/dose) over 30-60 min on Days 1/3/5 with GM-CSF administered (subcutaneously) on Days -4 to 5 at 4-week cycles. Here we present data on efficacy and safety outcomes by corticosteroid premedication on cycle 1 day 1 (C1D1) of naxitamab infusion. Response was scored by international criteria.

**Results:** At pre-planned interim analysis (data cut-off 31-dec-2021), 38/52 patients in the efficacy population and 54/74 in the safety population had received a corticosteroid premedication. Among patients

premedicated with corticosteroids, the overall response rate (ORR) was 42% [95%CI:26.3-59.2] and complete response (CR) rate was 29% [95%CI:15.4-45.9]. Notably, 61% of these patients had relapsed disease. Patients without corticosteroid premedication had ORR 71% [95%CI:41.9-91.6] with 64% CR [95%CI:35.1-87.2]. Notably, only 21% had relapsed disease. Hypersensitivity related Grade 3+ AEs reported during the C1D1 infusion were less frequent in patients who received systemic steroid premedication: bronchospasm (2 patients[3.7%] vs 3 patients[15.0%]); urticaria (3 patients[5.6%] vs 4 patients[20.0%]); anaphylactic reaction (0% vs 3 patients[15.0%]).

**Conclusions:** Differences in patient populations such as prior relapse preclude conclusion on effect of steroid premedication on naxitamab efficacy. However, steroid premedication appeared to lower the risk of severe hypersensitivity reactions. **Acknowledgement:** This study was funded by Y-mAbs Therapeutics, Inc.

EP333/#1641 | Poster Topic: AS05 SIOP Scientific Program/AS05.e Neuroblastoma

### EFFICACY AND SAFETY OF NAXITAMAB IN PATIENT SUBGROUPS WITH HIGH-RISK NEUROBLASTOMA

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**Background and Aims:** High-risk neuroblastoma (HR-NB) is the most common extracranial solid tumor in children, frequently presenting with bone marrow (BM; 70–89%) and bone (56–65%) metastases. Naxitamab is a humanized GD2-binding monoclonal antibody administered with granulocyte-macrophage colony-stimulating factor (GM-CSF) in patients with refractory/relapsed HR-NB in bone and/or BM. Response rates and median duration of response (mDoR) in subgroups by enrollment age, body weight (BW) and gender from a pre-planned interim analysis of ongoing Trial 201 (data cut-off 31-Dec-2021) are presented.

**Methods:** Trial 201 (phase II, NCT03363373) evaluates naxitamab+GM-CSF in patients with refractory/relapsed HR-NB with residual disease in bone/BM. Soft tissue and actively progressing disease were addressed prior to enrollment. Naxitamab (3mg/kg/dose) was administered intravenously over 30-60 min on Days 1/3/5 with GM-CSF administered subcutaneously on Days -4 to 5 every 4-weeks. Efficacy was evaluated by independent radiology and BM pathology review per INRC.

**Results:** Patients treated with naxitamab+GM-CSF (efficacy, n=52) had overall response rate (ORR) of 50% [95%CI:35.8-64.2], complete response (CR)=39%, and mDoR=not estimable (NE) [95%CI:24.9wks-NE]. ORR by subgroups with n≥8 patients: age 2 to <6yrs (n=27) ORR=44% [95%CI:25.5-64.7], CR=30% [95%CI:13.8-50.2], mDoR=NE [95%CI:NE-NE]; 6 to <12yrs (n=21) ORR=62% [95%CI:38.4-81.9], CR=52% [95%CI:29.8-74.3] mDoR=24.9wks [95%CI:11.0-NE]; BW <20kg (n=27) ORR=48% [95%CI:28.7-68.1], CR=33% [95%CI:16.5-54] mDoR=NE [95%CI:11.0-NE]; BW 20 to <40kg (n=20) ORR=55% [95%CI:31.5-76.9], CR=45% [95%CI:23.1-68.5], mDoR=25wks [95%CI:20.1-NE]; male patients (n=31) ORR=48% [95%CI:30.2-66.9]; female patients (n=21) ORR 52% [95%CI:29.8-74.3], mDoR by sex was not evaluated. No clinically relevant differences were seen in naxitamab safety (safety n=74) across the sub-groups.

**Conclusions:** Naxitamab is effective in HR-NB with residual disease in bone/BM regardless of age, BW, and gender. At median follow-up of 5.9 months, mDoRs were NE in most subgroups because of ongoing responses at data cut-off. Naxitamab safety across the sub-groups was consistent with previous reports.

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EP334/#310 | Poster Topic: AS05 SIOP Scientific Program/AS05.e Neuroblastoma

IS THERE A ROLE FOR HIGH-DOSE CHEMOTHERAPY (HDCT) WITH AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION (AHSCT) IN HIGH-RISK NEUROBLASTOMA IN RESOURCE-LIMITED SETTINGS?

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**Background and Aims:** High-dose chemotherapy (HDCT) with autologous hematopoietic stem cell transplantation (AHSCT) is an established treatment option for high-risk neuroblastoma. However, there is a lack of data on its efficacy and safety in low- and middle-income countries (LMICs). The aim of this study was to evaluate the out-

comes of patients with neuroblastoma who underwent AHSCT at our center.

**Methods:** We analyzed the data of 24 patients with high-risk neuroblastoma who underwent AHSCT between 2011 and 2020. The patients' data were extracted from the case records. Event-free survival (EFS) and overall survival (OS) were calculated from the day of stem cell infusion using the Kaplan-Meier method. None of the patients received immunotherapy.

**Results:** The study included 24 patients, with a median age of 5 years (2-14 years), and 75% were males. Surgical excision of the primary tumor was performed in 14 (58%) patients. Four patients received plerixafor for stem cell mobilization in addition to filgrastim. Four patients received melphalan conditioning, and busulphan and melphalan conditioning were used in 20 patients. Peripheral blood stem cell harvesting was performed in 23 patients, and bone marrow in one. The mean dose of CD34-positive stem cells infused was  $5.02 \times 10^6$ /kg. The median days of neutrophil and platelet engraftment were 12 days and 14 days respectively. The median duration of post-AHSCT follow-up was 14.5 months (1-136 months). Six patients were alive and in complete remission at the last follow-up. The median EFS and OS were 13 and 14 months, respectively. There was one transplant-related mortality, and one patient died due to dengue.

**Conclusions:** Outcomes in high-risk neuroblastoma remain poor in LMICs despite HDCT and AHSCT. The utility of AHSCT in the absence of improved survival, the high cost involved, and toxicity might not justify its use. Therefore, there is a need for increased access to immunotherapy in these countries to improve outcomes.

EP335/#1076 | Poster Topic: AS05 SIOP Scientific Program/AS05.e Neuroblastoma

MICE SENSITIVITY ANALYSIS OF EVENT FREE SURVIVAL IN HIGH-RISK NEUROBLASTOMA PATIENTS RECEIVING EFLORNITHINE (DFMO) MAINTENANCE TREATMENT WITH MATCHED EXTERNAL CONTROLS

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**Background and Aims:** Long-term survival in HRNB remains challenging. The primary cause of mortality is relapse. We reported that the risk



of relapse for HRNB patients in remission after upfront dinutuximab treated with DFMO was approximately half that of matched control patients from the COG trial, ANBL0032. Here, we evaluate the potential impact of missing covariate data (40% of control patients) on event free survival (EFS) using the multiple imputation by chained equations (MICE) sensitivity analysis.

**Methods:** Our phase 2 trial enrolled N=141 HRNB patients in remission post completion of disease treatment (2012–2016) for continuous DFMO treatment ( $\leq 2$  years;  $750 \pm 250$  mg/m<sup>2</sup> BID). ANBL0032 enrolled N=1328 HRNB patients (2001–2015) assigned to dinutuximab. Selection rules identified like patient groups eligible for matching, covariates of prognostic importance (n=11), and matching algorithm. Propensity-score matching (PSM) balanced cohorts on risk characteristics (1:3 ratio for treated:control). EFS was evaluated using unadjusted Cox model. MICE data sets (100 copies) were produced separately within each treatment arm. PSM covariates were ordered by increasing frequency of missing data. Each variable was imputed sequentially with an appropriate statistical model using observed and imputed covariates values with fewer missing observations. Each data set was analyzed as for primary analysis. Results were pooled using Rubin's method.

**Results:** N=92 treated patients and N=852 control patients met selection criteria (complete covariate data in n=91 and n=516, respectively. MICE confirmed the statistically significant EFS improvement with DFMO treatment: HR 0.48 (95% CI: 0.27, 0.86), p-value=0.0140 vs. HR 0.48 (95% CI: 0.27, 0.85), p-value=0.0114 (overall pooled analysis using complete covariate data).

**Conclusions:** MICE reproducibly confirms that HRNB patients in remission after standard upfront therapy treated with DFMO have approximately half the risk of relapse compared to matched control patients, supporting DFMO as maintenance treatment for HRNB.

EP336/#895 | **Poster Topic: AS05 SIOP Scientific Program/AS05.e Neuroblastoma**

#### IMPACT OF THE ORAL UNSATURATED FATTY ACIDS NUTRITION TO THE ANTI-TUMOR IMMUNITY IN MOUSE NEUROBLASTOMA MODEL

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**Background and Aims: Introduction:** Immunological effect induced by enteral nutrition is expected as the target for the novel anti-tumor nutrition immunotherapy. In our previous study, we reported that  $\omega 6$  unsaturated fatty acids rich enteral nutrition prolonged the survival period of mice compared to the  $\omega 3$  in mice neuroblastoma (Takeuchi et al, 2020 SIOP). Moreover, higher concentrations of arachidonic acid were observed in mice fed with  $\omega 6$  fatty acids rich nutrition (Takeuchi et al, 2021 SIOP). In this study we evaluated the relationship between the

oral intake of unsaturated fatty acids and survival periods, with paying attention to the inflammatory state of tumor bearing mice.

**Methods: Methods:** Female hemizygous TH-MYCNC Tg mice, which spontaneously progress neuroblastoma nodule, were fed with a  $\omega 3/6$  unsaturated fatty acids diet starting at the 6 weeks after birth. At 12 weeks, the mice were sacrificed. Cell surface antigen expression of tumor infiltrating lymphocytes and spleen cells were evaluated. Finally, intracellular expression of IFN- $\gamma$  in CD8  $\alpha$  positive splenocytes were evaluated using flow cytometer.

**Results: Results:** The ratio of tumor infiltration of CD8 a positive lymphocytes were also higher in  $\omega 6$  group ( $\omega 6$  vs  $\omega 3$ :  $10.8 \pm 3.4$  vs  $7.2 \pm 0.7$  %). The ratio of CD8 a positive splenocytes which expressing intracellular IFN- $\gamma$  were higher in  $\omega 6$  group compared to  $\omega 3$  feeding groups ( $\omega 6$  vs  $\omega 3$ :  $34.8 \pm 32.4$  vs  $7.6 \pm 8.6$  %). Moreover, compared to the splenocytes from  $\omega 6$  fed mice with tumor nodule, the ratio CD8  $\alpha$  positive splenocytes expressing IFN- $\gamma$  were higher in splenocytes from mice without tumor (tumor+ vs tumor-:  $52.7 \pm 32.5$  vs  $11.6 \pm 9.5$ ; p<0.01).

**Conclusions: Conclusion:** The  $\omega 6$  unsaturated fatty acids especially arachidonic acids are known to mediate inflammatory reaction, and inflammatory cytokine IFN- $\gamma$  has shown to inhibit cancer cell growth by activating cancer immunity. Our result indicated that oral intake of  $\omega 6$  unsaturated fatty acids rich feeding considered to promote anti-tumor effect by inducing the systemic inflammation.

EP337/#835 | **Poster Topic: AS05 SIOP Scientific Program/AS05.e Neuroblastoma**

#### DEVELOPMENT AND VALIDATION OF AN EPIGENETIC AND TRANSCRIPTIONAL GENE SIGNATURE FOR RISK STRATIFICATION IN NEUROBLASTOMA

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**Background and Aims:** Neuroblastoma (NB) is a pediatric cancer occurring in the peripheral nervous system and characterized by epigenetic and transcriptional abnormalities. The study aims to build an epigenetic and transcriptional prognostic model that optimizes the current protocols of molecular classification and even serves potential drug targets in NB.

**Methods:** We performed an integrative and unbiased analysis using public NB data and CRISPR-Cas9 screen both in vitro and in vivo and obtained 35 potential epigenetic and transcriptional genes. The LASSO model combined with Cox regression was performed to develop an epigenetic and transcriptional gene signature using GSE62564 (n=498). External validations were conducted using the other datasets (EGAS00001001308, n=139 and GSE16476, n=88) and the NB

samples from Shanghai Children's Hospital. Meanwhile, biological and clinical utility, immune cell subtypes and drug sensitivity were assessed.

**Results:** The 35 epigenetic and transcriptional genes were highly dependent to tumor viability. 26 of the 35 genes were included in the LASSO screen after the univariate Cox regression and MYCN exclusion. A prognostic epigenetic and transcriptional model including RUVBL1, LARP7, GTF3C4, THAP10, SUPT16H, TIGD1, SUV39H2, TAF1A, SMAD9 and FEM1B was established with the internal and external validation with biological experiments: the high-risk subtype compared to the low-risk subtype showed oncogenic and MYCN-related malignancy, poor prognosis and T-cell immunosuppression. MEK inhibitors were predicted to be potential therapeutic drugs in suppressing most of risky genes in NB.

**Conclusions:** The epigenetic and transcriptional gene signature represents a promising value for risk stratification in NB, and serves more evidence in therapeutic targets.

EP338/#246 | Poster Topic: AS05 SIOP Scientific Program/AS05.e Neuroblastoma

#### SECOND MALIGNANT NEOPLASMS IN NEUROBLASTOMA PATIENTS: CLINICAL DATA OF DMITRY ROGACHEV NATIONAL MEDICAL RESEARCH CENTER OF PEDIATRIC HEMATOLOGY, ONCOLOGY, IMMUNOLOGY

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**Background and Aims:** Intensification of therapy in intermediate/high risk patients with neuroblastoma (NB) resulted in improved overall survival. However, the survivors have a high incidence of long-term side effects of therapy, including second malignant neoplasms (SMN). The aim was to analyze the incidence of SMN in a cohort of Russian patients with intermediate/high risk NB.

**Methods:** The study included 176 patients with NB of the intermediate/ high risk group, diagnosed for the period 01.2012-12.2019, who completed specific treatment according to the modified German NB-2004 protocol at the national pediatric oncology center. Median follow-up was 58.7 months (range 16-124.8).

**Results:** Of the 176 patients, three cases (1.7%) developed a SMN. The types of SMNs included papillary thyroid carcinoma (n=2), acute myeloid leukemia (AML) (n=1). Age at diagnosis of NB was 39, 52, 55

months. AML was diagnosed in a boy three month after completion of therapy for the intermediate risk NB and relapse therapy (6 courses of topotecan/temozolomide, high-dose chemotherapy (TreoMel), radiotherapy to the retroperitoneal space, 21 Gy), metronomic therapy (vinblastine/celecoxib/cyclophosphamide/etoposide). The patient underwent specific therapy for secondary AML and alive with follow-up period of 25 months. Two papillary thyroid cancers (pT1bN0M0 and pT2N1bM0) were detected in patients with relapses of high-risk abdominal NB diagnosed 10 и 16 months after completion of therapy. One patient received first-line 131I-MIBG therapy and was diagnosed with primary hypothyroidism 12 months later. Both patients received high-dose regimens in the first line (TreoMel). Both patients underwent radical surgery and alive with the follow-up period of 3.8 and 10.7 months, respectively. The 5-year and 7-year cumulative incidence of SMN were 0.73% (95% confidence interval [CI] 0.01 – 5.07) and 2.75% (95% CI 0.88-8.42).

**Conclusions:** The intensive multimodal treatment strategy currently used to treat intermediate/ high risk NB can be associated with an increased risk of SMN. Comprehensive follow-up of these survivors is essential.

EP339/#521 | Poster Topic: AS05 SIOP Scientific Program/AS05.e Neuroblastoma

#### INITIAL RESULTS FROM THE FIRST MULTINATIONAL RETROSPECTIVE STUDY OF CLINICAL CHARACTERISTICS, RISK AND TREATMENT OF CHILDREN WITH NEUROBLASTOMA AND OTHER NEUROBLASTIC TUMORS IN LATIN AMERICA

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**Background and Aims:** Neuroblastoma is the most common extracranial solid tumor in children. Data about neuroblastoma from low- and middle-income countries is limited. We aim to evaluate clinical characteristics, risk distribution, and treatment modalities in patients diagnosed with neuroblastoma in Latin America.

**Methods:** Retrospective multicenter multinational study. We collected data on patients diagnosed with neuroblastoma and other neuroblastic tumors between 2010 and 2018 from 9 institutions in Argentina, Chile, and Uruguay.

**Results:** A total of 121 patients were included, 99 (81%) with neuroblastoma, 11(9%) with ganglioneuroblastoma, and 11(9%) with ganglioneuroma. Fifty-three patients (43%) were classified as high risk (HR), 16 (13%) as intermediate risk (IR), and 52 (43%) as low/very-low risk (LR). N-MYC amplification was performed in 90 patients (78%) (23 of them tested positive). Access to N-MYC testing was available at in-house laboratories in 2 of the 9 participating sites. All patients were evaluated at diagnosis with CT scans, MRIs (29%), MIBG scans (63%) and Tc99 bone scans (47%). First line treatments for HR patients consisted of chemotherapy (100%), surgery (77%), radiotherapy (45%), autologous stem cell transplant (ASCT) (49%) and anti-GD2 immunotherapy (7%). IR patients were treated with chemotherapy and surgery as first line treatment (87% and 93% respectively). LR patients were treated with surgery (88%) and chemotherapy (19%). A total 39 HR patients (69%) received second line and/or relapse therapy that consisted of combined chemotherapy (72%), surgery (20%), radiotherapy 10 (25%), ASCT (15%) and Immunotherapy with Racotumomab (10%). There were no reports on loss to follow-up, toxic deaths, or treatment abandonment.

**Conclusions:** Imaging and laboratory modalities to facilitate an accurate neuroblastoma risk classification (MIBG scans and NMYC amplification) are routinely used though not universally available in Latin America. Standards of care for first line treatment include chemotherapy, radiotherapy, surgery and ASCT. However, anti-GD2 immunotherapy has been largely unavailable for HR patients.

EP340/#505 | Poster Topic: AS05 SIOP Scientific Program/AS05.f  
Renal Tumours

## BEVACIZUMAB FOR RELAPSED OR REFRACTORY WILMS TUMOUR – REVIEW OF THE LITERATURE

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**Background and Aims:** Patients with advanced-stage diffuse anaplastic and/or blastemal-type Wilms tumour (WT), or those with subsequent relapses carry the highest risk of treatment failure to conventional intensive therapy. Knowing the challenges in identifying novel agents, a combination of antiangiogenic therapy with cytotoxic chemotherapy may have a synergistic effect. Bevacizumab is an antiangiogenic drug used to treat various adult solid tumours. The aim of this literature review was to identify the clinical outcomes of relapsed/refractory WT patients treated using bevacizumab-containing regimens.

**Methods:** A search was conducted using Pubmed and ClinicalTrials.gov. Search terms were: “Wilms” or “nephroblastoma” or “solid tumor” or “solid tumour” AND “paediatric” or “pediatric” or “children” AND “bevacizumab” or “Avastin”. Data collected included patient and disease characteristics, treatment regimens, and clinical responses/outcomes.

**Results:** Seven papers were identified. Among 15 evaluable patients (median age 9.5 years), there were two complete responses (CR), 6 partial responses (PR), 5 patients achieved stable disease (SD) and two patients had progressive disease (PD) on treatment. Five different treatment regimens were used, the most common being vincristine/irinotecan/temozolamide/bevacizumab (VITB, n=7). The VITB regimen was generally well tolerated and toxicities included mild myelosuppression, diarrhoea, and hypertension. Outcome at last follow-up was available in 12/15 patients; all had either PD (n=7) or died of disease (n=5). Median time to progression was 6 months.

**Conclusions:** This review suggests some effectiveness of bevacizumab in combination with other drugs (especially VITB) in heavily pre-treated patients with relapsed/refractory WT. Regimens containing bevacizumab were generally well tolerated. Bevacizumab is a feasible option to prolong survival for relapsed/refractory WT patients or bridge to other treatments but more trials/studies are needed to obtain additional evidence.

EP341/#814 | Poster Topic: AS05 SIOP Scientific Program/AS05.f  
Renal Tumours

## EXPLORING HOW THE LYMPHATIC VASCULATURE PATTERNS IN POST-CHEMOTHERAPY WILMS TUMOUR AND ITS ASSOCIATION WITH HISTOLOGICAL SUB-REGIONS WITHIN THE TUMOUR MICROENVIRONMENT

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**Background and Aims:** Lymphatic vessels maintain tissue fluid balance and resolution of inflammation in health and disease. Though lymphatic infiltration in some solid tumours is associated with metastatic spread, lymphatics also modulate protective anti-tumour immune surveillance. Comparatively, there is very little information on the role of lymphatic vessels in childhood kidney cancer. Here, we use three-dimensional (3D) imaging to examine lymphatic vessels in Wilms tumour, the most prevalent childhood kidney cancer.

**Methods:** Tissue volumes were subsampled from seven fresh nephrectomies for Wilms tumours ( $n = 27$  tumour sub-regions) and adjacent non-tumorous renal tissue ( $n = 14$  kidney cortex sub-regions). All tumours had been subject to a course of pre-operative chemotherapy. Specimens with  $<50\%$  necrosis were processed using wholemount immunofluorescence and optical clearing to enable 3D imaging of lymphatic vasculature. We compared 3D images for the presence of lymphatic vessels and their density, defined as the number of lymphatic vessels per unit volume of tissue.

**Results:** 3D imaging revealed lymphatic infiltration to be a feature of post-chemotherapy Wilms tumour. Distinct lymphatic patterns were observed dependent on defined histological sub-regions within the tumour microenvironment. Greater ( $p = 0.0039$ ) mean lymphatic density was observed in epithelial-predominant regions ( $959 \pm 160$  vessels per  $\text{mm}^3$ ) as compared to stromal-predominant regions ( $340 \pm 43$  vessels per  $\text{mm}^3$ ) or adjacent non-tumorous kidney ( $480 \pm 130$  vessels per  $\text{mm}^3$ ). Preliminary comparisons demonstrated blastemal regions to have the lowest lymphatic density.

**Conclusions:** These results demonstrate that lymphatic infiltration is a feature of the Wilms tumour microenvironment after chemotherapy. Differentiated epithelial tumour sub-regions possess highest lymphatic density, whereas lymphatic invasion is typically associated with adverse histological risk and poor clinical outcome in certain adult cancers. Our ongoing work may yield insights to harness the lymphatic vasculature for prognostic biomarkers, or manipulate these vessels to enhance targeted treatments, such as immunotherapy, for paediatric kidney cancers.

EP342/#903 | Poster Topic: AS05 SIOP Scientific Program/AS05.f Renal Tumours

#### NON-INVASIVELY IDENTIFYING STROMAL WILMS TUMOUR SUBTYPES USING MRI FROM MULTIPLE HOSPITALS

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**Background and Aims:** Identifying stromal Wilms tumour subtype could avoid intensification of therapy, where pre-operative chemotherapy has not caused tumour shrinkage. Currently, confirmation of stromal subtype relies on histological analysis of the excised tumour. The Apparent Diffusion Coefficient (ADC) derived from diffusion-weighted MRI (DWI) is related to cellular density and morphology. Stromal subtypes have increased ADC values compared to other subtypes. We assessed whether ADC could non-invasively identify stromal subtypes.

**Methods:** MRI data (post-chemotherapy, pre-surgery) from 49 patients with Wilms tumour were retrospectively collected from 6 UK hospitals. Patients underwent routine MRI scans, including DWI. DWI acquisition parameters varied within, and between sites. Tumour ROIs (Regions of Interest) were generated and verified by 2 radiologists. Areas of suspected necrosis were removed, using a previously published image-based method. ADC maps were formed from DWI data. The 25<sup>th</sup> percentile ADC within the viable ROIs was calculated. To distinguish stromal from other subtypes, a 5-fold validation (80% training, 20% test data) was performed, with an equal split of subtypes per training group. Average error metrics and an average threshold was calculated. This threshold was applied to the whole cohort ( $N=49$ ) and ROC (Receiver Operating Characteristic) analysis was conducted

**Results:** The 5-fold validation revealed average metrics for distinguishing stromal from other subtypes: Error rate: 30%, Sensitivity: 70%, Specificity: 70%. Area under curve from ROC analysis: 0.731. An ADC threshold ( $1.23 \times 10^{-3} \text{ mm}^2/\text{s}$ ) was determined and applied to the cohort (tumour ADC <sup>3</sup> threshold=stromal). Two 'mixed' tumours with high stromal components (50%, 60%) were incorrectly classified as stromal. No other subtypes were misclassified. Additionally, 63% of stromal cases (10/16) were correctly identified.

**Conclusions:** Stromal subtypes can be non-invasively identified with reasonably high sensitivity and specificity using MRI, despite varying DWI acquisitions. Such pre-surgical recognition may avoid unnecessary extension of pre-operative chemotherapy and aid surgical planning.

EP343/#1015 | Poster Topic: AS05 SIOP Scientific Program/AS05.f  
Renal Tumours

### PATTERNS OF CARE AND SURVIVAL OF RENAL TUMORS IN CHILDREN IN INDIA A RETROSPECTIVE MULTI-CENTRIC INPHOG STUDY (INPOG-WT-18-02)

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**Background and Aims:** Renal cancers account for 5-6% of all childhood cancers. Most common renal neoplasm is Wilms tumor (WT) or Nephroblastoma (90%). Frequently observed non-Wilms tumors (non-WT) include renal cell carcinoma (RCC), clear cell sarcoma of kidney (CCSK), malignant rhabdoid tumor of kidney (MRT), congenital mesoblastic nephroma (CMN), primitive neuroectodermal tumor (PNET) and renal lymphoma. In India there is paucity of data on outcomes with different centers following different protocols. Aims: To describe patterns of care in children < 18 years with renal tumors in India and to describe 2yr Event Free Survival (EFS) and Overall Survival (OS)

**Methods:** Seventeen Pediatric Oncology centers across India participated in this retrospective descriptive study. All children (<18 years) with primary renal tumors between January 2010 to June 2021 included. Relevant details recorded in pre-designed proforma.

**Results:** Total 443 children with renal tumors included in the study. Male:female ratio 1.5:1. Majority less than 4 years (74%). WT con-

stituted 91.%; CSSK next common (4.1%), remaining non-WT 5%. Commonest presentation abdominal distension or incidentally picked-up mass (87%). Others fever, weight loss, hematuria, hypertension in 13 % cases. Bilateral tumours seen in 7.4%; remaining unilateral tumours (Left 46.7% Right 44.7%). Stages I, II, III and IV were-109(24.6%), 113 (25.5%), 114 (25.7%) and 73 (16.5%) respectively. Lung was commonest site of metastasis followed by liver & bone. SIOP protocol followed in most patients (61.6%). Relapse seen in 59 (13.3%), 24(5.4%) lost follow-up and 33(7.4%) died. Relapse with discontinuation of treatment common cause of Death. OS at 20 months 85.7%. Tumour type (WTvs non-WT), stage, surgery type and neo-adjuvant chemotherapy showed statistically significant correlation with relapse and OS.

**Conclusions:** Despite different protocols being followed in centers across India, renal tumors have very good outcomes in children. This information will set the baseline and guide future studies.

EP344/#1484 | Poster Topic: AS05 SIOP Scientific Program/AS05.f  
Renal Tumours

### TREATMENT OUTCOMES AND SURVIVAL OF CHILDREN WITH WILMS TUMOR IN A COMPREHENSIVE PEDIATRIC CANCER CENTER IN SUB-SAHARAN AFRICA

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**Background and Aims:** Wilms tumor (WT) is a highly curable childhood cancer with more than 80% survival in high income countries (HICs). Survival in Sub-Saharan Africa is below 50%, which is significantly lower compared to HICs. We examined treatment outcomes and survival of children with WT treated using International Society of Pediatric Oncology-Renal Tumor Study Group 2016 UMBRELLA PROTOCOL.

**Methods:** A retrospective chart review of children diagnosed with Wilms tumor at Mulago National Referral Hospital, Uganda between January 2019 and December 2022. Kaplan-Meier curves used for Survival analysis.

**Results:** We included 109 patients with WT, median age was 3.2 years (Interquartile range (IQR), 2.4-4.7years) and 51% male. Sixty-one (56%) patients had unilateral localized disease (stages I-III), 39(36%) had stage IV, and 9(8%) had stage V disease. Among 80 patients with histological confirmation of WT, 45% and 51% had intermediate and high-risk histology respectively. Three (3%) patients had upfront nephrectomy, and 85(78%) had nephrectomy following neo-adjuvant chemotherapy. The median time from diagnosis to surgery was 2.1 (IQR, 1.7-3.9) months for stage I-III disease and 3.2 (IQR, 2.3-4.1) months for stage IV-V disease. Radiotherapy was indicated in 71 patients, and 57 (80%) received it. The median time from surgery to initiation of radiotherapy was 1.8 (IQR, 0.0-3.2) months. Twelve patients (11%) abandoned treatment. Two-year Overall Survival (OS) was 60.9%; 95% CI (49.5 - 70.5), with stage I-III OS 62.8%;95% CI (46.4 - 75.5) and stage IV-V OS 54.9%; 95% CI (37.7 - 69.2),  $P < 0.001$ . Two-year Event Free Survival (EFS) was 59.6%; 95% CI (48.4 - 69.3), with stage I-III EFS 60%;95% CI (44.2 - 72.9) and stage IV-V EFS 55%; 95% CI (38.8 - 69.6),  $P < 0.001$ .

**Conclusions:** EFS was 59.6%, a significant improvement in WT outcomes in our setting. Delayed surgery, radiotherapy and treatment abandonment are major challenges identified in treatment of our children. Focusing on these challenges could further improve survival.

EP345/#1845 | **Poster Topic: AS05 SIOP Scientific Program/AS05.f Renal Tumours**

#### DETERMINANTS OF OVERALL SURVIVAL RATES OF PATIENTS WITH WILMS TUMOUR AT PAEDIATRIC ONCOLOGY UNIT (POU), KORLE-BU TEACHING HOSPITAL (KBTH), GHANA

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**Background and Aims: BACKGROUND:** Wilms tumour (WT) commonest renal tumour in children.(1) The overall survival rates (OS) of patients with WT is 90% in high income countries (HICs)(2) (3), with a 15% recurrence of disease.(2)(3) However, in low & middle income countries (L&MICs), the OS varies from 11% to 46% resulting in the Collaborative Wilms Tumour Africa Project to improve OS.(4) **AIMS:** To determine the OS rates of patients with WT at POU, KBTH. To determine the predictors of OS rates of patients with WT at POU, KBTH.

**Methods** A hospital-based, retrospective study, data obtained from the POU database looking at the demographics, presentations, duration and type of neo-adjuvant and post-operative chemotherapy, surgical and pathological staging, radiotherapy and the associations with overall survival, morbidity and mortality in patients with WT.

**Results** One hundred and eleven patients seen in 5years, with an OS of rate of 50% with an abandonment rate of 11.7% and a mortality rate of 29.7%. Conversely, male sex had a higher incidence of WT than in

females in this study. A majority presented with unilateral disease with 6.3% as bilateral.(5)(6) Higher OS rates observed in patients with lower surgical and pathological staging of WT and two drug regimen.(7)(2) An advanced staging (8)(9), older age above four years and three drug regimen were linked to higher incidence of mortality (3) re-iterates the importance of early diagnosis and neo-adjuvant chemotherapy to reduce morbidity and mortality.(8)(10)

**Conclusions:** A multidisciplinary management approach in Wilm's tumour results in a high overall survival rates in children (90%). Good predictors of overall survival rates include low stage of disease and ages younger than four years. A joint action by healthcare workers for early diagnosis and prompt management directed at minimal drug dose and duration for improved OS and low morbidity and mortality.

**Acknowledgement:** Appreciation all the patients at POU, KBTH.

EP346/#1513 | **Poster Topic: AS05 SIOP Scientific Program/AS05.f Renal Tumours**

#### TUMOR BOARD FOR THE LATINAMERICAN PEDIATRIC ONCOLOGY GROUP (GALOP) RENAL TUMORS NETWORK

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**Background and Aims:** Multidisciplinary cancer tumor boards are essential to provide timely input from experts and improve patient care. Traditional face-to-face tumor boards became harder to access during the COVID-19 pandemic, though the use of virtual platforms have been important to overcome such barrier. A survey was performed among GALOP members in Latin America in 2022 that showed a high rate of interest in being part of a Renal tumor network (98.8%). We report on the experience of creating an on-line multidisciplinary renal tumor network in Latin America and the implementation of virtual tumor boards with regional and international experts.

**Methods:** We collected data about the monthly meetings held via zoom and that took place from June 2022 to March 2023. The Resonance GALOP Renal Tumor Network is a free online network that is part of the Resonance Health platform (<https://networks.resonancehealth.org/networks/lrtn/>).

**Results:** A total of 10 meetings have been held monthly. Pediatric oncologists, pediatric surgeons, pathologists, radiologists, and palliativists from 10 Latin American countries have participated in the meetings. Six educational sessions were presented and clinical cases were presented in 4 meetings follow by a brief update on the topic. The average number of participants per meeting was 50 (28-115), with an average participation peak of 39.9 (25-87). The most attended

meetings were the educational ones and the duration of the meetings had an average of 107 minutes (97-151).

**Conclusions:** The creation of the RTN was feasible and widely accepted by the interdisciplinary team that treats patients with renal tumors in Latin America. The challenge is to increase participation and translation of recommendations into final patient treatment.

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### THE IMPACT OF MULTIDISCIPLINARY MEETINGS ON THE DIAGNOSIS AND MANAGEMENT OF BRAZILIAN PATIENTS WITH RENAL TUMORS

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**Background and Aims:** Multidisciplinary meetings (MM) are extremely important in improving the quality of care for cancer patients. This approach is essential to review the diagnosis and treatment management and provide an important exchange of knowledge among the participants. We reviewed the pilot experience of the Brazilian Renal Tumor Group (GBTR) after the implementation of twice-weekly MM.

**Methods:** Seventy-four online meetings were held from Oct-2021 to Sep-2022. Images were shared in DICOM format and presented in real-time with an expert review regarding initial diagnosis, response assessment, and relapses. Pathological diagnoses were reviewed sharing the most representative macroscopic and microscopy images. The decision-making process was carried out in consensus with all participants following the SIOP-RTSG-UMBRELLA 2016 guidelines.

**Results:** An average of 6 meetings per month, with a mean of 113.5 minutes (59-117) were held. Two hundred and twenty-seven professionals from various specialties participated, ranging from 11 to 35 participants per meeting (mean=22). Of the 157 professionals, the majority were pediatric oncologists (67%) followed by pediatric surgeons (15%), pathologists (8%), radiologists (5%), and others. 250 cases were discussed from the 5 regions of the country (southeast: 29%; northeast 23%; south 19%; north 16%; midwest 10%) and 5 (2%) cases from other countries from Latin America. The main reasons for discussion were: clinical-radiological review (146), therapeutic approach (57), staging/ risk classification (30), and educational lectures (17). In 24% of the discussions, there was a significant change in the diagnosis and treatment.

**Conclusions:** This preliminary analysis has demonstrated that MM was essential to improve patient care. In addition, the MM has provided a friendly environment for the exchange of knowledge among all participants. We also observed an increasing number of cases registered by the GBTR in the UMBRELLA-RSTG-SIOP 2016 study.

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### CONTINUED CHALLENGES TO SURVIVAL OF WILMS TUMOUR IN SUB-SAHARAN AFRICA – A REPORT FROM CANCARE AFRICA - WILMS AFRICA PHASE II

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**Background and Aims:** Wilms tumour (WT) is one of the common and curable cancer types targeted by the Global Initiative for Childhood Cancer. Wilms Africa Phase I implemented an adapted WT treatment guideline in four hospitals, with improved end-of-treatment disease-free survival (68.5% vs 52%, P=0.002) and reduced treatment abandonment (12% vs 23%, P = 0.009). Two-year event free survival was 49.9%.

**Methods:** Wilms Africa Phase II introduced a revised WT treatment guideline as a multi-centre, prospective study conducted in seven hospitals, including 3 new sites in Ethiopia (2) and Zimbabwe. Funding was provided to employ local data managers with dedicated time. Eligibility criteria: age <16 years, unilateral WT, diagnosed between January 1<sup>st</sup> 2022 and October 1<sup>st</sup> 2023.

**Results:** We included 191 patients after the exclusion of 12 patients with a misdiagnosis. Median tumour size was 13.7 cm (range 3 - 42 cm) and 31%(60/191) had distant metastases detected. Neutropenia was documented in 6%(12/191) during preoperative chemotherapy. Fifty-eight percent of patients (111/191) had a nephrectomy. SIOP histological risk classification showed 7%(8/111) low risk, 79%(88/111) intermediate risk, 9%(10/111) high risk and 5%(5/111) results pending. Pathological stage was 38%(42/111) stage I, 17%(19/111) stage II, 36%(40/111) stage III and 5%(5/111) results pending. An end-of-treatment analysis of 191 included patients showed 47%(90/191) completed treatment alive without evidence of disease, 27%(52/191) had treatment abandonment, 14%(26/191) died during treatment,

9%(18/191) had persistent disease and 3%(5/191) are still on treatment. Treatment abandonment was 20%(23/113) versus 37%(29/78) in 'old' sites and newly joined sites, respectively ( $P=0.01$ ). Seventeen patients received radiotherapy in Ghana and Zimbabwe.

**Conclusions:** Two-year event free survival is expected to be below 50%. Patients continue to present late with advanced disease. Prevention of treatment abandonment remains an important challenge. Local evidence is essential to prioritise interventions. Future work will include continued efforts to provide family support and to improve multi-disciplinary collaboration.

EP349/#1003 | Poster Topic: AS05 SIOP Scientific Program/AS05.f  
**Renal Tumours**

**PROGNOSTIC IMPACT OF PRE-REFERRAL TUMOR RESECTION IN UNILATERAL WILMS TUMOR- A SINGLE INSTITUTIONAL EXPERIENCE FROM A LOWER MIDDLE-INCOME COUNTRY**

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**Background and Aims:** Wilms Tumor [WT] is the most common tumor in childhood. The objectives of this study were to evaluate the prognostic impact of pre-referral surgical resection of WT performed at non-oncology centers, and to strategize an improved care plan for this very curable pediatric tumor.

**Methods:** In this study conducted in a large pediatric cancer center in Pakistan, we retrospectively reviewed the electronic medical records of 149 patients with unilateral WT from September 2008 to August 2017. Based on treatment approach, cases were categorized into two groups: 1. Pre-referral Tumor Resection (PTR:  $n=75$ ) and 2. Post-neoadjuvant chemo Nephrectomy (PCN:  $n=74$ ).

**Results:** In PTR subset, median time to admission after PTR was 5 weeks (mean 11, SEM 2.8, Range: 2-202 weeks), with 53.3% ( $n=40$ ) presenting 4 weeks after PTR. Twenty patients underwent PTR after abdominal ultrasound only, with no prior CT scan. On baseline imaging studies, 58.7% ( $n=44$ ) had radiologically evaluable disease ( $n=21$ ) at presentation. Disease staging was uncertain in 23 cases because of no or inadequate histology specimens and/or lymph node sampling. The statistically significant differences were recorded for two subsets regarding tumor volume, extent and nodularity, renal vein and renal sinus involvement, lymph node status, tumor rupture and histopathologic features and tumor stage, with a 10-year EFS for PCN and PTR were 74.3% and 50.7% respectively ( $p$ -value  $<0.001$ ). In PTR subset,

EFS for those presenting within 4 weeks and after 4 weeks was 91.4% and 15.0% respectively ( $p <0.0001$ ).

**Conclusions:** Suboptimal pre-referral surgical interventions result in poor survival outcomes in unilateral WT. Our findings highlight the need for a comprehensive action plan for educating healthcare professionals engaged in WT diagnosis and referral process. PCN in a multidisciplinary team approach can reduce surgical morbidity and seems to be a better strategy to improve the survival rates in low-resource settings.

EP350/#508 | Poster Topic: AS05 SIOP Scientific Program/AS05.f  
**Renal Tumours**

**CLINICAL FACTORS ASSOCIATED WITH HEMATOLOGICAL TOXICITY IN CHILDREN RECEIVING POST-NEPHRECTOMY CHEMOTHERAPY FOR WILMS TUMOR: A SINGLE CENTER EXPERIENCE FROM MALAWI**

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**Background and Aims:** Wilms Tumor (WT) is the most common renal neoplasm in children. Risk factors for hematological toxicities and treatment-related mortality in post-nephrectomy patients receiving chemotherapy in Low-and-Middle-Income Countries (LMICs) is undefined.

**Methods:** This was a retrospective cohort study of patients with WT from 2019-2022 who received post-operative chemotherapy at Kamuzu Central Hospital in Malawi. Clinical data were recorded including nutritional status defined as per WHO guidelines. Hematological toxicity was defined by CTCAE v5 criteria. Odds Ratio (OR), corresponding  $p$ -values and 95% Confidence Intervals (CI) for associations between clinical characteristics and outcomes were calculated using a mixed-effects multivariable logistic regression accounting for multiple cycles per patient.

**Results:** A total of 326 chemotherapy cycles from 57 patients were identified. Median age was 52 months (interquartile range: 40-73). Distribution by stage comprised stage I: 19%; stage II: 12%; stage III: 46%; stage IV: 19%; and stage V: 4%. Malnutrition was present in 116 cycles (36%) and 34 (10%) had severe acute malnutrition (SAM). Vincristine-Actinomycin D-Doxorubicin (VAD) was administered in 132 cycles (40%); Vincristine-Actinomycin D (VA) in 93 (29%) and Cyclophosphamide-Etoposide (CE) in 90 (28%). Forty-nine cycles (15%) resulted in  $\geq$  grade 3 hematological toxicity and 27 (8%) had  $\geq$



grade 4. There were seven treatment-related deaths. CE was associated with both  $\geq$  grade 3 (OR: 6.2; 95% CI: 3.0-13.1;  $p < 0.001$ ) and  $\geq$  grade 4 (OR: 16.3; 95% CI: 5.6-47.6;  $p < 0.001$ ) toxicities. Malnutrition, age, and stage was not associated with hematological toxicity. However, SAM was associated with treatment-related mortality (OR: 9.4; 95% CI: 1.5-58.5;  $p = 0.02$ ).

**Conclusions:** Patients receiving CE had increased hematological toxicity. Although malnutrition was not associated with grade 3/4 toxicity, it was linked to toxic death. Nutritional support remains a critical component of the care for patients with WT in LMICs. Incorporation of CE should be guided by proper risk-benefit assessments.

EP351/#614 | Poster Topic: AS05 SIOP Scientific Program/AS05.f  
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#### NATIONAL TRAINEE-LED RETROSPECTIVE RE-AUDIT OF COMPLIANCE WITH THE CCLG RENAL TUMOUR BIOPSY RECOMMENDATIONS

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**Background and Aims:** The 2018 Children's Cancer and Leukaemia Group (CCLG) guidance recommends performing renal tumour biopsies only when there are age, imaging or biochemical features suggestive of a non-Wilms Tumour (WT). The Paediatric Oncology Trainees Group have completed a national re-audit of this guideline, following presentation of results of an initial audit in 2020.

**Methods:** Data was collected retrospectively at 14 principal treatment centres within England. All patients with unilateral renal tumours registered on the UMBRELLA study from 01/01/2021 to 31/12/2021 were included.

**Results:** Data were available for 93% (84/90) of the UMBRELLA registered patients. Overall, 48% (40/84) of patients received all recommended biochemical investigations (serum lactate dehydrogenase and calcium and urinary catecholamines), an improvement from 38% (28/73) in the initial audit. Renal biopsy was indicated in 43% (36/84) based on current guidance and performed in 38% of patients (32/84). Overall compliance with biopsy indications was 83% (70/84) vs 77% in the initial audit. In the age range typical for WT (6 months to <7 years), 38% (24/63) had an indication for biopsy and 32% (20/63) were biopsied; commonest indications were atypical imaging appearances

in 67% (16/24) and a raised lactate dehydrogenase in 21% (5/24). In patients with WT/nephrogenic rest (NR), biopsy was indicated in 39% (27/70) and performed in 31% (22/70). Biopsy was indicated and performed in all cases of rhabdoid tumour of the kidney and renal cell carcinoma.

**Conclusions:** The proportion of children with WT/NR who were biopsied is slightly reduced compared to the initial audit (40%), however remains significantly higher than the 18% reported in the international SIOP-WT-2001 trial. The current guidance is effective in identifying the majority of children with non-WT who require alternate management. Understanding the reasons for poor compliance in performing all recommended pre-treatment investigations and consistently higher biopsy rates is required.

EP352/#1013 | Poster Topic: AS05 SIOP Scientific Program/AS05.f  
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#### TREATMENT OUTCOME OF WILMS TUMOURS IN MOROCCO OVER 7 YEARS: MONOCENTRIC STUDY

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**Background and Aims:** The most prevalent kidney cancer in children is Wilms tumour (WT). This study evaluated the epidemiological characteristics, and treatment outcome of patients with WT

**Methods:** We performed a retrospective monocentric study of the medical records of all children who had a diagnosis of WT from 2015 to 2021, treated at our center. According to the SIOP 2001 classification, tumors were categorized into histological risk groups based on histology type. The GFA nephro 2005 protocol was used.

**Results:** Eighty-Six patients were treated. The median age at the time of diagnosis was 36 months (6 months -13 years); the sex ratio M/F was 0.8. The median time to diagnosis was 7 days (1 days - 1 year). The disease was bilateral in 10 patients (10%) and 31 patients (36%) had metastatic forms with 66% having pulmonary location. The median size of the tumour was 14.5 centimeters (2cm- 20 cm). The regressive histological type was the predominant type in 30%. Tumors were divided into low (9.3%) intermediate (53.5%) and high (37.2%) histological risk groups. The stage distribution was as follows. I, 26%; II, 21.4%; III, 39%; IV, 6.8%; and V, 6.8%. Most of the patients completed surgery (n: 81, 94%) and 25 patients received radiation therapy (29%). With a median follow-up time of 85 months, 74,2% of patients were alive, 20 % had died, 5.8% had lost follow-up. The overall survival (OS) was 75 % an the event-free survival was 72%. The 3-year OS rate was 85% for intermediate risk and 56% for high risk.

**Conclusions:** This study showed the patients had significant advanced stages, and a lot of metastatic forms. This resembles the profil of low-income nations in Africa and the Middle East. Although our study's survival rate is higher than other African nations, we need to strengthen our management to approach the survival of high-income countries.

EP353/#1400 | Poster Topic: AS05 SIOP Scientific Program/AS05.f  
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### SUCCESSFUL ESTABLISHMENT OF A PATIENT-DERIVED CELL LINE OF WILMS TUMOR

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**Background and Aims:** Wilms tumor (WT) is the most frequent malignant renal tumor of childhood. People with Down Syndrome are protected from its development. We aimed to study the molecular causes for this protection. The development of preclinical models allows the study of tumors in a more representative way and the testing of different treatments for a specific patient.

**Methods:** The study was approved by the Ethical Board. After obtaining the corresponding informed consent from the patient's parents, tumor samples were collected from two patients affected from WT on the day of the surgery, after appropriate preoperative chemotherapy. Tissue specimens were immediately processed: they were washed with saline solution, minced with scalpels, centrifuged (1000 rpm, 5 minutes), and treated with trypsin-EDTA for 10 minutes while shaking. Digested tumor was then plated on 100 mm cell culture dishes. Dulbecco's modified Eagle medium supplemented with 10% fetal bovine serum and 1% antibiotic and antimycotic mixture (DMEM-10) was used for all cell cultures. Medium was changed every 3 days.

**Results:** One of the tumor samples achieved adequate growth and it is still currently viable after 7 passages in culture, so a new cell line has been established. Characterization of the cell line and preclinical experiments are currently ongoing. The other tumor sample did not obtain any growth. To note, its corresponding pathology report showed 100% necrosis after preoperative chemotherapy.

**Conclusions:** Preclinical models represent an essential and harmless way to advance in translational research. The collaboration between hospitals and research centers is essential to promote scientific progress. This cell line will help us study the molecular causes that protect Down Syndrome from developing WT. Acknowledgments: Jérôme Lejeune Foundation, Álvaro Entrecanales Foundation, Universidad Francisco de Vitoria, HM Hospitals.

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Renal Tumours

### A LONG-TERM SURVEY OF 54 JAPANESE CHILDREN WITH RECURRENT NEPHROBLASTOMA

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**Background and Aims:** In Japanese prospective studies of pediatric renal tumors, the 5-year event-free survival and overall survival (OS) of nephroblastoma patients were 75%–90% and 89%–97%, respectively. However, recurrent nephroblastoma treatment in Japanese patients is unclear. This retrospective study aimed to determine the long-term survival and risk factors in such patients.

**Methods:** For recurrent cases reported to the Japan Wilms Tumor Study Group, a questionnaire was sent to 41 institutions (74 cases). Recurrence time, recurrence type, post-recurrence treatment, and outcome information were investigated.

**Results:** Survey forms were collected from 33 institutions (54 evaluable cases). Fifty-one patients without underlying disorders had a median time of 9.5 months from diagnosis to recurrence. Lung-only recurrence was observed in 18 cases, and other-type recurrence was in 33 cases. The 5-year OS of 51 cases was 70.6%; the cause of death was primary disease in 15 cases and treatment-related in one case. The 5-year OS in cases showing lung-only recurrence was superior to cases showing other-type recurrence (94.4% vs. 57.6%,  $p = 0.004$ ). In the other-type recurrence group, patients with high-intensity initial treatment and late recurrence (at least 10 months after diagnosis) had a worse 5-year OS than those with low-intensity or early recurrence (within 9 months from diagnosis) (28.6% vs. 70.8%,  $p = 0.013$ ).

**Conclusions:** Since salvage therapies are highly effective for lung-only recurrence, this study provided a basis to standardize post-recurrence treatment in such patients. New drug development is required for patients with other-type recurrence receiving high-intensity initial treatment and showing late recurrence.

EP355/#1334 | Poster Topic: AS05 SIOP Scientific Program/AS05.f  
Renal Tumours

### IS THE AGE OF PARENTS A RISK FACTOR FOR DEVELOPING NEPHROBLASTOMA IN A CHILD?

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**Background and Aims:** Parental age plays an important role in various childhood diseases and is also discussed as a risk factor for childhood cancer. We analyzed both the age of the mothers and of the fathers at birth of their child as a risk factor for the occurrence of nephroblastoma.

**Methods:** The analysis is based on data from SIOP9, SIOP93-01 and SIOP2001 from GPOH, including 3,991 patients from 1989-2020. Control data are received from the Federal Statistical Office from Germany containing all births in Germany from 1960-2019 (mothers: 22,342,629; fathers: 18,973,274) sorted by age of mothers and fathers. All data were adjusted to same observation periods. For the respected comparison of the mean values t-tests, Welch tests, comparative statistics and descriptive analyses were performed. Survival times were assessed with Cox regression and presented with martingale residual plots.

**Results:** Maternal age was available in 2,277 and paternal age in 2,176 patients with nephroblastoma. The mean age of mothers was  $29.68 \pm 5.39$  years compared to  $29.83 \pm 5.36$  years in the control group. The corresponding ages for fathers were  $32.77 \pm 6.39$  years and  $33.07 \pm 5.95$  years. There was no evidence of an higher maternal or paternal age in children with nephroblastoma. But fathers were significantly younger ( $p=0.028$ ) at the time of birth of their child with nephroblastoma. In addition, no significant differences in maternal and paternal age could be found for different histological types, in children with predisposition syndromes or in the outcome of patients.

**Conclusions:** A higher maternal or paternal age as a risk factor for an increased occurrence of nephroblastoma could not be found.

EP356/#701 | Poster Topic: AS05 SIOP Scientific Program/AS05.f  
Renal Tumours

## RENAL CELL CARCINOMA IN CHILDREN: THE RESULTS OF RETROSPECTIVE ANALYSIS

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**Background and Aims:** Renal cell carcinoma (RCC) is a rare malignant renal tumor in children. The aim of the study was retrospective analysis of the clinical and morphological characteristics and results of therapy of patients with RCC verified in the Department of Pathology in Dmitry Rogachev NMRC PHOI.

**Methods:** 42 patients aged 0-18 years with a confirmed diagnosis of RCC for the period 01.2012-05.2022 were registered. 28 patients with known clinical data were included in the final analysis. The analysis of the results was carried out on 01.06.2022.

**Results:** The median age was 11.0 years (range 3.0-16.9). The male:female ratio was 1.1:1. The median tumor volume ( $n=27$ ) was  $44 \text{ cm}^3$  (range 1.8 -  $547.7 \text{ cm}^3$ ). Distribution by clinical stages according to TNM system: T1 - 22 (78.5%), T2 - 4 (14.3%), T3 - 1 (3.6%), Tx - 1 (3.6%). Post-surgical N staging was as followed: N0 - 15 (53.6%), N1 - 4 (14.3%), Nx - 9 (32.1%). Stage M0 - 22 (79%), 6 (21%) - Mx. Preoperative chemotherapy per SIOP protocols was performed in 9 (32.1%), the initial tru-cut biopsy followed by surgery in 6 (21.4%) patients, 1 (3.6%) patient underwent an initial laparoscopic biopsy of the lymph nodes. In 1 (3.6%) case, a biopsy was performed followed by chemotherapy (incorrect diagnosis). The primary surgery was performed in 11 (39.3%) patients. The extent of surgery: R0 - 22 (78.6%), R1 - 2 (7.1%), Rx - 4 (14.3%). Translocation ( $n=9$ , 32.1%) and papillary ( $n=9$ , 32.1%) RCC prevailed. The median follow-up was 15.9 months (range 0.4-78.0). 26 are alive (92.8%). Metastatic progression was observed in 2 cases in 1.6 and 12.8 months, these patients died.

**Conclusions:** Characteristics of patients with RCC were consistent with the international data. Interdisciplinary discussion and surgical

treatment in specialized centers are mandatory for correct surgical tactics.

EP357/#333 | Poster Topic: AS05 SIOP Scientific Program/AS05.f  
Renal Tumours

#### DIRECT CORRELATION OF MRI-DWI AND HISTOPATHOLOGY OF PEDIATRIC RENAL TUMORS THROUGH A PATIENT-SPECIFIC 3D-PRINTED CUTTING GUIDE: A SINGLE-CENTER PROSPECTIVE STUDY

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**Background and Aims:** Invasive procedures to determine histology of pediatric renal tumors at diagnosis are discouraged within the SIOP-RTSG. In non-Wilms tumors (non-WTs) this may initiate misdiagnosis-based pre-operative chemotherapy. Furthermore, the more frequently occurring WT's often comprise of heterogeneous lesions, and risk assessment is based on post-surgical histological subtype, indicating clinical differences. MRI-DWI shows potential value as non-invasive biomarker through tumor characteristics and apparent diffusion coefficients (ADCs). This study aims to prospectively analyze MRI-characteristics of histological subtypes of WT's and non-WTs, with the purpose to non-invasively discriminate tumor types based on MRI-DWI.

**Methods:** Patients were included based on MRI and treated following the 2016-UMBRELLA protocol. In case of a total nephrectomy, a patient-specific cutting-guide based on the pre-operative MRI was 3D-printed, allowing direct comparison of imaging and histopathology. In case of non-eligibility for a cutting-guide, only whole-tumor ADC-values were measured. ADC-values of different diagnoses and patient- and solid tumor characteristics are statistically analyzed with correlation coefficients and the Mann-Whitney U-test.

**Results:** So far, 44 patients (47 lesions) with a median age of 2.6 years (1-177 months) were included. Thirty-seven lesions were WT's, of which 12/37 were regressive tumors. WT's appeared T2-hyperintense, T1-hypointense and predominantly heterogeneous. Median tumor volume of WT's at diagnosis was 589.7cm<sup>3</sup> (range 3.3-1956.9cm<sup>3</sup>), with limited median decrease or even increase (48.1cm<sup>3</sup>, range -332.7-561.5cm<sup>3</sup>) after pre-operative chemotherapy in stromal type WT's. On whole-tumor level, the median- and 25<sup>th</sup> percentile ADC after pre-

operative chemotherapy of stromal type WT's (7/37, mean 25<sup>th</sup> percentile ADC 1.212x10<sup>-3</sup>mm<sup>2</sup>/s) were significantly different (p=0.017) from epithelial and blastemal WT-lesions.

**Conclusions:** This ongoing prospective study shows stromal type WT's could be discriminated from more aggressive WT-subtypes, showing significantly higher median ADC-values and limited decrease in volume after pre-operative chemotherapy. These findings could be relevant for future decision-making in pediatric renal tumors, especially concerning high-risk tumors, bilateral cases and potential nephron sparing surgery.

EP358/#1288 | Poster Topic: AS05 SIOP Scientific Program/AS05.f  
Renal Tumours

#### CLINICAL AND WILMS TUMOR CHARACTERISTICS OF PATIENTS WITH HETEROZYGOUS GERMLINE DIS3L2 VARIANTS

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**Background and Aims:** Heterozygous germline *DIS3L2* variants were recently recognized to predispose to Wilms tumor (WT). Information on cancer penetrance and clinical/tumor characteristics of these patients is lacking, which challenges surveillance/management recommendations. Therefore, we aimed to describe an extended cohort of patients with WT and a heterozygous germline *DIS3L2* variant.

**Methods:** We collected clinical, tumor and family information of WT patients with heterozygous germline variants in *DIS3L2* by approaching national coordinators of countries participating in SIOP-RTSG and providers at individual institutions.

**Results:** Information of 22 probands from eight countries was collected. Four probands had relatives with WT and germline *DIS3L2* variant, resulting in a total of 26 patients. Germline variants were exon 9 deletions (n=22), nonsense (n=2) and frameshift (n=2) variants. The high percentage of exon 9 deletions (82% of probands) is presumably due to non-allelic homologous recombination between two flanking homologous LINE1-repeats. Genotyping of five Dutch patients did not reveal a founder effect. All patients whose asymptomatic parents were tested (n=14) inherited the variant. Median WT age was 41 months (range 19-101). In 15/16 patients with available tumor data, a somatic second hit was found. Two patients had bilateral WT, 8/26 patients had nephrogenic rests at histological examination and 8/26 patients had metastases. All patients had preoperative chemotherapy. Histology was blastemal in 7/26 patients, intermediate-risk 15/26, low-risk in 1/26 and unknown in 3/26. Additional phenotypes were autism spectrum disorder (n=1) and aberrant urethra (n=1). Four patients died during/after treatment, two relapsed (one died) and 22 reached complete remission.

**Conclusions:** Patients with WTs caused by heterozygous germline *DIS3L2* variants do not (yet) present a recognizable phenotype. *DIS3L2* variants are a cause for familial WT, but considering selection bias for referral to geneticists, penetrance seems low. In this (still small) cohort, there is a higher percentage of high-risk blastemal histology compared to sporadic WTs, needing further study.

EP359/#786 | Poster Topic: AS05 SIOP Scientific Program/AS05.f  
Renal Tumours

#### WILMS TUMOR IN CENTRAL AMERICA AND THE CARIBBEAN REGION (AHOPCA): IDENTIFYING OPPORTUNITIES TO IMPROVE QUALITY OF TREATMENT IN LOW AND MIDDLE-INCOME COUNTRIES

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**Background and Aims:** Pediatric cancer centers within AHOPCA adapted treatment guidelines from National Wilms Tumor Studies 4-5 to treat patients with Wilms tumor (WT). The guidelines recommended upfront nephrectomy (UN) unless the local multidisciplinary team considered preoperative chemotherapy (POC) (Vincristine/Actinomycin D/Doxorubicin) for 4-6 weeks in fragile patients and/or advanced disease at diagnosis, similar to the International Society of Pediatric Oncology (SIOP) approach.

**Methods:** A retrospective analysis of prospectively collected data from newly diagnosed patients with unilateral WT from 2012-2018, describing diagnostic characteristics, risk stratification, and outcomes. **Results:** Of 353 eligible patients, 247 (70%) received POC. Patients receiving POC had higher median initial tumor volume (590 mL vs 308 mL,  $p=0.0001$ ), and more often stage IV disease (74/247, 30% vs 3/106, 3%) compared to UN. The POC lead to partial response in 170/247 (69%) and a reduction of median tumor volume to 257 mL, 29/247 (12%) patients receiving POC didn't perform surgery because of abandonment (n=4), death (n=4), and progressive disease (PD, n=11). Tumor rupture/spillage was documented in 24/106 (22%) of UN and 50/218 (23%) of POC. While the guidelines considered patients receiving POC as local stage III, 69/218 (31%) were reassigned to Stage I-II after evaluation of histological findings, and 36/69 (52%) were spared radiotherapy. Anaplasia was reported in 42/324 (13%). The guidelines didn't apply the SIOP histological-risk classification in POC cases, and a retrospective analysis identified 19/31 (61%) cases with blastemal-type misclassified as intermediate risk. Abandonment-censored event-free survival (EFS) and overall survival (OS) rates were  $75\% \pm 2.4\%$  and  $78\% \pm 2.3\%$ , with UN and POC groups showing relapse/PD of 16% and 22%, and EFS of  $75\% \pm 4.3\%$  and  $66\% \pm 3.0\%$  ( $p=0.07$ ) respectively.

**Conclusions:** POC benefited patients with advanced disease, allowing for safe surgical procedures in our group. The implementation of the standard WT SIOP approach (POC and histological risk classification) is feasible and can improve the outcomes in the region.

EP360/#562 | Poster Topic: AS05 SIOP Scientific Program/AS05.g  
Bone Tumours

#### EPIDEMIOLOGY OF INFECTIOUS COMPLICATIONS IN POLISH PEDIATRIC PATIENTS WITH BONE TUMORS - A TEN YEARS PERSPECTIVE

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**Background and Aims:** Patients with bone tumors are treated with intensive chemotherapy resulting in neutropenia and immunosuppression. Aim: analysis of bacterial, fungal and viral infections in children with malignant bone tumors.

**Methods:** Retrospective analysis of 234 (140 Ewing's sarcoma (ES), 94 osteosarcoma (OSA)) children with newly diagnosed bone tumors between 2012 and 2021 in Polish pediatric oncology centers.

**Results:** Infections occurred in 110/234(47.0%) children, including 72/140(51.4%) with ES and 38/94(40.4%) with OSA. Median age: 13.9years (1month-22 years). BACTERIAL INFECTIONS. A total of 198 episodes were found 122 in ES, 76 in OSA. Time from diagnosis to first infection: 5 months. Bacteria were isolated from urine (70), blood (66), feces (55), wound (17), throat (1), conjunctiva (1), central catheter implantation site (1), joint fluid (1). The most common isolates were: *E.coli*(43), *Staphylococcus spp.*(46), *Klebsiella spp.*(31), *Clostridiolles difficile*(29), *P.aeruginosa*(20). Median therapy: 10 days (1-46). Treatment was successful in 98.0%(193/197). No deaths were observed from 2018-2021. Cumulative infection rate (2012-2021): 51.4%(ES), 40.4%(OSA)(OR 1.56, p=0.1, NS). Between 2020-2021 vs. 2012-2019, there was a significant 2.8-fold decrease in infections in ES (p=0.017; 95%CI=1.2-6.4) and a 3.1-fold increase in OSA (p=0.0215, 95%CI=1.2-8.2). FUNGAL INFECTIONS (IFI). There were 9 episodes of IFI (3probable, 6possible) occurred as urinary infection (2) and pneumonia (7). Time to infection: 0.6-12 months. Duration of therapy: 7-104days, survival 100%. VIRAL INFECTIONS. 26 infections were found in 22 patients: 13/140(9.3%) in ES and 9/94(9.6%) in OSA (p=ns), occurred 2 weeks-13 months after diagnosis: SARS-CoV-2(8), rotavirus (6), influenza (2), adenovirus (2), HHV6(1), norovirus (2), RSV (1), influenza (1), HSV+influenza (1), VZV (1). Treatment: acyclovir (HHV6- 8days, HSV- 5days, VZV- 5days), oseltamivir (influenza, 5days), in gastrointestinal infections and SARS-CoV-2 symptomatic treatment. Death was observed in 1/8(12.5%) of patients with SARS-CoV-2(ES patient) infection.

**Conclusions:** A high rate of bacterial complications was found in children with bone tumors, while fungal and viral infections were episodic. Between 2020 and 2021, there was a significant decrease in bacterial infections in ES patients, while an increase in OSA patients.

EP361/#1460 | Poster Topic: AS05 SIOP Scientific Program/AS05.g Bone Tumours

#### CLINICAL CHARACTERISTICS, TREATMENT, AND SURVIVAL OF CHILDREN AND ADOLESCENTS WITH OSTEOSARCOOMA: EXPERIENCE IN A PEDIATRIC CANCER CENTER IN MEXICO

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**Background and Aims:** Osteosarcoma is the most common bone tumor in children. Advances in chemotherapy and local control make it possible to increase survival. The objectives were to describe the clinical characteristics, management, and survival in children and adolescents with osteosarcoma.

**Methods:** Descriptive-retrospective study. Seventy-four patients diagnosed with osteosarcoma were included. (from 2007 to 2022).

**Results:** The median age was 13 years, the male predominance was 63.5%, the affected anatomical site: femur 52.7%, tibia 23%, humerus 10.8%, and the median size of the primary tumor was 10 cm. The most frequent osteoblastic histological subtype was 70.3%. Metastatic disease was 35%, and the main site of metastasis was the lung.

Neoadjuvant chemotherapy was administered to 85% of the patients according to the institutional protocol (alternating regimens of ifosfamide-doxorubicin, cisplatin-etoposide) and from the year 2020 with the EURAMOS protocol. Adjuvant chemotherapy was administered in 78.4%.

In the patients who received the institutional protocol, 22.6% developed renal toxicity associated with the use of ifosfamide and cisplatin, 9.5% severe hematological depression, 3.8% ototoxicity due to cisplatin, and 1.9% cardiotoxicity due to anthracyclines. And in the patients who received the protocol-EURAMOS, adverse effects to methotrexate occurred in 20% and severe hematological depression in 10%.

Local control performed: amputation 44.8%, disarticulation 37.9%, limb salvage 12.1%. Good histological response in 24.3% (Huvos necrosis system).

Median follow-up was 60 months, overall survival (OS)  $48.7 \pm 7.3\%$ , and event-free survival (EFS)  $33\% \pm 6\%$ . In patients with metastatic disease, OS was  $26 \pm 10\%$  and EFS  $13.5 \pm 7.2\%$  compared with patients with a localized disease with OS  $61 \pm 9.2\%$  and EFS  $42.5 \pm 7.9\%$ .

**Conclusions:** The success in the survival of osteosarcoma lies in timely detection. Barriers to limb salvage are large tumor size and metastatic disease at diagnosis. It is necessary to design appropriate to strengthen referral systems.

EP362/#1051 | **Poster Topic: AS05 SIOP Scientific Program/AS05.g Bone Tumours**

## TREATMENT OF RECURRENCE OF OSTEOSARCOMA IN CHILDREN

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**Background and Aims:** The results of treatment of recurrence of osteosarcoma depend on the operability of the tumor, the interval of occurrence of relapse, the use of chemotherapy.

**Methods:** From 2009 to 2022, 19 children with relapsed osteogenic sarcoma, aged from 9 to 18 years, were treated in the children's department of the Kyiv Oncology Center, the average age was 14 years. Recurrences were observed in 11 of 33 children with a local form of osteosarcoma and in 8 of 13 children with metastatic osteosarcoma. The number of relapses in one patient was from 1 to 8. In case of single metastases in the lungs, an atypical lung resection was performed, in case of multiple metastases in the lungs and bone metastasis, pre-operative chemotherapy, removal of metastases, and postoperative chemotherapy were performed. Chemotherapy and surgery were performed in 6 children with recurrence of the local form of osteosarcoma, in 4 only atypical lung resection, in 1 child the parents refused treatment. 8 patients with metastatic osteosarcoma and combined relapse underwent chemotherapy. Primary chemotherapy was carried out according to protocol ISG-SSG 1 or UNDIOR-99. Relapse chemotherapy was based on 1st line chemotherapy drugs: methotrexate  $12\text{g}/\text{m}^2$ , ifosfamide  $15\text{g}/\text{m}^2$ , carboplatin  $600\text{ mg}/\text{m}^2$  + etoposide  $600\text{ mg}/\text{m}^2$  and 2nd line of chemotherapy: endoxan  $2.5\text{g}/\text{m}^2$  + etoposide  $500\text{ mg}/\text{m}^2$ . Gemzar with docetaxel was used in adjuvant chemotherapy.

**Results:** Out of 11 children with recurrence of local osteosarcoma, 7 children (63.6%) remain alive with a follow-up period of 6 months to 12 years. 5-year overall survival was 68% ( $p < 0.05$ ). All children with recurrence of metastatic osteosarcoma died within 8 months to 7 years from the start of anti-relapse treatment.

**Conclusions:** The effectiveness of first-line chemotherapy is an important prognostic indicator ( $p < 0.05$ ) of the survival of children with relapsed osteogenic sarcoma.

EP363/#1379 | **Poster Topic: AS05 SIOP Scientific Program/AS05.g Bone Tumours**

## UNRAVELLING OF BRCA2 MUTATION IN A CHILD WITH HEPATOBLASTOMA AND EWING SARCOMA

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**Background and Aims:** **Background:** Familial cancer predisposition syndromes account for 10% of all paediatric cancers. We report here

a child diagnosed with Hepatoblastoma at the age of 1 year, who subsequently developed Ewing sarcoma at 7 years with next generation sequencing (NGS) revealing underlying BRCA2 mutation. This is the first report of such an association, to the best of our knowledge.

**Methods:** We reviewed literature for genetics and syndromic association of Hepatoblastoma and Ewing sarcoma as second malignant neoplasm and hereditary cancer predisposition syndromes.

**Results:** A developmentally normal 7-year-old girl, second born child of a non-consanguineous marriage with no significant family history of malignancies presented at 1-year of age with SR Hepatoblastoma and was treated with PLADO chemotherapy and right hepatectomy. After a disease-free interval (DFI) of 5 years, she presented with Ewing sarcoma of left scapula, which was treated with COG AEWS0031 protocol and scapulectomy. NGS done (considering 2 embryonal malignancies) on somatic cell detected germline heterozygous mutation of BRCA2 gene [variant c.9117+2del]. Family was counselled regarding screening protocol for further BRCA2 associated malignancies in the child and BRCA2 mutation screening in first degree relatives.

**Conclusions:** BRCA2 mutations causing childhood cancers are very rare, limited to case reports of association with non-Hodgkin lymphomas in children (St. Jude Life study) and medulloblastoma. There has been no indication to test for BRCA1/2 in children with rare exception of Fanconi anaemia, where association of embryonal malignancies are well known. Our experience highlights the need to do genetic sequencing in all children with multiple cancers and the need to research on BRCA1/2 genes in pathogenesis of embryonal cancers.

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#### TANDEM HIGH-DOSE CHEMOTHERAPY AND AUTOLOGOUS STEM CELL TRANSPLANTATION FOR INITIAL PULMONARY METASTASES

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**Background and Aims:** Metastatic osteosarcoma has a poor prognosis, a long-term survival rate below 20%. The role of high dose chemotherapy and autologous stem cell transplantation (HDC/ASCT) in high risk osteosarcoma is still unclear compared to conventional chemotherapy, and the optimal conditioning regimen is not established. We retrospectively analyzed the outcome of tandem HDC/ASCT in osteosarcoma with pulmonary metastases.

**Methods:** Among patients with osteosarcoma treated at Seoul National University Children's Hospital from 2014 to 2022, 10 patients received tandem HDC/ASCT for pulmonary metastases at diagnosis. After neoadjuvant chemotherapy, primary tumor was surgically removed. Metastatectomy was followed after one cycle of adjuvant chemotherapy. Tandem HDC/ASCT was performed in complete remission. We used melphalan, etoposide, and carboplatin (MEC) for the first ASCT and busulfan plus melphalan (BuMel) for the second ASCT.

**Results:** The median age at diagnosis was 12.2-years-old (range 6.5-13.8). Tumor necrosis rates following neoadjuvant chemotherapy were 90% in 2 patients (20%), 50-89% in 5 patients (50%), 10-49% in 2 patients (20%), and <10% in 1 patient (10%). The median follow-up duration was 34.5 months (range 3-82). The 2-year event free survival was 45.0% and overall survival was 90%. Of the five events (50%), one was treatment-related mortality (TRM) and four cases were relapse. Salvage chemotherapy was done in relapsed patients. The causes of death in three patients (30%) were TRM, secondary malignancy (therapy-related myelodysplastic syndrome), and progression of osteosarcoma, respectively. All patients achieved engraftment after each HSCT. Neither veno-occlusive disease (VOD) nor thrombotic microangiopathy occurred in the first HDC/ASCT. During the second HDC/ASCT, 3 patients (30%) were treated for severe VOD.

**Conclusions:** Despite of high toxicity, overall survival of tandem HDC/ASCT with MEC/BuMel was feasible. Even in the case of relapse, most patients showed response in salvage chemotherapy. A prospective study is needed to identify efficacy of HDC/ASCT for metastatic osteosarcoma.

EP365/#51 | Poster Topic: AS05 SIOP Scientific Program/AS05.g Bone Tumours

#### CARDIAC FUNCTION IN PEDIATRIC EWING SARCOMA DURING AND AFTER TREATMENT: A LONGITUDINAL STUDY

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**Background and Aims:** We evaluated the prevalence and determinants of cardiac dysfunction during and after treatment in children with Ewing sarcoma treated on the EFT 2001 protocol.

**Methods:** This retrospective study included children aged 0-18 years with Ewing sarcoma treated at our centre with the EFT 2001 protocol (anthracycline cumulative dose 360mg/m<sup>2</sup> and cyclophosphamide 11800mg/m<sup>2</sup>) with/without radiation therapy from January 2001 through December 2018. Cardiac assessments were done at baseline, after every 2 cycles of doxorubicin, and at post-treatment follow-up. Undernutrition was defined as weight/BMI-for-age <2SD. The



cumulative incidence (risk) of cardiotoxicity was calculated with death as a competing risk, and subset analysis using nutrition and gender.

**Results:** Among 650 eligible patients, median age at diagnosis was 12 years and median follow-up 56 months (range 1-252 months). Eighty-five patients (13%) developed cardiotoxicity, at a median time of 13 months (range:1-168 months). Five,16, 8, 32 and 24 patients developed cardiac dysfunction at <120 mg/m<sup>2</sup>, 120-240 mg/m<sup>2</sup>, 240 mg/m<sup>2</sup>, 300 mg/m<sup>2</sup> and 360 mg/m<sup>2</sup> respectively. The cumulative incidence of cardiac dysfunction in the overall cohort and undernourished was 5.8% and 9.2% at 12months, 13% and 18% at 24months, 13% and 19% at 36months, 13% and 20% at 48months, 14% and 21% at 5years and 15% and 24% at 10 years. At a median cardiac follow up of 25 (range: 3-212) months, 21 (24.7%) patients had normalization of left ventricular function whereas 9(10.6%) patients died of cardiac toxicity. Age at diagnosis (7-12 years OR5.1, 13-18 years OR3.9), female sex (OR2.3), undernutrition (OR2.9) and chest wall location (OR8.7) were risk factors for cardiotoxicity on multivariable analysis.

**Conclusions:** Children with Ewing sarcoma have a high incidence of cardiac toxicity persisting years after therapy, underlining the need for life-long surveillance. Undernourished children are at a higher risk for cardiac dysfunction even at lower cumulative anthracycline doses, and need more stringent monitoring.

EP366/#1668 | **Poster Topic: AS05 SIOP Scientific Program/AS05.g Bone Tumours**

#### EWING SARCOMA. A NEW LOOK. EXPERIENCE OF THE RESEARCH INSTITUTE NAMED L.A. DURNOV

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**Background and Aims:** Ewing sarcoma (ES) is the second most common malignant tumor of the bone system in children and adolescents, characterized by a highly aggressive course. Despite the achievements of modern oncology, the treatment of ES remains an actual and little-studied problem.

**Aims:** To improve survival rates for patients with Ewing's sarcoma

**Methods:** We ran a comparative study of examination and treatment of 330 patients staged IIA-IVB treated at the DOiG Research Institute or the period from 2009 to 2022 using protocols MMES-99, n=210, and ES-2017, n=120. The average follow-up time for patients was 59.0±43.1 months and 30.8±16.3 months, respectively (p=0.0000001). The intensification in the MMES-99 protocol was carried out due to the escalation of the dose of alkylating agents, in the ES-2017 protocol – due to the compression interval and the use of the most effective chemotherapy drugs (vincristine/doxorubicin/ifosfamide).

**Results:** 270 (84.6%) patients were diagnosed with classical ES – 167 (61.9%) of them had localized form, 103 (38.1%) of them had disseminated form, 50 (15.4%) – extraskelatal ES - 35 (69.4%) of them had localized form, 15 (30.6%) had disseminated form. During the follow-up, 100 (31.4%) patients died, progression was detected in 120 (37.6%). The 3-year overall survival rate in localized forms of ES treated according to the MMES-99 protocol was 80.7±3.9, compared with 85.8±6.5 in patients treated according to the ES-2017 protocol. Progression-free survival for patients treated by ES-2017 was also better. The incidence of febrile neutropenia with the use of the ES-2017 protocol was 10 times less than with the MMES-99 protocol, and amounted to 4% and 42%, respectively (p=0.0001). Thus, the ES-2017 protocol is more effective and less toxic.

**Conclusions:** Intensification of treatment by using of “interval compression” and selection of chemotherapy drugs is more effective and safer than the previously used treatment protocols.

EP367/#678 | **Poster Topic: AS05 SIOP Scientific Program/AS05.g Bone Tumours**

#### DETERMINANTS OF TUMOR NECROSIS AND ITS IMPACT ON OUTCOME IN NON-METASTATIC OSTEOSARCOMA TREATED WITH A TWO-DRUG NON-HIGH DOSE METHOTREXATE REGIMEN – A RETROSPECTIVE INSTITUTIONAL ANALYSIS

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**Background and Aims:** Tumor necrosis post neoadjuvant chemotherapy in osteosarcoma is an adverse prognostic factor. Treatment escalation among patients with poor necrosis treated with 3-drug high-dose methotrexate-based protocol has failed to improve outcomes. This study aimed to elucidate the factors affecting tumor necrosis and its impact on outcome among patients of non-metastatic osteosarcoma treated with two-drug non-high dose methotrexate-based regimen in a low-middle income setting.

**Methods:** A retrospective single-institutional study was conducted on non-metastatic osteosarcoma patients treated at our institute between 2003-2019. Patients who underwent upfront surgery, no surgery or without available tumor necrosis data were excluded. Patients were treated uniformly with 3 cycles of cisplatin/doxorubicin before surgery. Patients with poor necrosis (<90%) were further treated with alternating 6 cycles of cisplatin/doxorubicin and ifosfamide/etoposide; those with good necrosis (≥90%) received 3 cycles of cisplatin/doxorubicin. Multivariable logistic regression and cox regression analyses determined the factors predicting good necrosis and the independent impact of necrosis on event-free survival (EFS) and overall survival (OS) respectively.

**Results:** Of 640 registered osteosarcoma patients, 280 patients (median age 17 years; male 67.1%; median symptom duration 4 months) were included for analysis. 73 patients (26%) achieved good necrosis. Median EFS was 37.5 months; median OS was not reached. Symptom duration  $\leq 4$  months (OR=2.34;  $p=0.037$ ), and serum alkaline phosphatase (ALP)  $\leq 450$  IU/l (OR=3.32,  $p=0.003$ ) predicted good necrosis. Poor necrosis was an independent predictor of inferior EFS (HR=2.24,  $p=0.01$ ) along with large baseline tumor size ( $>10$ cm) (HR=2.07;  $p=0.002$ ) and symptom duration  $\leq 4$  months (HR=1.68;  $p=0.041$ ). Similarly, poor necrosis also independently predicted inferior OS (HR=3.52;  $p=0.004$ ) along with large tumor size (HR=2.26;  $p=0.005$ ) and symptom duration  $\leq 4$  months (HR=2.04;  $p=0.02$ ).

**Conclusions:** Patients with shorter symptom duration and lower ALP achieved good necrosis post 2-drug neoadjuvant chemotherapy. Poor necrosis continues to be an independent prognostic factor for survival outcomes, despite treatment escalation.

EP368/#769 | Poster Topic: AS05 SIOP Scientific Program/AS05.g Bone Tumours

#### WDR62 EXPRESSION IN OSTEOSARCOMA

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**Background and Aims:** Osteosarcoma (OS) is the most common primary bone tumor in children, adolescents, and young adults. The WD-40 repeat containing 62 (WDR62) is a centrosome-associated gene located in the 19g13.12 human chromosome and is involved in DNA replication and cell cycle progression. The aim of this study is to investigate the role of WDR62 in the pathogenesis of human osteosarcoma and to understand the molecular basis of osteosarcoma.

**Methods:** Actin and WD Repeat Domain 62 (WDR-63) antibodies were purchased from Abcam (Cambridge, MA, USA). In this study, WDR62 expression was evaluated by immunohistochemistry using formalin-fixed and paraffin-embedded (FFPE) osteosarcoma tissue specimens and western blot. 38 FFPE human osteosarcoma were retrieved from our files. The study was approved by the ethics committee. Western blotting and immunohistochemistry were carried out according to the current CAP (College of American Pathologists)-guidelines.

**Results:** Based on 38 clinical specimens, WDR62 expression was substantially increased in osteosarcoma tissues. Positive WDR62 protein expression was mainly located in nuclei. WDR62 was highly expressed in the areas of fibroblastic-osteoblastic productions, but the expression was similar to the expression of osteoid. The expression could not identify specific patterns apart from the relatively low expression of WDR62 in unfavorable histology osteosarcoma (telangiectatic osteosarcoma). WDR-62 showed a higher expression in the osteosarcoma cell lines of U2OS and SAOS2 than in the normal osteoblast cell line of hFOB1.19. WDR-62 was expressed higher in SASO2 in compar-

ison to U2OS. The expression of WDR62 was mainly observed at 166 kDa.

**Conclusions:** The findings of this study show the overexpression of WDR62 in human osteosarcoma. There is potential for the use of WDR62 as a biomarker in the diagnosis of osteosarcoma as it is possibly associated with tumorigenesis. WDR62 might be a novel prognostic marker and a potential chemotherapy target for osteosarcoma.

EP369/#1527 | Poster Topic: AS05 SIOP Scientific Program/AS05.g Bone Tumours

#### ASSESSMENT OF PHYSICAL FUNCTIONALITY AND QUALITY OF LIFE IN CHILDREN SURVIVING MALIGNANT BONE TUMOURS: EXPERIENCES FROM A TERTIARY CARE CENTRE IN A DEVELOPING COUNTRY

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**Background and Aims:** Children with bone malignancies are prone to physical disabilities due to the tumour as well its therapy. Issues are magnified in paediatric population due to skeletal and psychological immaturity. Children living in India have to face challenges owing to poor living conditions, limited services for the physically challenged and social stigma of physical disability. This study aims to conduct a holistic assessment of survivors of childhood bone malignancies in matters of physical disability and overall quality of life.

**Methods:** Prospective cross-sectional assessment of physical functionality was done using Paediatric balance test and Timed up and go test (TUG) in patients with bone malignancies who came for follow up. Health related QoL was assessed using PedsQL test.

**Results:** Total of 12 patients were evaluated with median follow up time being 26 months. 66% had tumour of lower limbs, 25% of axial skeleton and 16% of upper limbs. Ten (83%) had undergone a surgery (limb salvage surgery in all). The mean TUG score (11.9 secs) was more affected compared to Pediatric balance test (51.8). All patients with lower limb and axial skeleton tumors had limb length shortening and difficulty in running and squatting while no major restrictions in upper limb tumours. Muscle strength at the affected joint was lower than normal in 10/12 (83%). PedsQL score was significantly affected in emotional and schooling domains and was lower in males and for those staying in rural areas.

**Conclusions:** With advances in therapy, survival of bone cancer patients has improved but focus on physical rehabilitation is neglected in developing countries. Physical disabilities adversely impact emotional wellbeing and scholastic performance, especially in poorly equipped parts of the country. Timely physical rehabilitation, psychological counselling and a strong social support should be an integral part of treatment of bone malignancies to help the survivors achieve a better quality of life.

EP370/#935 | Poster Topic: AS05 SIOP Scientific Program/AS05.g  
Bone Tumours

### FIRST-LINE ANTI-GD2 THERAPY IN PATIENTS WITH NEWLY DIAGNOSED EWING SARCOMA

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**Background and Aims:** Despite multimodal therapy, the prognosis of patients with metastatic/inoperable Ewing sarcoma (ES) remains poor, indicating the urgent need for novel therapies. The disialoganglioside GD2, a well-established tumor-associated antigen, has been shown to be expressed by 40–90% of ES cells, making it a suitable therapeutic target in ES. Here we report 6 cases with newly diagnosed localized or metastatic, GD2-positive ES, treated with the anti-GD2 antibody dinutuximab beta (DB) during the last 4 years.

**Methods:** Four patients presented with metastatic disease and 2 patients with localized, but with inoperable primary tumour. GD2 expression was confirmed in all 4 patients by immunohistochemistry in paraffin-embedded tumour specimen. All patients received induction+consolidation chemotherapy (VIDE/VAI-2 patients or VDC/IE-4 patients), surgery just of the primary tumour, five patients received local irradiation and two patients irradiation of the metastatic sites. 4 patients received 1 cycle of DB (10 mg/m<sup>2</sup>/day over 10 days), followed by surgery. The remaining 4 cycles of DB were given as consolidation. The other two patients, who had no surgeries, received 5 cycles as consolidation.

**Results:** Two patients had no primary tumor after the induction therapy; 4 patients exhibited remaining primary tumours; three of them received surgery. Two of these 3 patients presented with complete necrosis of their primary tumor upon histologic evaluation and one patient-with 98% necrosis. One patient was still with inoperable disease. All 6 patients achieved complete remission and five of them are still without relapse and one patient suffered late relapse. The median duration of response from diagnosis was 38 months [range 32-46 months]. Treatment with DB was well tolerated, with no severe side effects.

**Conclusions:** First-line anti-GD2 immunotherapy in patients with GD2-positive ES appears to be promising, without severe toxicity and there is still a need for clinical trial to confirm the results.

EP371/#131 | Poster Topic: AS05 SIOP Scientific Program/AS05.g  
Bone Tumours

### EFFICACY AND SAFETY OF PAZOPANIB IN THE TREATMENT OF PEDIATRIC SARCOMA: RETROSPECTIVE COHORT STUDY

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**Background and Aims:** The presence of frequent genetic alterations activating the tyrosine kinase (TKI) signaling pathway has recently led to a more targeted therapeutic approach. We describe our institutional experience using pazopanib for pediatric sarcomas.

**Methods:** We performed a retrospective, IRB approved, chart review of all patients with sarcoma treated with pazopanib off-study at Ankara University Pediatric Oncology Clinic between 2019–2021.

**Results:** Twenty-five patients were identified. Median age at commencement of pazopanib treatment was 13 years old (range 4 to 18 years; 15 male: 10 female). Median duration on treatment with pazopanib was 16 months (range, 2 to 33). The median duration between the diagnosis of sarcoma and the beginning of pazopanib was 17.0 months (range, 1 to 80 months). Twelve of 25 patients due to metastatic disease at diagnosis, pazopanib was started with first-line chemotherapy and/or continued as maintenance therapy (Group 1). In the remaining 13 of 25 patients, received a second-line chemotherapy with pazopanib was administrated due to relapsed disease (Group 2). Nine patients (36.0%) (2 patients in group 1 and 7 patients in group 2) had died from progressive disease ranging between 13 and 70 months (median 33 months) after the diagnosis. OS rate was 64,0% in the entire cohort; group 1 and group 2 were 83,3%, and 46,2%, respectively. The overall median OS was 69.4 months. No new pazopanib-related adverse effects were identified.

**Conclusions:** Pazopanib appears to be an effective treatment for pediatric sarcoma. Treatment with pazopanib is well-tolerated and could have a role to maintain response in patients with pediatric sarcoma. Further studies are needed to better define the use of this regimen in the upfront management of those patients.

EP372/#1788 | Poster Topic: AS05 SIOP Scientific Program/AS05.h  
Soft Tissue Sarcomas

### ROLE OF BONE EROSION IN ORBITAL RMS. A REPORT FROM EPSSG RMS 2005 PROTOCOL

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**Background and Aims:** Orbital RMS tend to be delimited into the orbital cavity. In some patients the tumor can erode the bone and extend in the surrounding areas. The grade of erosion may be different. The aim of this analysis was to analyze the cohort of patients with orbital RMS included in the EpSSG RMS20005 protocol to better characterize the role of bone erosion (BE) as risk factor.

**Methods:** In the absence of a validated grading system we arbitrarily defined 3 grades of BE: minimal BE (scalloping, thinning of the bone), moderate (focal bone lysis or cortical interruption) or extensive (complete cortical destruction, with tumor crossing the pre-existing bone barrier).

**Results:** 199 patients were included in our analysis. Patients with extensive BE had more frequent PM extension ( $p = 0.0004$ ), volume  $> 5$  cm ( $p = 0.0008$ ) and T2 invasiveness ( $p = 0.0019$ ), compared with minimal/moderate erosion subgroups. With a median follow-up of 70.4 months, 183/199 (91%) patients are alive, 83% in first complete remission. EFS and OS at five years respectively of 75.8% (69.2-81.3), 76.9 (70.3-82.2), 91.6 (86.7-94.8). BE alone was not associated with a higher event ratio. Grouping patients in two cohorts no/minimal/moderate BE and extensive BE, events were more frequent in patients with extensive BE vs no/minimal/moderate BE (9/21, 42% vs 39/178, 21% respectively;  $p = 0.03$ ). Metastatic relapse was more frequent in extensive BE group ( $p = 0.009$ ). Considering just the presence/absence of BE, OS seems to be better in no-BE group, without any difference in EFS. Including also BE entity in survival analysis, both EFS and OS seem to be better in the group without BE (78 vs 57%,  $p 0.01$  and 94 vs 71% at 5 years,  $p < 0.0001$ ).

**Conclusions:** BE seems to be relevant especially in case of extensive erosion, with a worse events ratio, metastatic events, EFS, OS.

EP373/#178 | Poster Topic: AS05 SIOP Scientific Program/AS05.h  
Soft Tissue Sarcomas

### RESULTS OF THE PHASE 2 COHORT OF LENVATINIB (LEN) PLUS EVEROLIMUS (EVE) IN RECURRENT/REFRACTORY CHILDHOOD SOLID TUMORS, PERFORMED IN COLLABORATION WITH THE CHILDREN'S ONCOLOGY GROUP

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**Background and Aims:** Angiogenic signaling and mTOR-mediated activation have been implicated in driving several childhood cancers. In

the phase 1 part of Study 216, the RP2D was LEN 11mg/m<sup>2</sup>/day+EVE 3mg/m<sup>2</sup>/day in 28-day cycles. We report results of 3 cohorts from the phase 2 portion.

**Methods:** Patients 2-21 years old with recurrent/refractory Ewing sarcoma (EWS), rhabdomyosarcoma (RMS), and high-grade glioma (HGG) were enrolled using a 10+10 Simon's optimal 2-stage design per cohort. Measurable disease per RECISTv1.1 (EWS, RMS) or RANO (HGG) was required, tumor responses were investigator-reported. The primary endpoint was ORR at week (wk) 16; secondary endpoints included best overall response, duration of response, and safety.

**Results:** Phase 2 enrolled 41 patients (EWS n=10; RMS n=20; HGG n=11). As of the final database lock (Nov 14, 2022), none were receiving treatment/in follow-up. One patient with HGG withdrew before first imaging assessment and thus was unevaluable for efficacy. In the RMS cohort, a partial response (PR) in stage 1 prompted cohort expansion; subsequently, a 2nd PR was observed. ORR of the RMS cohort was 10.0% (n=2/20) at wk16; no objective responses were observed for EWS or HGG. Durations of the 2 PRs were 2.1 and 2.8 months. Thirteen patients (EWS: n=4; RMS: n=6; HGG: n=3) had a best response of stable disease (SD); 4 (EWS n=2; RMS n=1; HGG n=1) had SD lasting  $\geq$ 23 weeks. Common ( $\geq$ 35%) treatment-related AEs included hypertriglyceridemia, proteinuria, diarrhea, decreased lymphocyte/white blood cell counts, increased blood cholesterol, fatigue, and decreased platelet count; 56.1% required dose modification of either agent. Eight deaths (disease progression n=7; encephalopathy unrelated to treatment n=1) occurred  $\leq$ 28 days after last dose.

**Conclusions:** Although LEN+EVE did not achieve predetermined study thresholds for antitumor activity, some prolonged SD was observed. The safety profile was manageable and consistent with individual agent profiles and the combination as seen in adult studies.

EP374/#875 | Poster Topic: AS05 SIOP Scientific Program/AS05.h Soft Tissue Sarcomas

#### PROSPECTIVE PHASE I/II TRIAL OF AN INDIVIDUALIZED PEPTIDE VACCINE IN PEDIATRIC AND YOUNG ADOLESCENT PATIENTS WITH METASTASIZED FUSION-DRIVEN SARCOMAS FOLLOWING STANDARD TREATMENT - PERVISION

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**Background and Aims:** Children, adolescents and young adults with metastasized, gene fusion-driven solid tumors display dismal prognosis. Within the framework of the German DKTK consortium the phase I/II study PerVision, a prospective multicenter peptide vaccination trial, will evaluate whether a patient-individualized fusion peptide vaccination induces an antigen-specific T-cell response and may contribute to tumor control. Metastatic fusion-driven rhabdomyo-, Ewing- and synovialsarcoma patients (age < 40 y) in first or second complete remission or partial response with no signs of active disease will be included. Individual vaccination peptides will be derived from the sarcoma-specific fusion breakpoint and administered as s.c. injection. After the end of standard treatment, patients will receive 3 vaccinations. The study intends to enroll 21 patients. Primary aim of this study is to evaluate immunogenicity (specific T cell response) along with safety/toxicity. Here we report on two patient-individualized fusion peptide vaccination approaches.

**Methods:** In order to assess feasibility of this approach, two patients were vaccinated with a fusion-derived peptide: 1. a 15 y. female patient with a DNAJB1-PRKACA fusion-positive fibrolamellar hepatocellular carcinoma and 2. a 16 y. male patient with a EWSR1-FLI1 fusion-positive Ewing sarcoma.

**Results:** In both patients, fusion-peptide specific T-cell responses were elicited. 1: DNAJB1-PRKACA-derived HLA class I and II ligands induced multifunctional CD4+ T cells. Cellular antigen presentation of DNAJB1-PRKACA-derived peptides was demonstrated by mass spectrometry-based immunopeptidome analysis. Single-cell RNA sequencing further identified multiple T cell receptors from DNAJB1-PRKACA-specific T cells (Bauer et al., Nat. comm. 2023). 2: 41 days after the first inoculation, T-cell clonal expansions specific for two of three EWSR1-FLI1-fusion peptides were detected. The three highest frequency T cell clones had unique, private CDR3 binding regions.

**Conclusions:** These two index patients indicate that patient-individualized peptide vaccines are able to induce a T-cell response in fusion-driven tumors.

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### PROTON RADIOTHERAPY FOR PARAMENINGEAL RHABDOMYOSARCOMA: COMPLICATIONS AND LONG-TERM OUTCOMES OF TREATMENT IN CHILDREN

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**Background and Aims:** Radiotherapy is a leading method of local treatment of patients with parameningeal rhabdomyosarcoma (PM-RMS). The use of proton radiotherapy is currently quite limited. This abstract presents the long-term treatment results and the complications of proton therapy in the treatment of children with PM-RMS within a single center.

**Methods:** The study included 25 patients of the medical center named after Sergey Berezin who received proton therapy from 2018 to 2022. Information was collected by a retrospective analysis of medical histories, examining medical documentation requested at the place of residence of patients and examining patients directly at our center.

**Results:** The average patients' age at diagnosis was 4 years old (from 2 to 11). The embryonic histological variant was verified in 68% of the patients, alveolar - in 32%. The local stage of the disease was diagnosed in 36% of the patients, 28% of the patients had metastases in the regional lymph nodes and 36% of the patients had distant metastases. We identified a single case (4%) of intracranial spread. The median prescribed dose was 50.4 Gy (41.4-55.8 Gy). The average follow-up period was 23.4 months. Three-year overall survival (OS) was 70%, and three-year event-free survival (EFS) was 65%. Early adverse events of proton therapy (the first 3 months) included: dermatitis (100%), mucositis (100%), dryness of mucous membranes (60%), sinusitis (24%), acute purulent otitis media (4%), hoarseness (4%), and nosebleeds (4%). Among the late complications (3 months after proton therapy) were: facial hypoplasia (44%), tooth damage (16%), chronic dryness of mucous membranes (12%), chronic nasal congestion (4%), and visual impairment (4%).

**Conclusions:** Proton therapy provides good disease control and survival for patients with PM-RMS. The results are comparable to those seen worldwide. Proton therapy has acceptable toxicity and a limited number of severe complications, which makes it possible to use it with children with PM-RMS.

EP376/#963 | Poster Topic: AS05 SIOP Scientific Program/AS05.h Soft Tissue Sarcomas

### ANGIOSARCOMA IN CHILDREN: THE RESULTS OF RETROSPECTIVE ANALYSIS

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**Background and Aims:** Angiosarcoma (AS) is a rare soft tissue sarcoma (STS), which accounts for 0.3% of pediatric STS. The aim of the study was to describe cases of AS in children treated in the Dmitry Rogachev NMRC PHOI.

**Methods:** A retrospective analysis of patients with a histopathologic diagnosis of AS for the period 01.2012-01.2022 was done. Demographic, clinical data and results of therapy were analyzed. Patients were treated according to different German Cooperative Weichteilsarkom Studiengruppe (CWS) guidelines.

**Results:** Five patients were included in the analysis. The median of age was 5.2 years (range 2.9-5.7). Male: female ratio was 0.66:1 The tumor was in the soft tissues (n=3) and in the bones (n=2). Tumor size was >4 cm in 4 cases. The median of tumor volume was 119 cm<sup>3</sup> (range 34-1560). Lymph nodes involvement was detected clinically in 1 case. No distant metastases at the time of diagnosis were recorded. Primary R1 resection was performed in 2 (40%) cases, 3 patients (60%) underwent tumor biopsy. Four patients received VDC (vincristine/ doxorubicin/ cyclophosphamide) and paclitaxel courses; 1 - I<sup>2</sup>VAd/I<sup>2</sup>VA courses. The objective response (2 - complete (CR), 1 - partial) was achieved in 3/5 cases. Local control of these 3 patients consisted of R1 resection with local radiation therapy (n=2) and definitive RT (n=1). 2/5 patients progressed on therapy. 1/5 patient relapsed with isolated bone metastasis after CR. Then patient achieved secondary CR after gemcitabine/doxetaxel regimen, surgery and RT, but later died with multiple brain metastases. Two patients who received VDC/paclitaxel are alive without events with 32 months median follow-up

(range 6-37), 3 patients died because of the disease progression in 4, 32 and 37 months after diagnosis.

**Conclusions:** Our data confirmed the aggressive behavior of AS in children. Chemotherapy based on paclitaxel and doxorubicin in combination with local control allows achieving long-term disease control in some patients.

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#### RHABDOMYOSARCOMA-A 6 YEARS RETROSPECTIVE REVIEW OF 40 PATIENTS TREATED AT THE PEDIATRIC ONCOLOGY UNIT, KORLE-BU TEACHING HOSPITAL, ACCRA GHANA

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**Background and Aims:** Rhabdomyosarcoma (RMS) is the most common pediatric soft-tissue sarcoma accounting for 40% of Soft tissue sarcomas. In Ghana, it makes up 87.7% of soft tissue sarcomas and 5.7% of childhood cancers. The aim of this study was to describe the epidemiological and clinical characteristics and outcome of children with Rhabdomyosarcoma.

**Methods:** We retrospectively reviewed 40 medical records of children diagnosed with Rhabdomyosarcoma at the Pediatric Oncology unit of the Korle-Bu University teaching Hospital from January 2016 to January 2021.

**Results:** The Male: female ratio was 1.5:1.3. More than half were between 0- 5 years (57.5%). Mean duration of symptoms was 5.6 weeks with 71.5% (29/40) presenting more than 1 month from onset of symptoms. The main primary tumour location sites were head/neck (42.5%), genitourinary system (GUS) (22.5%) and abdomen (17.5%) with the bladder being the commonest genitourinary site (5/9). The Alveolar rhabdomyosarcoma was the commonest Histologic subtype in the head and neck region (5/9). Almost half of the embryonal tumours (5/12) were found in the genitourinary system. In 88.2% of the cases, tumour size was >5cm. Out of 40 patients, 32(80%) were initiated on treatment, 4(10%) died at presentation, 4(10%) switched directly to palliative care. For those initiated on treatment, 87.5% (28/32) had either a relapse or resistant disease, 25% (8/32) completed treatment, 21.9% (7/32) switched to palliative care, 28.1% (9/32) abandoned treatment and 25% (8/32) died during treatment.

**Conclusions:** Rhabdomyosarcoma is more common in males and in children <10 years of age. Common sites are Head/neck, genitourinary tract and abdomen. Alveolar Histology was common in the head/neck region while embryonal Histology was common in the GUS. Large tumour size at presentation due to delayed presentation with resultant poor outcome. There is need for continuous education of the public and health care workers on the early signs of childhood cancers and prompt referral to improve outcome.

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#### PRIMARY EXTREMITY RHABDOMYOSARCOMAS: CLINICAL FEATURES AND TREATMENT RESULTS

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**Background and Aims:** Rhabdomyosarcomas constitute 3-4% of childhood cancers. About 15% are localized in the extremities. While this location is associated with poor prognosis, many other poor prognostic factors are also associated with them. The objective of this study was to report our institutional experience with extremity rhabdomyosarcomas over a 30-year period.

**Methods:** From 1990 to 2021, 334 children diagnosed with RMS in our center. Of these, 32 (9.6%) children with extremity primary were evaluated retrospectively.

**Results:** There were 25 males and 7 females with a median age of 6 years. Most common complaints were swelling. Mean duration of symptoms was 4.0±3.2 months. The primary site was the upper extremity in 34.4% of patients and the lower extremity in 65.7%. Most common tumor location was thigh (25%) and upper arm (15.6%). The mean tumor dimension was 7.3±4.1 cm. Histopathological subtype was embryonal in 13 patients (40.6%), alveolar in 11 (34.4%), spindle cell in 1 (3%) and pleomorphic in 1(3%). Localized lymph node and systemic metastasis was found in 31.2% and 47% of patients, respectively. Fifty percent of the cases had Stage IV-Group IV, 22% had Stage III-Group III disease. In addition to chemotherapy, 56.6% received radiotherapy and 64% underwent surgery. Within a median 27 months of follow-up, 43.3% of the patients had primary refractory/progressive disease and 40% had relapsed. Three-year event-free and overall survival rates were 17.2% and 44.4%. Age, tumor location, histopathological subtypes had no effect on survival rates. Male gender, tumor size over 5 cm, high clinical and surgical stage, and high risk group were associated with significantly lower survival rates.

**Conclusions:** There were a male preponderance (M/F:3.6) in extremity rhabdomyosarcomas. Contrary to classical knowledge, the age of adolescent and alveolar histopathology did not constitute the majority. It was determined that survival rates in extremity rhabdomyosarcomas were quite poor, especially in the high-risk group.

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**COMPLETE AND DURABLE RESPONSE TO LAROTRECTINIB TREATMENT IN A TEENAGER WITH METASTATIC MALIGNANT PERIPHERAL NERVE SHEATH TUMOR HARBORING LMNA-NTRK1 GENE FUSION**

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**Background and Aims:** Neurotrophic tyrosine receptor kinases (NTRK 1-3) fusions have been identified in a range of pediatric cancers. Among children with cancer NTRK fusions can be detected in less than 1% of cases and around 5% of children with soft tissue sarcomas. ETV6-NTRK3 fusion is the most frequently reported. Malignant peripheral nerve sheath tumor (MPNST) is a rare soft tissue sarcoma and its prognosis is linked to location, size, histologic features and metastatic status.

**Methods:** Herein, we describe a 14 year old male with localized MPNST of the right foot with complete surgery, a mitotic index of 12 and size 5.4cm x 4cm. He completed 5 cycles of adjuvant chemotherapy with IFOSFAMIDE+DOXORRUBICINE with no evidence of disease. Patient developed asymptomatic right pleural metastasis at 6 months off therapy, pathology confirmation of relapse was done after complete surgery of lesions. LMNA-NTRK1 fusion was diagnosed one month after metastasectomy and access to larotrectinib was pursued while patient off any other therapy. At 1 year off therapy he developed a 2<sup>nd</sup> relapse involving soft tissue in right hemithorax, right pulmonary nodules and pleura, soft tissue tumor was excised with positive margins and received adjuvant radiation with 55.8 Gy. Larotrectinib was started during radiation therapy.

**Results:** Imaging at 3 months on therapy showed complete response in lung and pleura. Currently patient is still on treatment (started on August'2021) and remains free of disease and without significant related adverse effects.

**Conclusions:** Although NTRK fusions are rare overall in pediatric cancer there are patients that will definitively benefit from looking for such fusions as effective targeted therapy exists and is becoming more available worldwide. Length of therapy and long-term toxicity are just a couple of questions that remain unanswered. Economic status and government regulations (not yet approved in Mexico) may limit access to this potential lifesaving therapy for selected patients.

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**THE HISTONE DEMETHYLASE INHIBITOR GSKJ4 INHIBITS TUMORIGENESIS OF EMBRYONAL RHABDOMYOSARCOMA BY TARGETING THE KDM6B-MAD2L1/CDC20 AXIS**

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**Background and Aims:** Embryonal rhabdomyosarcoma (ERMS) is the most common aggressive soft-tissue sarcoma in children with a dismal prognosis and limited therapeutic options. In this study, we showed that GSKJ4, a novel small-molecule inhibitor of the histone demethylase KDM6B (Jumonji d3, JMJD3), exerted a significant anti-tumor effect on ERMS and then investigated the underlying molecular mechanisms.

**Methods:** High-throughput screening for epigenetic drug targets that inhibit the tumorigenesis of ERMS was performed. An integrative analysis of data obtained by RNA sequencing and the publicly available TCGA database was performed to identify potential targets of GSKJ4. ERMS cell lines and xenograft models were used to investigate protein functions.

**Results:** GSKJ4 treatment and KDM6B knockdown remarkably suppressed ERMS cell proliferation, clone formation, and migration, induced cell cycle arrest, and promoted apoptosis. Mechanistically, GSKJ4 exerted its anti-tumor effect by promoting H3K27me3 methylation at the promoter region of MAD2L1/CDC20, which suppressed the expression of these genes. Finally, we demonstrated the synergistic effect of GSKJ4 combined with M2I-1 in vivo and in vitro. Importantly, we confirmed the clinical correlation of the expression levels of KDM6B, MAD2L1, and CDC20 with the prognosis of ERMS patients.

**Conclusions:** Altogether, we identified that GSKJ4, a selective inhibitor of KDM6B, plays an anti-tumor role in ERMS by modulating the epigenetic regulation of MAD2L1 and CDC20. These findings not only provide novel insights into the molecular basis of ERMS oncogenesis but also suggest a therapeutic approach for ERMS.

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**EXTRANODAL SPREAD OF INTERDIGITATING DENDRITIC CELL SARCOMA TREATED WITH THE HELP OF A REMOTE TUMOR BOARD**



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**Background and Aims:** Interdigitating dendritic cell sarcoma (IDCS) is a very rare neoplasm commonly occurring in males of middle-age and mainly involving the lymph nodes but rarely affecting extranodal sites. It is arising from the antigen-presenting cells of the immune system. We report a case of extranodal IDCS in a 20 month-young female involving the head from right axilla to left fronto-temporal and gingival areas since 8 months treated successfully in remote rural area.

**Methods:** The kid was presented to our Butaro cancer center of Excellence (BCCOE) from a Provincial Hospital with a tissue block for immunohistochemistry (IHC) as suspected of a rhabdomyosarcoma or high grade lymphoma. The following stains available at Butaro: Negative CD45, CD3, CD20, PAX5, AE1/AE3 and positive S100 (cytoplasmic and nuclear) were not conclusive but suggestive of histiocytic sarcoma. The block was sent to Brigham and Women's hospital for additional stains and review and the following profile: Positive PU.1, S-100, lysozyme (dot-like) and negative CD163, CD1a, Langerin, PAX5, CD30, ALK and Desmin confirmed an IDCS.

**Results:** This infant was about to undergo palliative care upon results of uncommon pediatric cancer till our pathologist argued the local team and headed the presentation of the case to our tumor board with Boston experts. They recommended to try the combination of cyclophosphamide, doxorubicin hydrochloride, vincristine sulfate, and prednisone (CHOP) 1cycle and assess the response given the superficial nature of many of the lesions. Three weeks of first CHOP dose ended up with the disappearance of the maxillo-fronto-temporal masses of 4, 3 and 4 cm diameter respectively. The good feedback to tumor board gained approval of chemotherapy continuation to 6 cycles with 60mg/m<sup>2</sup>/5days prednisolone at each cycle.

**Conclusions:** The child is still well surviving at 2 years from end of chemotherapy, the CHOP showed success to treating an infant with extranodal IDCS.

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### INTRA-ABDOMINAL DESMOPLASTIC SMALL ROUND CELL TUMOR: THE EUROPEAN PEDIATRIC SOFT TISSUE SARCOMA STUDY GROUP (EPSSG) EXPERIENCE

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**Background and Aims:** This study describes the clinical findings of a consecutive series of pediatric and adolescent patients with a diagnosis of intra-abdominal desmoplastic small round cell tumor (DSRCT) prospectively enrolled in European pediatric Soft tissue sarcoma Study Group (EpSSG) protocols: the BERNIE study, the EpSSG MTS 2008 study, and the EpSSG NRSTS 2005 study.

**Methods:** Patients < 21 years, with a diagnosis of DSRCT arising in the abdomen were included. All trials recommended a multimodal approach including intensive multidrug chemotherapy and loco-regional treatment with surgery and/or radiotherapy whenever possible.

**Results:** The analysis included 32 cases (median age 13.7 years, male: female ratio 1.5:1). Three patients had localized tumors, 7 had regionally disseminated disease, and 22 extra-peritoneal metastases. All but one patient received multidrug chemotherapy and 11 had maintenance chemotherapy. Loco-regional treatment consisted of surgery only in 7 cases, surgery plus adjuvant radiotherapy in 10 and radiotherapy

only in 6. Among the 17 cases who had radiotherapy, 6 had irradiation of the primary site, 10 had whole abdominopelvic radiotherapy plus boost to macroscopic residual disease and one had irradiation to lung metastases only. With a median follow-up of 76 months (range, 18-124), 5-year event-free and overall survival (OS) were 19.7% and 21.0%, respectively. EFS was significantly worse for patients who did not receive loco-regional treatment (p-value 0.007).

**Conclusions:** The study confirmed that the outcome of patients with DSRCT remains dismal and did not improve over recent years despite an intensive multimodal treatment approach.

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### SYNOVIAL SARCOMA IN CHILDREN- LESSONS LEARNT OVER A DECADE OF MULTIMODALITY TREATMENT

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**Background and Aims:** Recent risk-based multimodality therapy in children and young adults has shown Overall survival (OS) of >70% in localized synovial sarcoma (SS). We studied the clinical profile, outcomes and prognostic factors of SS treated over a decade.

**Methods:** Children  $\leq$  15 years with histologically proven, treatment-naive synovial sarcoma from 2011 to 2021 were retrospectively analyzed. Primary was imaged by CT/MRI scan and staging was done by CT chest. Patients with resectable disease were offered surgery upfront. Those with unresectable disease, tumors >5cm, deep or visceral location, and impingement on neural structures were offered chemotherapy (cumulative doses: ifosfamide-45g/m<sup>2</sup>, vincristine-18mg/m<sup>2</sup>, doxorubicin-300mg/m<sup>2</sup>). Surgery was planned at 9-12 weeks and adjuvant radiotherapy (RT) was given as per standard guidelines.

**Results:** Of 272 patients with Non-Rhabdomyosarcoma Soft-Tissue Sarcomas, 53(19.5%) were SS. Median age was 11.5 years (range, 1year-15 years), M:F- 3:1. Forty-three (81.1%) patients had localized disease [regional lymph nodes involved-7(13%)]. Ten patients (18.9%) had metastases (lung-9, lung and bone marrow-1). Histology was monophasic-27 (50.9%), biphasic-6(11.3%), poorly differentiated sarcoma-10(18.9%[GC1] %), not otherwise specified-10(18.9%). Primary

was appendicular in 28 (52.8%, upperlimb-6, lowerlimb-22), axial in 25 (47.2%, head and neck-11, pelvis-2, others-12). Twelve (22.6%) had osseous primary. The median tumor size was 9cm (range,2-21cm). Tumor size>5cm was noted in 47/53(88.6%). Forty-two patients which included 2 patients with lung metastases were evaluable for outcomes. Local therapy was surgery-5(11.9%), definitive RT-5 (11.9%), surgery and RT-32(71%). At a median follow-up of 39months (range,26-52months), 3year Event Free Survival (EFS) and OS of the whole cohort were 52% (95%CI:0.37-0.72) and 62% (95%CI:0.47-0.82) respectively. Tumor size>9cm (HR-2.8, 95%CI:1.0-7.5, p=0.036) was prognostic for EFS and OS (HR-3.7, 95% CI:1.3 to 10.5, p=0.014). Definitive RT as local therapy in those patients with unresectable tumors adversely affected EFS (HR-10.3,95%CI:2.8-38.0, p=0.000) and OS (HR-4.5, 95% CI-1.1-19.2, p=0.037).

**Conclusions:** Children with localized synovial sarcoma had relatively good outcomes despite large tumor size in the cohort. Large tumor size and unresectability portends poor outcomes.

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### POORLY DIFFERENTIATED CHORDOMA: AN AGGRESSIVE VARIANT DISTINCT FROM CONVENTIONAL CHORDOMA OCCURRING IN CHILDREN

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**Background and Aims:** Paediatric poorly differentiated chordoma (PDC) is a distinct, aggressive variant of chordoma involving clivus and sacrococcygeal region and connotes a dismal prognosis. We aimed to study the histomorphology, immunohistochemistry (IHC) and clinical characteristics of PDC.

**Methods:** We studied a series of 12 paediatric patients diagnosed with PDC in last 10 years in our institute. Tumour morphology and immunohistochemistry was reviewed. Treatment and follow-up information was sought from electronic medical records.

**Results:** Age range of 12 patients was 1 to 15 years with a median of 5 years. M:F ratio was 5:1. Nine patients had tumours at base of skull while 3 were at the sacrococcygeal region. Two patients had lung metastasis at presentation. Histomorphology showed epithelioid/ rhabdoid cells arranged in sheets. Physalipherous cells was not observed. All tumours showed positivity for Brachyury, epithelial marker and loss of expression of INI 1 on IHC. Only 2 patients could be treated with surgery and radiotherapy (RT), 6 with RT

alone and 3 received chemotherapy in combination with RT. Follow-up information was available in 6 patients; 3 had died of disease while 3 were alive with disease including one with lymph nodal metastasis.

**Conclusions:** PDC is a rare variant of chordoma which differs from the conventional type in terms of its paediatric age distribution, clival location, rhabdoid histomorphology, INI1 loss on IHC and dismal prognosis. All 12 children had large, aggressive, destructive rapidly growing tumours; two patients also had lung metastasis at presentation. Multimodal therapy was offered to the patients; however, refractoriness to treatment was evident. Histologically, the 'rhabdoid' phenotype and loss of INI1 loss was a distinctive feature. None of the tumours exhibited 'physaliferous' cell morphology typically seen in conventional chordoma. Thus, high index of suspicion and appropriate IHC (INI1 and Brachyury) was important for making the accurate diagnosis of this rare tumour.

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*Retinoblastoma*

#### BASELINE RETINOBLASTOMA SURVIVAL DATA FOR A WHO GLOBAL INITIATIVE FOR CHILDHOOD CANCER FOCUS COUNTRY: THE PHILIPPINES

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**Background and Aims:** By 2030, retinoblastoma survival in the WHO Global Initiative for Childhood Cancer (GICC) countries should reach at least 60%. The Philippines, the 1st focus country in the Western Pacific region, has no baseline population-based survival statistics. We present data from Philippine General Hospital, a large setting 2 retinoblastoma referral center seeing 15 % or 30 of 200 of cases expected annually.

**Methods:** Demographic and clinical data were collected on newly diagnosed patients from January 2014-December 2021. Study end point was December 2022.

**Results:** There were 233 patients with a male: female ratio of 1.2:1. Median age at diagnosis was 29 months with a median symptom-to-diagnosis lag time of 17 months. The most common presenting symptom was leukocoria (82%). Patients had unilateral disease in 71.7% (N=167), 25.3% bilateral (N=59), and 2.6% trilateral disease (N=6). Majority had extra-ocular disease at diagnosis: International Retinoblastoma Staging System (IRSS) Stage 0: 0.4% (N=1); Stage I: 45.9% (N=107); Stage II: 3.4% (N=8); Stage III: 28.3% (N=66); Stage IV: 18.9 % (N=45); and unknown 2.6% (N=6). At study end point,

51.9% (N=121) were alive; 36.1% (N=84) died; 7.3% (N=17) refused (2.6%; N=6) or abandoned treatment (4.7%; N=11); 2.6% (N=6) lost to follow-up, and 2.1% (N=5) transferred centers. The timing of abandonment was during chemotherapy. The 1 and 3-year overall survival was 54.7% and 55.3%, respectively, with survival highest for Stage I (97.8% and 96.3%, respectively) and lower for Stages III (51.3% and 24.5%, respectively) and IV (12.1% and 0%, respectively). The 1 and 3-year abandonment-sensitive overall survival was slightly lower (61.3% and 48.1%, respectively) and followed similar trends by stage as the overall survival.

**Conclusions:** Low survival rates are due to late diagnosis and treatment abandonment. Strategies for early detection, prompt referral and treatment adherence should be prioritized in the national pediatric cancer action plans to meet WHO GICC goals.

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*Retinoblastoma*

#### CARBOPLATIN-INDUCED OTOTOXICITY IN CHILDREN TREATED FOR RETINOBLASTOMA: A CROSS-SECTIONAL STUDY OF 42 SURVIVORS

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**Background and Aims:** The chemotherapy regimen of carboplatin, vincristine, and etoposide (JOE), administered intravenously, is commonly used for retinoblastoma. Assessment of high-frequency hearing loss (HL) is infrequently reported in survivors of retinoblastoma. The aim was to evaluate HL in survivors of retinoblastoma who had received carboplatin-containing systemic chemotherapy.

**Methods:** The single-center, cross-sectional study was conducted from 2021-2022. Patients with retinoblastoma treated from 2011-2019 were enrolled. Manual otoscopy and immittance audiometry were performed to exclude patients with middle ear pathology. The hearing assessment was performed by otoacoustic emissions test, conventional (500-8000 Hz), and high-frequency (9000-20,000 Hz) pure-tone audiometry. There is a lack of a grading scale for HL at high-frequencies.

**Results:** Forty-two survivors of retinoblastoma were enrolled. Among the 53 eyes, 81% had intraocular and 19% extraocular retinoblastoma. The median number of cycles of JOE received was 6 (IQR: 6-9.3). The median cumulative carboplatin dose was 3,152 mg/m<sup>2</sup> (IQR: 2,214-4,564). The median age at diagnosis and hearing evaluation were 32.5 months (IQR: 19-43.5) and 88.5 months (IQR: 19-43.5), respectively. The median duration from diagnosis to hearing assessment was 50.5 months (IQR: 30-78.5). Pure tone audiometry revealed high-frequency (9,000-20,000 Hz) sensorineural hearing loss in 17 (40.5%)

survivors. The majority (65%) had bilateral HL. Two children among the 17 also had HL (40 dB) at conventional pure tones (8,000 Hz). The HL was not clinically perceptible in any survivor, and a hearing aid was not indicated. There was a lack of association of HL with age at diagnosis ( $p=0.12$ ), duration from diagnosis to audiometry ( $p=1.00$ ), weight-for-age ( $p=0.79$ ), socioeconomic status ( $p=0.14$ ), or cumulative carboplatin dose ( $p=0.25$ ).

**Conclusions:** High frequency (9,000-20,000 Hz) HL was observed in 17 (40.5%) of the 42 survivors of retinoblastoma who had received a carboplatin-containing chemotherapy regimen. The HL was, however, not clinically noticeable. A periodic hearing assessment is recommended to assess the progression of ototoxicity.

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Retinoblastoma

#### ADVANCED RETINOBLASTOMA WITH EXCELLENT TREATMENT OUTCOME DESPITE CHALLENGES- A REPORT FROM EASTERN INDIA

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**Background and Aims:** Retinoblastoma (RB) is the commonest ocular malignancy in children and has excellent outcome for vision and life if detected early. We present data on advanced RB from a cancer center in Eastern India.

**Methods:** Retrospective data collected and analysed on MS Excel for 60 months (Jan 2017-Dec 2022). Patients who received at least 1 cycle of chemotherapy were included in the analysis

**Results:** 64 children received curative intent chemotherapy. Investigations included examination-under-anaesthesia and MRI scan. Median age was 2.4 years (IQR 1.7, 3.7 years). Males: Female ratio 1.56:1. Family history was present in 5(4 bilateral 1 unilateral). Unilateral disease was present in 36/64(56%), bilateral in 28/64(44%). Commonest presenting symptom was white reflex (46/64=71%), fungating tumour seen in 2/64(3%). Symptoms were present for 1-2 months in 36/64(56%), >6 months in 15/64(23%). Stage III was seen in 6/36(17%) unilateral RB and 2/29(7%) bilateral RB. In unilateral RB 29/36(80%) had Group E, 6/36(17%) had Group D. Of 58 eyes in 29 children with bilateral RB, 37/58(63%) had advanced disease (Group D/E). Upfront enucleation done in 18/36 (50%) children with unilateral RB, 13/36 (36%) had delayed enucleation. Eye and vision saved in 5/36

(14%). In bilateral RB upfront enucleation of the worse eye done in 2/58(3%) eyes, delayed enucleation in 16/58(27%) eyes. Vision in both eyes saved in 11/29(38%) patients. None lost both eyes. High-risk histopathological features present in 27/49(55%) enucleated eyes. RB1 gene mutation data was available in 10 patients, mutation detected in 6/10, all bilateral RB. Two patients died of progression. Treatment was completed in 55/64(86%), abandoned in 7/64(11%). Fever neutropenia was the commonest toxicity (13/64=20%). Carboplatin hypersensitivity seen in 8/64 (12%). Three years EFS and OS were 87.6%(75.6-93.9) and 96.3%(85.8-99.1) respectively. Three year EFS was 95.6%(83.6-98.9) discounting abandonment.

**Conclusions:** Patient assistance may help in reducing abandonment, the main event impacting an otherwise excellent outcome.

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Retinoblastoma

#### PROGNOSTIC VALUE OF MOLECULAR MARKERS IN UNILATERAL RETINOBLASTOMA TREATED BY FIRST-LINE ENUCLEATION

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**Background and Aims:** At diagnosis of retinoblastoma, clinical and imaging features contribute to decide between eye-sparing treatments and enucleation. In case of enucleation, histopathological features further stratify the oncological risk and guide the decision on adjuvant treatments. Recent retrospective studies identified molecular markers with a possible additional prognostic value. We explore here the relationship between these molecular markers and the clinical outcome.

**Methods:** Ninety cases were selected from two French prospective cohorts of primary enucleated unilateral retinoblastoma patients with adjuvant chemotherapy adapted to histopathological risk factors. The tumor DNA was deeply sequenced using an in-house gene panel. We focused on molecular markers that are deemed pejorative (subtype 2, MYCN amplification, BCOR mutation, ARID1A mutation, 6p gain) and studied their association with clinical features, post-enucleation histopathological risk factors, and local or metastatic relapse.

**Results:** Forty-three cases of subtype 2, 6 cases with MYCN amplification, 8 cases with BCOR mutations, 1 case with ARID1A mutation

and 20 cases with 6p gain were identified. Adjuvant chemotherapy was indicated respectively in  $n=14/43$ ,  $n=3/6$ ,  $n=3/8$ ,  $n=0/1$  and  $n=7/20$  cases. In comparison, cases without identified molecular factors required adjuvant chemotherapy in  $n=16/55$  instances. These results suggest there is no significant association between the proposed molecular risk factors histopathological factors requiring adjuvant treatments. Additionally, molecular factors were not associated with orbital or metastatic relapses as no event was reported in the series over a median follow-up of 5.2 years.

**Conclusions:** Based on a well-documented series of primary enucleated eyes, we found no correlation between selected molecular markers and histopathological risk factors, adjuvant therapies or relapse. This suggests that these molecular markers do not provide post-enucleation prognostic information in patients treated by first-line enucleation. They may however serve to refine the stratification of enucleated retinoblastomas and help de-escalate adjuvant therapies.

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*Retinoblastoma*

#### PSYCHOSOCIAL SUPPORT NEEDS REPORTED BY PARENTS OF RETINOBLASTOMA SURVIVORS

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**Background and Aims:** Retinoblastoma guidelines promote the provision of psychosocial support to affected families. However, and it is unclear if families affected by retinoblastoma access support services in a consistent, timely and equitable manner. We aimed to determine the psychosocial support needs of retinoblastoma parents and to uncover which needs are met or unmet.

**Methods:** This was a quantitative, cross-sectional study. Eligible participants were parents and caregivers of children with retinoblastoma across Canada. Participants completed a paper or online questionnaire, collecting data pertaining to (i) participant demographics and (ii) use of and need for psychosocial support. The primary outcome measure was the proportion of retinoblastoma survivors and parents with  $\geq 1$  unmet psychosocial support need.

**Results:** Forty parents took part in the study. Of these, the majority were women ( $n=32$ ), White ( $n=31$ ) and had one child affected by retinoblastoma ( $n=37$ ). All participants answered the demographic survey, while 32/40 (80%) completed the psychosocial support needs survey. The proportion of parents with  $\geq 1$  unmet informational need was 81% (26/32). The average number of information needs per participant was 7.3 (SD  $\pm 3.5$ ). The most commonly stated information needs were for (i) long-term screening for second cancers (18/32, 56%); (ii) mental health counseling (15/32, 47%); (iii) complementary and alternative therapies (12/32, 38%); and (iv) vision loss rehabilitation (12/32, 38%). The proportion of parents with  $\geq 1$  unmet service need was 88%

(28/32). The average number of service needs per participant was 4.3 (SD  $\pm 3.1$ ). The most commonly stated service needs were for (i) family counseling (16/32, 50%); (ii) mental health counseling (14/32, 44%); (iii) camp programs and retreats (13/32, 41%); and (iv) vision loss rehabilitation (13/32, 41%).

**Conclusions:** Parents and caregivers of children with retinoblastoma have significant psychosocial support needs. Clinical and research teams should focus on filling this gap in care.

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*Retinoblastoma*

#### CONSERVATIVE MANAGEMENT OF BILATERAL INTRAOCULAR RETINOBLASTOMA IN BAMAKO

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**Background and Aims:** Conservative treatment of early stages of retinoblastoma has greatly improved the overall survival rate. The aim was to evaluate the results of conservative management of bilateral intraocular retinoblastoma in Mali.

**Methods:** The study covered the period from 01/01/2011 to 31/12/2019. We included children with bilateral intraocular retinoblastoma. After a CEV-type neoadjuvant chemotherapy, the most affected eye was enucleated, and the contralateral eye was preserved by local treatment.

**Results:** Eighteen cases were included. The median age was 11 months with a sex ratio of 0.66. The mean time to diagnosis was 5 months. The most common presentation was leucocoria. All patients received a funduscopic examination under a general anaesthesia, ocular ultrasound and a CT scan. The eyes classified (D) represented 40%. The distribution of conservative treatment modalities was as follows: Thermochemotherapy ( $n=12$ ; 66%); intra-vitreous melphalan ( $n=6$ ; 33%). After conservative treatments thirteen patients had useful vision, and two patients had no vision. At the completion of treatment, eleven patients were in complete remission, with a follow-up of 3 years. Five children were still undergoing treatment. Three patients had tumor progression and received bilateral enucleation.

**Conclusions:** Conservative management for early detected retinoblastoma provides promising results. Awareness raising about the initial symptoms should be intensified among the population and the health-care providers. Acknowledgments: We would like to thank AMCC, IOTA and GFAOP.

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Retinoblastoma

### SURVIVAL AND RELAPSE PATTERNS IN UNILATERAL RETINOBLASTOMA: ROLE OF CLINICAL-HISTOPATHOLOGIC FEATURES

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**Background and Aims:** Enucleation for retinoblastoma (RB) is a common treatment modality in developing countries owing to advanced intraocular disease at presentation. Histopathologic risk factors (HRF) as choroidal, optic nerve and scleral infiltrations (specially combined ones) and clinical presentation (glaucoma, buphthalmus, pseudocelulitis) have been associated with poorer prognosis. Risk of relapse supports need for intensive chemotherapy. Defining criteria for neo- and adjuvant therapy may improve outcomes of enucleated cases and also avoid unnecessary adjuvant treatment for low risk patients. Aim: to determine clinical and histopathologic features of enucleated unilateral retinoblastoma and to evaluate role of more intensive chemotherapy in outcome.

**Methods:** Retrospective study of enucleated unilateral retinoblastoma from 1997 to 2022 with histopathology and medical record review at National Cancer Institute-Brazil. Data from clinical presentation, staging HRF, chemotherapy use, relapses and outcome were analysed.

**Results:** Of 190 unilateral cases, 97 (50,5%) were enucleated. Median age at diagnosis: 27 months (range 4 to 85); 49 female (50,5%); glaucoma and/or buphthalmus as initial presentation: 17 cases (17,5%). Extraocular cases n=7 (7,1%) with median lag time 8,2 months (range 4.1 to 16). Only 39 were considered extraocular and/or high risk (clinical and pathologic) received chemotherapy (40%). There were 13 relapses (13,4%). Among 58 low risk patients (60%), only 4 relapses: 3 orbital which received intensive treatment and are alive without evidence of disease (1 had per-operative rupture) and 1 with CNS dissemination which died (restaged as higher staging after pathologic review). Among 38 patients which received chemotherapy, 7 relapses: 3 extraocular cases with leptomeningeal disease and died; 4 combined ocular involvement had CNS disease progression and also died (1 with abandonment). Failures predominated historically during the use of a less intensive chemotherapy. After chemo intensification in 2012, only 2/13 relapsed (both with glaucoma at diagnosis). Mortality was 12, 3% (n=12): 1 acute myeloid leukemia (AML) as second neoplasm; 1 with congenital heart disease and 10 from disease progression.

**Conclusions:** Adequate clinical and histopathology evaluation of retinoblastoma who undergo enucleation are mandatory to assign

relapse risk. These data suggest that adjuvant chemotherapy may not be needed in unilateral retinoblastoma with low risk of relapse and intense adjuvant chemotherapy in high and very high risk patients may be effective in preventing extraocular relapse.

EP392/#302 | Poster Topic: AS05 SIOP Scientific Program/AS05.i  
Retinoblastoma

### ANALYSIS OF CLINICAL DATA AND PROGNOSIS OF 835 CHILDREN WITH BILATERAL RETINOBLASTOMA IN BEIJING TONGREN HOSPITAL

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**Background and Aims:** To analyze the characteristics of single center and bilateral retinoblastoma in recent 16 years and the differences and changes of clinical prognosis.

**Methods:** The clinical data of 835 children with bilateral RB were collected from 2790 children with retinoblastoma who were treated in our hospital from September 13, 2005 to March 13, 2021. SPSS20.0 statistical software was used for statistical analysis to identify the clinical characteristics and risk factors of RB in children.

**Results:** 443 males (53.1%), 392 females (46.9%). The median age was 20.4 month. Among them, there were 17 cases of trilateral RB; 41 cases (5.4%) with distant tissue and organ metastasis; 2.8% (23/835) had a definite RB family history; The first symptom was white pupil sign, accounting for 63.4% (529/835), followed by strabismus, accounting for 15.4% (129/835). The median follow-up time was 50.69 months. 412 cases with unilateral enucleation accounted for 49.3%, 29 cases with bilateral enucleation accounted for 3.5%, and 394 cases without enucleation accounted for 47.2%. There were 42 deaths, 119 drup up and 674 survived. OS was 94.13% (674/716). the average survival time was (123.732 ± 1.247) months, and 95% CI was 121.289~126.176. Univariate prognostic risk factor analysis showed that in 2015-2020 (P=0.047), trilateral RB (P=0.001), distant tissue and organ metastasis (P=0.001), lymph node metastasis (P=0.001), and no enucleation of eyeball (P=0.037) could affect the prognosis; COX multivariate survival analysis showed that distant tissue and organ metastasis was an independent risk factor affecting the survival of bilateral RB (P=0.001).

**Conclusions:** The incidence rate of infants with bilateral RB is high, other clinical features are not specific, and the overall prognosis is good. Attention should be paid to the prevention and treatment of distant tissue and organ metastasis.

EP393/#1586 | Poster Topic: AS05 SIOP Scientific Program/AS05.i  
*Retinoblastoma*

#### AVAILABILITY OF SOCIAL DETERMINANTS OF HEALTH DATA IN THE ELECTRONIC HEALTH RECORD OF PEDIATRIC EYE CANCER PATIENTS

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**Background and Aims:** Social Determinants of Health (SDOH) have been shown to significantly influence the development and treatment of cancer outcomes. We aimed to (i) determine the availability of SDOH data in the electronic health record of eye cancer patients managed at The Hospital for Sick Children (SickKids) and (ii) characterize the population by SDOH.

**Methods:** This was a retrospective cohort study between 1 June 2018 and 23 May 2022. Study subjects were eligible if they: (i) were diagnosed with eye cancer; (ii) primarily managed at SickKids; and (iii) resided in Ontario. Data collected included: sex, birthdate, ethnicity, preferred language, need for interpreter, postal code, public insurance status, and diagnosis (ICD-10-CM). Postal code was used to deduce neighborhood income quintile, geographic location, and urban/rural status. Data was analyzed using summary statistics.

**Results:** The study population consisted of 235 patients representing the following diagnoses: C69.2 Retinoblastoma (225/235, 95.7%), C69.4 Malignant neoplasms of ciliary body (1/235, 0.4%), C69.6 Malignant neoplasm of orbit (6/235, 2.6%), and C69.9 Malignant neoplasm: Eye, unspecified (3/235, 1.3%). Sex, birthdate, postal code and insurance were recorded for 99% of patients. Preferred language was documented for 93%. Ethnic group and need for language interpreter were available for 0%. The male: female ration was 1:1, and 39% were aged 5-13 years at the time of study. English was the most common preferred language (84%). The majority (99%) were registered with the Ontario Health Insurance Program, 89% resided in urban areas, and 44% resided in Central Ontario. The most common neighbourhood income quintile was the highest quintile (25%).

**Conclusions:** The documentation of SDOH for eye cancer patients was variable, with little attention paid to recording ethnicity, and need for language interpreter. This highlights the need to develop standard practices for collecting SDOH data to assemble complete data sets and eliminate barriers to data collection.

EP394/#1404 | Poster Topic: AS05 SIOP Scientific Program/AS05.i  
*Retinoblastoma*

#### ROAD TO DIAGNOSIS OF RETINOBLASTOMA –NEED TO CREATE AWARENESS FOR EARLY DIAGNOSIS. EXPERIENCE FROM A DEVELOPING COUNTRY

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**Background and Aims:** A strong disparity exists between the developed and developing countries in the stage at diagnosis and outcomes of children with retinoblastoma. We aimed to assess the duration of time lag between the onset of symptoms and the diagnosis of retinoblastoma.

**Methods:** This descriptive study enrolled 80 children with a diagnosis of retinoblastoma. Details regarding the presenting features and its duration were collected. The first person contacted after the presenting symptoms and the interval between the onset of symptoms and final diagnosis were collected.

**Results:** Among the 80, 53(66.3%) had unilateral disease and 27(33.8%) had bilateral retinoblastoma. Two of them were identified within 3 weeks of life by the parents. Leukocoria was the most common presentation in 58(72.5%) children. Symptoms of retinoblastoma were first picked up by parents in 65(81.3%) and only 3(3.8%) were picked up by the pediatricians during routine vaccination/review. Seven children (8.8%) had family history of retinoblastoma. None of the babies with positive family history of retinoblastoma underwent screening. Parental delay was seen in 25(31.3%) and physician delay was observed in 16 (20%) cases. Ophthalmologists were the first person to be contacted in 59 (73.8%) cases, of which only 10 children (12.5%) were diagnosed as retinoblastoma. The mean interval between onset of symptoms and the first visit to physician was 58 days and mean interval between onset of symptoms and final diagnosis was 96 days and mean interval between diagnosis and treatment initiation was 21 days. Forty-three children (53.8%) underwent enucleation. The age at presentation of symptoms and the first person of contact for symptoms had statistical significance with diagnostic delay.

**Conclusions:** National level awareness programs among community and health care providers for early diagnosis is required. Government and NGOs support is essential to provide the optimal care to save the vision of these children.

EP395/#1189 | Poster Topic: AS05 SIOP Scientific Program/AS05.i  
*Retinoblastoma*

#### RETINOBLASTOMA OVER THE YEARS: RETROSPECTIVE LOOK IN NUH

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**Background and Aims:** This is a retrospective study to review the outcome of children diagnosed and treated for retinoblastoma from January 2006 to December 2021 in the division of paediatric oncology. Over the years we have undertaken intraarterial chemotherapy administration. Only some of the patients are included in this study. We aim to report on the outcome of our patients by applying the new AJCC staging system.

**Methods:** DSRB approval was obtained. Patients listed in our division database were identified. Patients who received intraarterial chemotherapy but not under our service are not included. Information were taken from the electronic health records. Staging system were based on the IRSSS, IIRCS and AJCC.

**Results:** Forty one children were seen (age range 1-72 mos, median 14 mos). Sixty eyes were affected, bilateral (20) and unilateral (21). Clinical presentations were leukocoria (27), strabismus (10), redness (4), screening (2), proptosis (2), pain (2), buphthalmos (1), nystagmus (1), poor focus (1). Staging/Grouping: STage0=8; StageI=27; StageII=2; StageIII=0; StageIVa=3; StageIVb=1. Intraocular Groups: A=4; B=11; C=3; D=16; E=18. Thirty-four eyes were enucleated (primary 16, secondary18). Of ten primary, intraocular grouping: D=2; E=8. AJCC: cTb1=1; cT2a=1; cT2b=2; cT3C=3; cT3e=1; cT4a=1. Six had high-risk histopathologic features. One died. Twenty six eyes were preserved. Intraocular grouping: A=4; B=10; C=3; D=5; unknown=2; AJCC T1a=12; T1b=5; T3c=1; T2b=6. Chemotherapy were systemic (n=22); intraarterial (3); combined (n=1). Two died from progressive disease and sepsis. Eighteen eyes had secondary enucleation. Clinical grouping: D=9; E=7; unknown=1. Clinical grouping: D=9; E=7; unknown=1. AJCC: cT2a=5; cT2b=4; cT3a=1; cT3b=1; cT3c=5; cTx=1. Two had recurrence. Eyes saved following chemoreduction: Group A=4/4(100%); B=10/11(91%); C=3/3(100%); D=5/16(31%); E=0(0/18). Adverse events following systemic chemotherapy: neutropenia, thrombocytopenia, fever, bacteremia, septic death (1); hearing loss and hypomagnesemia.

**Conclusions:** Globe salvage is possible with early detection. Advanced disease at presentation remains a challenge.

EP396/#1806 | Poster Topic: AS05 SIOP Scientific Program/AS05.i Retinoblastoma

#### BARRIERS AND FACILITATORS TO IMPLEMENTING RED REFLEX TEST GUIDELINES FOR RETINOBLASTOMA DIAGNOSIS AS DETERMINED BY PATIENTS, HEALTHCARE PROVIDERS AND RESEARCHERS

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**Background and Aims:** The top retinoblastoma research priority in Canada - as established by patients, healthcare providers and researchers - is early diagnosis. The red reflex test (RRT) is a simple ubiquitous procedure for the early diagnosis of ophthalmological conditions, including retinoblastoma. While effective, a false negative RRT may delay diagnosis, resulting in irreversible vision loss or death. There is a paucity of information about what constitutes a gold standard RRT which we addressed elsewhere in a systematic review. The purpose of this project was to uncover potential facilitators and barriers to implementing RRT guidelines for retinoblastoma diagnosis.

**Methods:** A hybrid workshop for retinoblastoma patients, health professionals and researchers was organized and led by 7 meeting facilitators. The three-part workshop consisted of (i) listening to stories of retinoblastoma patients complicated by delayed diagnosis; (ii) sharing preliminary findings from the systematic review of RRT procedures; and (iii) participating in a facilitated group discussion about the facilitators and barriers for implementing RRT guidelines. Ideas were recorded during the workshop and later organized by theme and content

**Results:** The workshop was attended by 13 patients (2 online, 11 in person) and 12 non-patients (healthcare providers and researchers; 6 online, 6 in person). Attendees asserted that implementation of a RRT guideline would be enhanced by; (i) empowering families to advocate for RRTs and (ii) timely education about the importance of RRTs and the RRT guidelines. Barriers to implementation of RRT guidelines identified by attendees included (i) inconsistent use and interpretation of RRT by primary care physicians; and (iii) unavailability of RRT during virtual appointments.

**Conclusions:** Implementation of RRT guidelines may be enhanced by empowering patient families and creation of an educational tool for primary care physicians and patient families alike.

EP397/#1532 | Poster Topic: AS05 SIOP Scientific Program/AS05.i Retinoblastoma

#### GENDER BIAS AND TREATMENT ADHERENCE BEHIND THE POOR OUTCOME OF RETINOBLASTOMA IN A LOWER-MIDDLE INCOME COUNTRY: A 5-YEAR ANALYSIS OF SOCIAL FACTORS

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**Background and Aims:** Multiple socio-economic factors affect the outcome of pediatric cancers. Care of retinoblastoma patients in lower-middle income countries (LMICs) lags behind high-income countries. Objective of this study was to identify the socio-economic factors contributing to the outcome of retinoblastoma patients in a large Indian center.

**Methods:** This was a retrospective study that included all retinoblastoma patients diagnosed at our center between year 2017-2021. Data were collected from hospital records regarding the age, gender, presenting symptoms, lag time, number of siblings, family income, education and prior contact with healthcare. Outcome parameters like survival and regularity of survivorship follow ups were documented. Patients lost to follow up were contacted telephonically to document important outcome measures.

**Results:** Total 382 patients were enrolled. While 59.6% had unilateral retinoblastoma, 40% had it bilaterally and 46.6% patients had extraocular disease. There was significant difference between lag time of unilateral vs bilateral disease (6 vs 4 months,  $p < 0.05$ ). Females had delayed presentation than males (6.5 vs 4 months,  $p < 0.05$ ). While 86.3% patients had leukocoria, 23.5% presented with proptosis. Baseline CNS metastasis was present in 8.9% patients, while 2.6% had bony or marrow metastasis. In a median follow-up time of 3.5 years, 32.9% of patients were lost to follow-up. After telephonic tracking of the entire cohort including the lost to follow ups, 30.9% patients had died. Female patients were more likely to be lost to follow up ( $\chi^2 = 9.1$ ,  $p = 0.002$ ) and there was higher probability of death in the lost to follow-up cohort ( $\chi^2 = 30.9$ ,  $p = 0.0001$ ).

**Conclusions:** While a large number of patients present with extraocular and metastatic disease, even in intraocular disease treatment adherence remains a challenge in LMICs. We highlight the significant gender related delay in presentation and loss to follow up in girls with retinoblastoma in our setting that further adds to the already poor overall outcome.

EP398/#704 | Poster Topic: AS05 SIOP Scientific Program/AS05.i Retinoblastoma

#### ENROLLMENT AND PATIENT PREFERENCES IN PARTICIPATION IN A RARE PEDIATRIC EYE CANCER BIOBANK

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**Background and Aims:** Biobanking holds potential to transform poor outcomes of rare pediatric eye cancers (R-PECs), which are neoplastic lesions of the retina, choroid, orbit, iris, eyelid, conjunctiva, and optic nerve. A biobank dedicated to R-PECs was developed as an arm of a pediatric ophthalmology biobank at The Hospital for Sick Children (Toronto, Canada) to house a large number of specimens and associated data. We aimed to describe the enrollment and preferences of participants in the R-PEC biobank.

**Methods:** Eligible patients included those diagnosed with a R-PEC who, due to standard of care, had a specimen extracted not required for clinical purposes or underwent significant imaging. A broad informed consent model was utilized, allowing storage of specimens and data for future use in unspecified research; patients were provided with the option to opt-out of specific research components. With patient/substitute-decision-maker informed consent, specimens and associated clinical data were collected and stored.

**Results:** From June 2020 to February 2023, 57 patients were approached for study participation, and 52 provided written informed consent (91% consent rate). Of consented participants: 69% agreed to research by industry, 94% to genome sequencing research, 88% to development of organoids/cell lines, 90% wished to be informed of carrier status, and 77% agreed to future research contact. Specimens were contributed by 71% of participants. Participants covered six diagnoses (retinoblastoma, angiolymphoid hyperplasia with eosinophilia, juxtapapillary retinal capillary hemangioblastoma, optic nerve glioma, retinal astrocytic hamartoma, rhabdomyosarcoma) and contributed 90 aliquots (including tumour, vitreous humour, and aqueous humour).

**Conclusions:** Understanding patient preferences and perspectives towards aspects of research may help us tailor communications and catalyze high impact research aligned with patient interests. Future steps include onboarding partner sites to increase enrollment, collection of bioimages, generation of additional resources such as tumour organoids, and promotion of the biobank to scientists to stimulate use of available resources.

EP399/#23 | Poster Topic: AS05 SIOP Scientific Program/AS05.i Retinoblastoma

#### "IT'S NOT MEANT TO BE FOR LIFE, BUT IT CARRIES ON": A QUALITATIVE INVESTIGATION INTO THE PSYCHOSOCIAL IMPACT OF RETINOBLASTOMA

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**Background and Aims:** Retinoblastoma (Rb) is a rare cancer of the retina diagnosed in ~50 children in the UK annually, with 45% of cases due to hereditary factors. Whilst highly curable, Rb can have huge

impact on the wellbeing of individuals long after remission. Existing research has highlighted the need for psychosocial support in this population, however the nature of this is under-researched and largely unavailable. This qualitative study aimed to explore living beyond Rb and challenges that may be faced as a result.

**Methods:** Between June 2022 and January 2023, we conducted focus groups with 15 teenagers (13-19 years) and interviews with 17 young adults (TYA; 20-29 years) with a history of Rb. A narrative approach explored life-stories of individuals and aimed to gain clear understanding of transition to adulthood, seeking views on challenges experienced and current psychosocial support they access or felt could be beneficial. Analysis used reflexive thematic analysis.

**Results:** TYA discussed increased anxiety, both related to social needs and health. This included concerns about second cancers, body image, and passing on Rb genes to future children. For many, they internalised Rb and the domination of this on their identity. There was also a focus on a lack of targeted psychological support, and the need for education amongst others about the long-term impact of childhood cancer.

**Conclusions:** TYA who have had Rb are at increased risk of anxiety and identity-related distress. This is particularly apparent for those with the hereditary variant, as well as those who were treated with enucleation and therefore have a visible difference that others can detect. There is a high need for targeted Rb psychosocial support, which is supported by existing evidence and supports our plan to develop a novel psychoeducation intervention for this population.

EP400/#143 | Poster Topic: AS05 SIOP Scientific Program/AS05.i  
*Retinoblastoma*

#### NON-METASTATIC EXTRA-OCULAR RETINOBLASTOMA: OUTCOMES OF MULTIMODAL THERAPY

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**Background and Aims:** This study aims to evaluate the treatment and the impact of histopathological features after neoadjuvant chemotherapy on the outcomes of children with extra-ocular retinoblastoma.

**Methods:** Patients with non-metastatic extra-ocular retinoblastoma corresponding to International Retinoblastoma Staging System (IRSS) II and III registered between 2006 to 2021 were included in the

analysis. The demographic details, laterality, clinical presentation, preoperative treatment, surgery, histopathology, chemotherapy, radiotherapy, and outcomes were reviewed.

**Results:** Eighty-four patients amounting to 18.2% of all registered patients with retinoblastoma, were seen in the study period. Propolis or fungating mass was present in 48% at presentation. IRSS II disease was observed in 14 patients, IIIa in 69, and IIIb in 1 patient. Sixteen patients did not pursue treatment, and 68 were offered standard multimodal treatment. Forty-six patients received neoadjuvant chemotherapy, while 22 underwent upfront surgery. Disease progression while receiving treatment occurred in 28%; all had IRSS III disease. Progressions were more common after surgery (74%) than while receiving neoadjuvant chemotherapy (26%)  $p=0.004$ . Early relapses occurred in 28% at a median of 2 months from the completion of therapy and 11 months from diagnosis. More than 50% of the patients had died within one year of diagnosis. The 5-year EFS and OS are 45% and 48%, respectively. The EFS was better for stage II; however, it was not statistically significant (58.3% vs. 41.8%;  $p=0.2$ ). The presence of high-risk features on postchemotherapy histopathology was significantly associated with an inferior outcome (37.6% vs. 74.3%;  $p=0.01$ ). Massive choroid invasion (26.7% vs. 63.6%;  $p=0.02$ ) and PLONI (31.3% vs. 57.2%;  $p=0.04$ ) notably had poor EFS.

**Conclusions:** Extra-ocular retinoblastoma is an aggressive disease marked by disease progression while on treatment and early relapses after completion of therapy. PLONI and massive choroidal invasion are high-risk features associated with inferior outcomes.

EP401/#512 | Poster Topic: AS05 SIOP Scientific Program/AS05.i  
*Retinoblastoma*

#### THE RETINOBLASTOMA JOURNEY MAP: A PATIENT-CENTRED PATHWAY OF CARE

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**Background and Aims:** Retinoblastoma treatment is complex, and the treatment and follow-up plan for each patient may differ. Pathways of care have been shown to enhance quality of care, improve patient outcomes, promote patient safety, increase patient satisfaction, and optimize the use of healthcare resources. This study describes the process of co-designing, with patient families, a pathway of care called the "Retinoblastoma Journey Map", and its evaluation among a pilot group of parents of newly diagnosed patients.

**Methods:** Human-centred design was utilized to ideate, prototype and refine the Retinoblastoma Journey Map. Parents of children newly diagnosed with retinoblastoma were recruited to use and evaluate the Retinoblastoma Journey Map alongside their clinical management. Mixed-methods data was collected on feasibility, acceptability, usability and perceived impact on communication, self-efficacy, anxiety, depression and quality of physician-patient interaction.

**Results:** The Retinoblastoma Journey Map was created to include set of 25 stickers covering 3 themes: clinical treatment (13), medical education (1) and milestones (11). The Retinoblastoma Journey Map was piloted with 12 families and found to be feasible, acceptable and usable. No significant effect on communication, self-efficacy, anxiety, depression or quality of patient-physician interaction was observed. Participant discussions and written feedback resulted in the identification of 6 themes: (i) Primary Use of the Map; (ii) Challenges Using the Map; (iii) Perceived Impact of the Map; (iv) Perceived Limitations of the Map; (v) Feasibility, Acceptability and Usability; and (vi) Unmet Needs.

**Conclusions:** Following a patient-identified research priority aiming to improve knowledge, a pathway of care for retinoblastoma was co-created with researchers, health professionals and patients. While the anticipated effects on communication and patient-physician interaction were not observed, a new use 'legacy building' came out of the evaluation. Patients identified that this important impact of the map, allowing families to document the pathway of care and educate their child at a later date.

EP402/#1157 | Poster Topic: AS05 SIOP Scientific Program/AS05.i Retinoblastoma

#### A MATHEMATICAL MODEL TO UNDERSTAND RETINOBLASTOMA CONSIDERING THE CLOSEST GENETIC CIRCUITRY OF THE RB GENE AT EARLY STAGES AND ITS FEEDBACK WITH THE EPIGENETIC LANDSCAPE

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**Background and Aims:** Retinoblastoma is a pediatric malignancy caused by loss of function and biallelic inactivation of the RB gene. This loss of function reflects abnormal regulation in signaling pathways that alter the cell cycle, resistance to apoptosis, adhesion, division, and cell reprogramming.

**Methods:** It is important to know the functioning of the RB gene with the closest genetic circuit of the E2F and TGF- $\beta$  genes, the cyclin-dependent kinases E/Cdk-2 and D/Cdk4-6, as well as the non-coding RNA miR17~92 for understanding the origin and prognosis of tumorigenesis.

**Results:** In this direction, we propose a mathematical model to describe the attractor states and cell lineage that underlie the prereplicative

stage of the cell cycle using the closest genetic circuit of the gene RB. The results of our model show that the dynamics for cell development and differentiation correspond to different basins of attraction in the epigenetic landscape.

**Conclusions:** In conclusion, cell lineage emerges as a dynamic evolution from undifferentiated to differentiated basins of attraction in different cell types.

EP403/#1565 | Poster Topic: AS05 SIOP Scientific Program/AS05.i Retinoblastoma

#### GLOBE SALVAGE IN ADVANCED INTRAOCULAR RETINOBLASTOMA: NO BENEFIT OF HIGH DOSE CARBOPLATIN-ETOPOSIDE-VINCRIStINE AND SUBSEQUENT CHEMOTHERAPY INTENSIFICATION - A RETROSPECTIVE ANALYSIS OF 300 EYES

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**Background and Aims:** Globe salvage is a priority in the treatment of retinoblastoma. In countries where patients present at advanced stages, the optimal first line therapy has not been defined. We examine the utility of high dose Carboplatin-Etoposide-Vincristine (CEV) for globe salvage in advanced intraocular retinoblastoma (IORB).

**Methods:** A retrospective analysis was carried out on all patients of advanced (group D and E) IORB enrolled in a 5-year period. Details of chemotherapy regimen, globe salvage, histopathology, intra-arterial chemotherapy, toxicity and treatment outcome were gathered, along with socio demographic data. Telephonic interview was performed for patients who were lost to follow up.

**Results:** Of 200 patients enrolled, with 300 involved eyes, group D and E made up 39% and 53% of the eyes respectively. Globe salvage was achieved in 68% of Group D eyes. Of those Group E eyes in which globe salvage was attempted, 37% were successful. No significant difference was found between globe salvage rates with standard dose CEV and high dose CEV (59% vs 55%  $p = 0.7$ ) or average number of cycles given in these two groups to achieve globe salvage (6.8 vs 7.4,  $p = 0.49$ ). If response was suboptimal, chemotherapy was intensified sequentially (standard dose CEV to high dose CEV followed by augmentation with Cyclophosphamide and Doxorubicin), this was found to have no significant difference in globe salvage compared to continuation of baseline chemotherapy (53% vs 56%  $p = 0.8$ ).

**Conclusions:** In this study, high dose CEV does not appear to offer any benefit over standard dose CEV in globe salvage in group D and

E retinoblastoma. Considering the incidence of toxicity as well as the cost and extra hospital visits for administration of growth factor when giving high dose or augmented chemotherapy, reexamination of the need for chemotherapy intensification in these patients should be considered.

EP404/#1720 | Poster Topic: AS05 SIOP Scientific Program/AS05.i Retinoblastoma

#### FEASIBILITY AND SAFETY OF VINCRIStINE, TOPOTECAN AND CARBOPLATIN CHEMOTHERAPY IN CHILDREN WITH RETINOBLASTOMA - OBSERVATION FROM A TERTIARY CANCER CENTRE FROM LOW-MIDDLE INCOME COUNTRY

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**Background and Aims:** Most widely used systemic chemotherapy regimen for retinoblastoma involves combination of vincristine, etoposide and carboplatin. Etoposide is associated with increased risk of secondary malignancies. Topotecan based regimens have been found to be effective for patients with advanced intraocular retinoblastoma. In our study, we assessed safety and feasibility of vincristine, topotecan and carboplatin (VTC) regimen in children with Retinoblastoma.

**Methods:** We collected data of 17 children, (25 eyes) with retinoblastoma, treated with VTC (Vincristine: 1.5 mg/m<sup>2</sup>/dx1, Topotecan: 1.5 mg/m<sup>2</sup>/dx5, Carboplatin: 450 mg/m<sup>2</sup>/dayx1) regimen at a tertiary cancer center in India, between March 2022 and November 2022. The clinical details and toxicities for each patient were noted.

**Results:** Male and female ratio was 1.8:1. Median age at presentation was 30.5 months (IQR- 12 to 47 months). Positive family history was present in 11.7% (n=2). Nine (52.9%) children had unilateral disease. Stage 0, I, II, III, and IV disease was seen in two (14.28%), three (28.57%), two (21.4%), and five (35.7%) and zero children respectively. Two (8%), three (12%), two (8%), two (8%) and sixteen (64%) eyes had group A, B, C, D, and E disease respectively. Enucleation was carried out for 40% cases (n=10). High-risk features on histopathology were present in 80% (n=8) of enucleated eyes. VTC was given as a second-line regimen in 5 (36.7%) children. None of the children with group A, B, or C disease required enucleation. Anemia and thrombocytopenia (≥grade 3) were the most common complication observed in 40% (n=10) patients. Other grade 3 or more toxicities were neutropenia (28%, n=7), febrile neutropenia (28%, n=7), enterocolitis (17.6%, n=3), and sepsis (11.8%, n=2). One child (7.1%) died during treatment.

**Conclusions:** Topotecan-based regimens can be used to eschew etoposide-associated secondary malignancies. The toxicities associated with the regimen in our study were mainly associated with myelosuppression and manageable in most cases.

EP405/#396 | Poster Topic: AS05 SIOP Scientific Program/AS05.i Retinoblastoma

#### THE CLINICAL AND GENETIC CHARACTERISTICS OF RETINOBLASTOMA PATIENTS IN A SINGLE CENTER WITH FOUR NOVEL RB1 VARIANTS

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**Background and Aims:** The goal of this study is to assess the clinical and genetic characteristics of children diagnosed with retinoblastoma.

**Methods:** All cases diagnosed with RB and received treatment and follow-up on the Ophthalmology and Pediatric Oncology Department, October 2016 to May 2021 were evaluated retrospectively. The RB1 gene was analyzed by next generation sequencing (NGS) technique in DNAs obtained from peripheral blood samples of the patients.

**Results:** The mean age was 24.6 (median: 18.5, range: 3–151) months. There were 15 (22.3%) Group D eyes and 39 (58.2%) Group E eyes. The RB1 gene was sequenced by the NGS method in 19 patients. Heterozygous RB1:NM\_000321.3: c.54\_76del (p.Glu19AlafsTer4) variant was detected in a 15-month-old female with bilateral RB. Heterozygous RB1:NM\_000321.3:c.1814+3A>T variant was detected in a 5.5-month-old male with bilateral RB. The intronic RB1:NM\_000321.3:c.1332+4A>G variant was detected in pt 14, a 13-month-old male with unilateral RB. The RB1:NM\_000321.3: c.575\_576del p.Lys192SerfsTer10 variant was found in an 18-month-old female with an allele frequency of 37%. These variants have not been reported in the literature and mutation databases. The mean follow-up was 38.5±34.7 (range: 1–149) months. After eye-conserving treatments, secondary enucleation in 14 eyes (20.8%). The globe salvage rate was 86.6% in group D (13 of 15 eyes), and 30.7% in group E (12 of 39 eyes).

**Conclusions:** In our study 80% of the study patients were groups E and D. Currently, retinoblastomas are diagnosed in late stages in our region. We describe four novel variants and one of them was found in two different patients. This data is very important for assessing prognosis. It serves as a guide for estimating the long-term risk of secondary malignancy as well as the short-term risk of developing additional malignancies in the same eye and the other eye.

EP406/#661 | Poster Topic: AS05 SIOP Scientific Program/AS05.j Liver Tumours

#### INCREASED SURVIVAL IN CHILDREN WITH MALIGNANT LIVER TUMORS IN DENMARK 1985-2020

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**Background and Aims:** Malignant liver tumors in children are rare and national outcomes for this group are rarely reported. This study mapped the paediatric liver tumors in Denmark from 1985 through 2020 and reports on incidence, outcome and long-term adverse events. **Methods:** We identified all paediatric malignant liver tumors from the Danish Childhood Cancer and National Pathology Registries and reviewed the case records for patient and tumor characteristics, treatment and clinical outcome.

**Results:** We included 79 patients with malignant liver tumors in the analyses; Overall crude incidence was ~2.29 per 1 million children (<15y) per year, with 61 hepatoblastomas, 9 hepatocellular carcinomas and 9 other hepatic tumors. Overall, 5 y survival was 84%, 78% and 44% respectively. For hepatoblastomas, age > 8 y and diagnosis before year 2000 were statistical significant predictors of a poorer outcome. Liver transplantation was performed in 16% of the cases with an overall survival of 80% compared to 84% for patients receiving surgery. Adverse events were: Reduced renal function in 12% (GFR<90), reduced cardiac function in 7% (EF<55) and impaired hearing function in 48% (Boston 2-4).

**Conclusions:** Survival for hepatoblastomas in Denmark is increasing and comparable with international results. Stratifying treatment factors in current protocols were confirmed to be significant in the Danish cohort. Hearing loss is the major treatment related side effect and affects about 50% of the patients.

EP407/#1170 | Poster Topic: AS05 SIOP Scientific Program/AS05.j Liver Tumours

#### OUTCOME OF A NATIONWIDE MULTICENTER PHASE II CLINICAL TRIAL FOR LOCALIZED HEPATOBLASTOMA: REPORT FROM JAPAN CHILDREN'S CANCER GROUP LIVER TUMOR COMMITTEE TRIAL, JPLT3-S,I

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**Background and Aims:** Complete resection of the primary tumor is essential for survival of patients with hepatoblastoma (HB). In our previous trial JPLT-2, the outcome of patients with unresectable tumors was still unsatisfactory. We considered that these patients may benefit from chemotherapy given in a timely manner and surgeries including liver transplantation (LTx) performed at optimal timings. We designed a trial (JPLT3-I) for intermediate risk (IR) HBs with central pathology, radiology, and surgical review to facilitate accurate diagnosis and early referral of patients requiring LTx. For standard risk (SR) HBs, we evaluated the feasibility of cisplatin monotherapy (JPLT3-S).

**Methods:** IR was defined as non-metastatic tumors with AFP≥100 ng/ml meeting either of: (1) PRETEXT IV (2) positive PRETEXT annotation factors (E,F,H,M,N,P,V) (4) age >3 years. SR consisted of all other non-metastatic tumors. SR patients were treated with 6 cycles of cisplatin monotherapy. IR patients were treated with 6 cycles of cisplatin/doxorubicin (PLADO).

**Results:** Between January 2013 to December 2018, 39 SR and 33 IR eligible patients were enrolled. The 3-year event-free survival for SR and IR were 97.6% and 78.6%, respectively. 3-year overall survival were 100% (SR) and 88.9% (IR). In SR patients, response to preoperative cisplatin was PR in 83%, SD in 14%, and PD in 3%. IR patients achieved PR in 91%, SD in 6%, and PD in 3% in response to preoperative PLADO. Microscopic resection of the liver tumor was achieved in 97% of SR and 94% of IR. These included 5 primary LTxs. Progression and relapse tended to occur in relatively older patients or patients whose tumors have unfavorable features (i.e., HCN-NOS)

**Conclusions:** Treatment results of the JPLT3-S,I study improved from the JPLT-2 study and were comparable to those from other international clinical trials. PLADO seemed to be sufficient for a majority of IR. Cases with unfavorable features may need different strategies.

EP408/#300 | Poster Topic: AS05 SIOP Scientific Program/AS05.j  
Liver Tumours

### CORRELATION ANALYSIS OF THE EFFECT OF VENOUS TUMOR THROMBUS ON THE PROGNOSIS OF 279 CHILDREN WITH HEPATOBLASTOMA

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**Background and Aims:** To study the characteristics of imaging diagnosis and histopathological diagnosis combined with tumor thrombus in children with hepatoblastoma and its influence on prognosis.

**Methods:** 279 HB patients were collected in the pediatric of Beijing Tongren Hospital from Jan 2009 to Jan 2019. The group of HB cases with tumor thrombus was as the study group. To collect clinical data of HB for comprehensive diagnosis and treatment. SPSS software was used to analyze the correlation between age, pathological classification, AFP, tumor rupture, immunohistochemistry and tumor thrombus formation, diagnosis and treatment strategy and prognosis.

**Results:** There were 137 cases of tumor thrombus group and 142 cases of non-tumor thrombus group in this group. 171 vs 107 of male vs female. The median age was 1.95-y old. 2.2%. There were 5 cases (1.8%) in the low-risk group, 91 cases (33.7%) in the medium-risk group, and 183 cases (64.5%) in the high-risk group. The median follow-up time was 47 months, 79 cases died (28.3%), 200 cases survived (71.7%), 43.1% (59/137) in the tumor thrombus group, and 14.1% (20/142) in the control group. The 3-y OS was 51.8% and the 3-y DFS was 38.0% in the tumor thrombus group; In the control group, the 3-y OS was 73.2%, and the 5-y DFS was 49.3%.  $P < 0.001$  (survival prognosis of study group vs control group). There was a statistically significant difference of OS and DFS between the tumor thrombus groups. The risk of death in the tumor thrombus group was higher than that in the non-tumor thrombus group. The risk of metastasis in tumor thrombus group was higher than that in control group ( $P < 0.05$ ).

**Conclusions:** In this study, the age of onset and Ki-67 expression level are independent risk factors affecting the incidence of tumor thrombus. Age of onset, intrahepatic metastasis, distant metastasis and tumor thrombus are independent risk factors affecting the prognosis of HB children.

EP409/#407 | Poster Topic: AS05 SIOP Scientific Program/AS05.j  
Liver Tumours

### RELATIONSHIP BETWEEN THE SERUM LEVELS OF ALPHA-FETOPROTEIN AT THE END OF TREATMENT AND THE PROGNOSIS IN PATIENTS WITH HEPATOBLASTOMA

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**Background and Aims:** New prognostic factors need to be explored to further improve the individualized treatment in patients with hepatoblastoma (HB). This study is to determine the relationship between the serum level of alpha-fetoprotein (AFP) at the end of treatment and the prognosis in patients with HB.

**Methods:** Retrospective studies were conducted in consecutive patients who had finished the first-line therapy without progression. The patients at very low risk underwent surgery only. The patients at low risk underwent surgery followed by C5V (cisplatin+5-fluorouracil+vincristine) chemotherapy. The patients at intermediate risk received chemotherapy with C5VD (CSV plus doxorubicin) and surgery. The patients at high risk received chemotherapy with C5VD alternating with IIV (Ifoshamide+Irinotecan+Vincristine) and surgery. Peripheral serum levels of AFP of the patients were detected at different time points.

**Results:** A total of 72 patients were included in the study. There were 2, 14, 25, and 31 patients in very low, low, intermediate, and high risk groups. At the end of first-line treatment, 46 patients (63.9%) had serum levels of AFP  $\leq 10$ ng/ml, and 55 patients (76.4%) achieved complete remission (CR). Compared to the patients with AFP  $> 10$ ng/ml at the end of first-line treatment, patients with AFP  $\leq 10$ ng/ml had significant lower recurrence rate (15.2% vs. 65.4%), better three-year event-free survival (3yr-EFS) rates (80.7% vs. 31.4%) and overall survival (OS) rate (96.6% vs. 63.0%). In patients achieving CR, the 3yr-EFS and OS rates were higher among those with AFP  $\leq 10$ ng/ml than AFP  $> 10$ ng/ml. In patients without CR, the 3yr-OS rate was higher in patients with AFP  $\leq 10$ ng/ml than AFP  $> 10$ ng/ml. The multivariate analysis indicated that serum AFP  $> 10$ ng/ml at the end of first-line treatment was an independent prognostic predictor.

**Conclusions:** The prognosis of HB patients with serum AFP  $> 10$ ng/ml at the end of first-line treatment is dismal and treatment should be reinforced.

EP410/#1039 | Poster Topic: AS05 SIOP Scientific Program/AS05.k  
Germ Cell Tumours

### DELAYED DIAGNOSIS OF SACROCCYGEAL GERM CELL TUMORS: CLINICAL CHARACTERISTICS AND CHALLENGING MANAGEMENT

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**Background and Aims:** Sacrococcygeal germ cell tumors (SGCTs) include mature and immature teratomas, yolk sac tumors, and other malignant tumors. They are considered as a neonatal surgical

emergency because of their high potential for malignant transformation if diagnosed after the age of two months. The aim of our study was to assess the impact of late management in SGCTs on their oncological and functional prognoses.

**Methods:** This was a descriptive, retrospective study realised in our pediatric surgery department over a period of 10 years (October 2010–October 2020). It included all SGCTs diagnosed after the age of two months.

**Results:** We collected 6 cases of SGCTs with a delayed diagnosis. The sex ratio was 0.2. The mean age of the patients at diagnosis was 14.7 months (3 months – 24 months). Only one case had prenatal diagnosis. The absence of an obvious mass at birth was noticed in five cases. Most presenting symptoms are due to the mass effects of the tumor (4 cases). Digital rectal examination shows the presence of presacral mass in all cases. An elevated serum value of alpha-feto protein was found in half of the cases. Metastases at diagnosis were identified in three patients. Radiological and biological features were in favour of malignant germ cell tumors in three cases and mature teratomas in the other three cases. Three patients underwent chemotherapy preoperatively. Surgery was performed in five patients. Pathological examination revealed four mature teratomas and one yolk sac tumor. A sacrococcygeal yolk sac tumor was found after recurrence of benign teratoma. Urinary retention was reported in two patients after surgery. The mortality was 16.7%.

**Conclusions:** Early diagnosis in SGCTs is associated with better prognosis. The incidence of malignancy increases if resection is delayed; worsening the prognosis even though survival rate in malignant tumor has been improved by recent chemotherapy.

EP411/#1229 | Poster Topic: AS05 SIOP Scientific Program/AS05.k Germ Cell Tumours

#### INCIDENCE AND PREDICTORS FOR ONCOLOGIC ETIOLOGY IN CHINESE CHILDREN WITH PITUITARY STALK THICKENING

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**Background and Aims:** With increasing use of magnetic resonance imaging (MRI) in evaluation of children with endocrine disorders, pituitary stalk thickening (PST) poses a clinical conundrum due the

potential for underlying neoplasm and challenges in obtaining tissue biopsy. Existing literature suggested Langerhans cell histiocytosis (LCH) to be the commonest (16%) oncologic cause for PST, followed by germ cell tumors (GCTs, 13%) (CCLG 2021). As cancer epidemiology varies according to ethnicity, we present herein the incidence and predictors for oncologic etiologies in Hong Kong Chinese children with PST.

**Methods:** Based on a territory-wide electronic database, we reviewed patients <19 years who presented with endocrinopathies to three referral units between 2010 and 2022. Records for patients who underwent at least one MRI brain/pituitary were examined (n=1670): those with PST (stalk thickness  $\geq 3.5$ mm) were included, while patients with pre-existing cancer, other CNS and extra-CNS disease foci were excluded.

**Results:** Twenty-eight patients (M:F=10:18) were identified. Median age at diagnosis of PST was 10.9 years (range: 3.8–16.5), with central diabetes insipidus (CDI) and precocious puberty being the most frequent presenting endocrine disorders. At median follow-up of 4.7 years, oncologic diagnoses were made in 14 patients (50%), including 13 GCTs (46%; germinoma=11, non-germinoma=2), and one LCH (4%). Among patients with GCT, 10 were diagnosed based on histology, two by abnormal tumor markers, and one by combination of histology and markers. Three patients with germinoma were initially misdiagnosed as hypophysitis/LCH. Cumulative incidence for oncologic diagnosis was significantly higher in boys, patients with PST  $\geq 6.5$ mm, CDI or  $\geq 2$  pituitary hormone deficiencies at presentation, and evolving hypopituitarism (all  $p < 0.05$  by log-rank).

**Conclusions:** Higher rate of GCT was observed in Chinese children with endocrinopathy and isolated PST. Predictors identified may guide healthcare providers in Asia on clinical decision-making. Serial measurement of tumor marker is essential in management.

EP412/#649 | Poster Topic: AS05 SIOP Scientific Program/AS05.k Germ Cell Tumours

#### OUTCOME ANALYSIS OF EXTRA-CRANIAL MALIGNANT GERM CELL TUMORS IN CHILDREN AND ADOLESCENTS: A SINGLE CENTER EXPERIENCE FROM INDIA

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**Background and Aims:** Pediatric germ cell tumors (GCT) are chemosensitive tumors associated with excellent outcomes, even in stage IV disease. However, the results in low-middle-income countries (LMIC) are less than satisfactory for various reasons. We aim to study the clinicopathological features and treatment outcomes of children aged  $\leq 18$  years with extra-cranial malignant GCT.

**Methods:** Pertinent data of all the children with GCT from July 2016–February 2022 were collected from the hospital records retrospectively. Children's Oncology Group (COG) staging was used to classify GCTs. Children received chemotherapeutic regimens PEb or JEB (Etoposide, bleomycin with cisplatin/carboplatin, respectively) depending on age at diagnosis  $\geq 11$  years or  $< 11$  years, respectively. All the low-risk (LR) patients (completely excised teratomas and stage-I gonadal tumors) did not receive any other therapy, whereas high-risk (HR) (stage IV ovarian, stage III/IV extragonadal GCTs) and the remaining intermediate-risk (IR) patients received six and four cycles of chemotherapy, respectively.

**Results:** Thirty-eight children were analyzed with an equal male-to-female ratio and a median age of 2.1 years. The mean follow-up duration was 2.3 years. Mature teratoma was the commonest (12) diagnosis, followed by yolk sac tumor (YST) and MMGCT (mixed malignant GCT), seven equally. Extragonadal GCTs (22; 57.9%) were more common than gonadal GCTs (16; 42.1%), with retroperitoneum as the primary site in 9 (23.68%) children and ovary being the most frequent gonadal site in 10 (26.3%). We observed almost equal distribution of LR (13), IR (13), and HR (12) disease among the patients. Four patients relapsed, four expired (all disease-related), and 1 abandoned the treatment. The 3-year EFS and OS were 72.1% and 86.8%, respectively, with LR and IR ( $p=0.009$ ) being favorable prognostic factors.

**Conclusions:** The LR and IR GCTs had very good results in our study. However, the outcome in HR patients might be improved by adopting intensive therapeutic strategies and balancing treatment-related toxicities.

EP413/#1287 | Poster Topic: AS05 SIOP Scientific Program/AS05.k Germ Cell Tumours

#### CIRCULATING MIR-371A-3P ASSAY FOR DETECTING MALIGNANT GERM CELL TUMOURS: FURTHER PROGRESS TOWARDS CLINICAL ADOPTION

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**Background and Aims:** MicroRNAs (miRNAs/miR-) are short, non-protein-coding RNAs that are dysregulated in cancer. MiR-371a-3p, universally overexpressed in malignant germ-cell-tumours (GCTs), rep-

resents a highly promising circulating biomarker for GCT diagnosis and follow-up, regardless of patient age, tumour site, or subtype (seminoma/yolk-sac-tumour/embryonal carcinoma). We identified and developed a highly sensitive multiplexed pre-amplified qRT-PCR-based assay for its detection/quantification in biofluids. Here, we further characterise assay performance, including confirmation of an 'indeterminate' range, interlaboratory concordance, and age/gender comparisons in controls.

**Methods:** Serum from patients with malignant GCTs ( $n=44$ ) and without ( $n=31$ ; controls) was used for miRNA isolation, prior to multiplexed pre-amplified qRT-PCR. For some experiments, control serum was spiked with synthetic miR-371a-3p mimic, allowing use as a malignant GCT 'substitute'. For the baseline control study, three age groups were employed: 0-11 years (y; pre-pubertal;  $n=20$ ), 11-18y (peri-pubertal/adolescent;  $n=20$ ), 18-45y (adult;  $n=20$ ), with 10 males and 10 females in each group.

**Results:** The separate sample quality-control (QC) step described in the original protocol had no advantages compared with incorporation into a single multiplexed methodology, with appropriately revised PCR Cq thresholds utilised. Therefore, a revised multiplexed pre-amplified qRT-PCR protocol was established for both QC and diagnostic test, which gave highly concordant results in different laboratories (Cambridge, UK and UTSW, Dallas, US). Circulating miR-371a-3p levels were independent of sample haemolysis, and normalisation to the endogenous housekeeping miRNA miR-30b-5p shown to be unnecessary (although retained for QC), further simplifying the test. This allowed raw miR-371a-3p Cq levels to be used for quantification. A region of overlap between malignant GCT cases and controls, previously defined as the 'indeterminate range' (Cq 28-35), was further evidenced. In controls, there was no difference in circulating miR-371a-3p levels by age or gender.

**Conclusions:** A simplified protocol which reduces reagent/assay costs can be used for the detection of malignant GCTs, with no additional considerations for age/gender required.

EP414/#1263 | Poster Topic: AS05 SIOP Scientific Program/AS05.k Germ Cell Tumours

#### TESTICULAR GERM CELL TUMOUR CELLS RELEASE MICRORNA-CONTAINING EXTRACELLULAR VESICLES RESULTING IN PROMALIGNANT CHANGES IN CELLS OF THE TUMOUR MICROENVIRONMENT

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**Background and Aims:** MicroRNAs (miRNAs/miR-) are short, non-protein coding RNAs that are dysregulated in malignant germ cell tumours (GCTs), with universal over-expression of miR-371~373 and miR-302/367 clusters regardless of patient age, tumour site, or subtype (seminoma/yolk-sac-tumour/embryonal carcinoma). These miRNAs are released into the bloodstream, presumed via extracellular vesicles (EVs), and represent promising biomarkers. Here, we comprehensively examined the role of EVs, and their miRNA cargo, on (fibroblast/endothelial/macrophage) cells representative of the testicular GCT (TGCT) tumour microenvironment (TME).

**Methods:** Small RNA next generation sequencing was performed on 34 samples, comprising representative malignant GCT cell lines/EVs and controls [testis fibroblast (Hs1.Tes) cell-line/EVs and testis/ovary samples]. TME cells received TGCT-derived EV treatment, miRNA quantification by qRT-PCR, and a miRNA overexpression system (miR-371a-OE) to perform functional assays and assess mRNA changes.

**Results:** TGCT cells secreted EVs into culture media. MiR-371~373 and miR-302/367 cluster miRNAs were over-expressed in all TGCT cells/subtypes compared with control cells and were highly abundant in TGCT-derived EVs, with miR-371a-3p/miR-371a-5p the most abundant compared with normal EVs. Fluorescent labelling demonstrated TGCT-derived EVs were internalised by all TME cells. TME (fibroblast/endothelial) cell treatment with EVs derived from different TGCT subtypes resulted in increased miR-371~373 and miR-302/367 miRNA levels, and other generic (e.g., miR-205-5p/miR-148-3p), and subtype-specific (seminoma, e.g., miR-203a-3p; yolk-sac-tumour, e.g., miR-375-3p) miRNAs. MiR-371a-OE in TME cells resulted in increased collagen contraction (fibroblasts) and angiogenesis (endothelial cells), associated with dysregulation of mRNAs and relevant cellular pathways.

**Conclusions:** TGCT cells communicate with non-tumour stromal TME cells through release of EVs enriched in oncogenic miRNAs, likely contributing to tumour progression.

EP415/#736 | **Poster Topic: AS05 SIOP Scientific Program/AS05.k Germ Cell Tumours**

#### ONCOLOGIC AND ENDOCRINOLOGIC OUTCOME OF CHILDREN AND ADOLESCENTS WITH TESTICULAR AND OVARIAN SEX CORD STROMAL TUMORS

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**Background and Aims:** Sex cord stromal tumors (SCST) are hormonally active and rare. Aim is to describe their endocrinology presentation and outcome.

**Methods:** All patients (<19 years of age) included in the national TGM-13 registry between 2014 and 2021 were selected. Additional endocrinology data from three large centres were added. After primary resection, patients with ruptured, disseminated or incompletely resected SCST received chemotherapy.

**Results:** Seventy-eight patients, 63 ovarian and 15 testicular tumors, were included. Germline DICER1 pathogenic variant was present in 9/17 Sertoli-Leydig tumors. Sixty-one ovarian tumors (97%) were FIGO stage I. Adjuvant chemotherapy was delivered for 15 patients: 12 FIGO IC, 1 FIGO IX, 2 FIGO III. Seven had recurrence (3 FIGO IA, 2 FIGO IX, 2 FIGO III) leading to one death. Three-year progression-free survival is 89% (95% CI 76%-95%). Testicular tumors were TNM stage pSI (14 cases) or pSIIIA (1 case), eight had tumorectomy and seven total orchiectomy. None experienced recurrence. Forty-one patients (34 female, 7 male) had endocrinology data reviewed: 18 were pre-pubescent and 23 had an ongoing puberty or were pubescent at diagnostic. Endocrine disorders were initially present in 29/34 girls and 2/7 boys, and started to regress within two months after surgery for 27/28 patients with available data. At the end of the follow-up (with a median of 25 months post-diagnosis), 15/41 patients had endocrine abnormalities: gynecomastia persisted in 2 boys and in 2 prepubescent girls, 4/7 prepubescent girls at diagnosis presented precocious or advanced puberty during the follow-up, 8/21 pubescent girls had persistent hyperpilosity, menstruation disorders or hot flashes. Final height was in normal ranges [-1.7 SD: +2.3 SD] for all patients.

**Conclusions:** SCST carry a favourable prognosis. Tumorectomy appears safe in testicular primary. Endocrinology disorders, common at diagnosis, usually regress rapidly, but may persist thus justifying an endocrinology follow-up. Final height was not affected.

EP416/#579 | **Poster Topic: AS05 SIOP Scientific Program/AS05.k Germ Cell Tumours**

#### EVALUATE THE POST CHEMOTHERAPY RESPONSE IN PEDIATRIC OVARIAN GERM CELL TUMORS WITH CT SCAN

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**Background and Aims:** Background: Ovarian germ cell tumours (OGCTs) are rare pediatric tumours and histologically heterogeneous. The treatment approach for these tumours have evolved and surgery currently is the gold standard and upfront resection recommended for localised OGCT. Though upfront surgery achieves complete resection however in large size tumours, it is associated with undue morbidity. Neo-adjuvant chemotherapy is administered for tumours with peritoneal or omental deposits on baseline imaging. This study attempts to evaluate the response of chemotherapy on OGCT, and correlate it with the histologies. Aim: Evaluate the OGCT response to neo-adjuvant chemotherapy by CT scan and correlate with histology and tumour markers.

**Methods:** Retrospective study. Sample size: 25 cases Inclusion Criteria: The paediatric patients from birth till 15 years diagnosed as OGCT based on histopathology/imaging findings with raised tumour markers and imaging available in hospital database. Exclusion Criteria: Incomplete medical records or non-availability of digital DICOM CT images in hospital PACS.

**Results:** The largest tumour dimension in the baseline scan ranged from 24 cm to 5.3 cm, average -13.7cm, and the tumour volume ranged from 26cc to 4268 cc. Post chemotherapy the tumour size reduced, largest tumour dimension ranged from 22cm to 2cm, average - 8.1cm and the tumour volume ranged from 4.1cc to 3880cc. 16 Patient showed > 75% volume reduction, 4 patient showed 50 to 75 % volume reduction and 3 patient had 25 to 50 % and 3 had < 25 % volume reduction. The histology showing maximum responders were yolk sac tumour and dysgerminomas.

**Conclusions:** Significant tumour size reduction by neoadjuvant chemotherapy is achieved in dysgerminomas and yolk sac tumours. This may alter the management of localised large OGCT in future. The correlation of chemotherapy response with histology will help to predict the possible response and accordingly offer upfront surgery or neoadjuvant chemotherapy without undue morbidity.

EP417/#32 | Poster Topic: AS05 SIOP Scientific Program/AS05.k  
*Germ Cell Tumours*

#### THE PROGNOSTIC VALUE OF IMMUNOHISTOCHEMICAL STUDIES IN DIAGNOSIS AND TREATMENT OF OVARIAN GERM CELL TUMORS OF CHILDHOOD AND ADOLESCENCE

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**Background and Aims:** To study the effectiveness of immunohistochemical studies in diagnosis and tactics treatment of germ cell ovarian tumors of childhood and adolescence.

**Methods:** We observed 30 patients with malignant ovarian germ cell tumors. The diagnosis put by using standard, accepted methods of determination of tumor markers AFP, CA-125 and HCG. Of the 30 patients, 12 (52%) were aged 1 to 14, 18 (48%) of 15 to 18 years. All patients after operation was carried out immunohistochemical study with bcl-2 oncoprotein and p53 suppressor gene.

**Results:** Of the 30 (100%) in 6 patients (20%) was high expression of the oncoprotein bcl-2, 9 (30%) - moderately severe, 15 (50%) - was low expression. The study of tumor suppressor gene p53 revealed that in 8 (26.6%) patients had high expression, in 12 (40%) - moderately severe in 10 (33.3%) - was low expression. Conducted immunohistochemical studies have shown that in the group with high positive expression of bcl-2 and p53 had a more aggressive course of tumor process, followed in these patients revealed early recurrences and metastases, which required a more aggressive course of chemotherapy (6 to 8 courses by scheme BEP, PVB or VEP), and in the group with low or negative expression of p53 and bcl - 2 effective schemes and more sparing regimens (4 to 6 courses of BEP scheme, EP)

**Conclusions:** The performed immunohistochemical studies have shown that the definition of indicators oncoprotein bcl - 2 and the gene - the p53 tumor suppressor is not only diagnostic value but also has important prognostic and selection of treatment of ovarian germ cell tumors of childhood and adolescence

EP418/#580 | Poster Topic: AS05 SIOP Scientific Program/AS05.l  
*Rare Tumours and Histiocytosis*

#### CHALLENGES IN TREATING PEDIATRIC COLORECTAL CARCINOMA IN A LOW-MIDDLE-INCOME COUNTRY

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**Background and Aims:** Colorectal carcinoma is rare in young children globally. Moreover, there are limited treatment options and adequate surgical skills available in LMIC to manage these children presenting in the advanced stages of the disease. The aim of this study is to explore the challenges faced in treating these children in resource-limited settings.

**Methods:** A retrospective cohort study was conducted in the Pediatric Oncology department of UCHS & Children's Hospital Lahore Pakistan from January 2018 to December 2022 and the data was analyzed using SPSS 26.

**Results:** A total of 48 patients were included in this cohort with a mean age of 12.2 and median age of 13 years, and an M: F ratio of 2:1. The most common site was Rectosigmoid 73%, followed by rectum 17%, transverse colon 4%, ascending colon 4%, and jejunum 2%. 96% had high-grade pathology with 60% signet ring, 21% mucinous, and 19% adenocarcinoma. 27% of cases had distant Mets (liver, bone, lungs) and 41% regional dissemination. Palliation was advised at initial diagnosis in 23%, during treatment 27%, and not recommended in 50%. Among 50% offered treatment, 6% defaulted treatment, 17% were well, 14% expired and the rest relapsed. Surgery, chemotherapy followed by RT was given in 17%, surgery, and chemotherapy (FOLFOX6) in 42% and surgery alone in 11% and chemotherapy alone in 15%, and no Rx in 15% of cases. Biopsy was done via colonoscopy in 31%, true cut in 15%, and open laparotomy in 54%. 60% of these children presented with intestinal obstruction. Stomas were made in 52%. Genetic testing was not available in the hospital. Five children were associated with familial cancers/CMMRD.

**Conclusions:** Children with colonic cancer, presenting at advanced stages resulting in dismal survival emphasize the need for early diagnosis, timely referrals, improved surgical skills, and access to genetic testing for their better survival in LMIC.

EP419/#1206 | Poster Topic: AS05 SIOP Scientific Program/AS05.I  
*Rare Tumours and Histiocytosis*

#### THE EFFECT OF BEVACIZUMAB (AVASTIN) IN TREATING JUVENILE RECURRENT RESPIRATORY PAPILOMATOSIS

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**Background and Aims:** Repetitive growth of papillomas in the respiratory tract causes high healthcare costs and low quality of life. This case report analyzes the effects of bevacizumab (Avastin) in treating Juvenile onset recurrent respiratory papillomatosis (JoRRP). The case presentation includes recurrent JoRRP symptoms in a sixteen-month female who experienced noisy breathing, stridor, poor oral intake, and hoarseness. Despite that the patient underwent more than 25 surgical interventions and being treated with alpha interferon, upon finding bilateral papillomatosis, omega-shaped epiglottis, and arytenoid edema, the JoRRP escalated. Clinical improvements started upon bevacizumab (Avastin) administration, in 5mg/kg to 10 mg/kg dose range for 60 to 90 minutes. The patient's clinical response signaled that bevacizumab is effective in treating JoRRP and improving quality of life. Evidence from more studies reported that bevacizumab influences new

disease management protocols and control. Thus, bevacizumab is an evidence-based remedy for JoRRP to reduce lesions that obstruct the tracheal airway without compromising the patient's quality of life.

**Methods:** Administration of bevacizumab (Avastin), in 5mg/kg to 10 mg/kg dose range for 60 to 90 minutes.

**Results:** The initiation of systemic angiogenesis inhibitor bevacizumab (Avastin) 5mg/kg and then increased to a maximum of 10 mg/kg over 60-90 minutes, she showed dramatic clinical improvements. Post five cycles of intravenous bevacizumab a laryngoscope showed impressive regression of residual papilloma with no evidence of recurrent lesions.

**Conclusions:** JoRRP is a rare devastating, disease of the airway causing mild hoarseness to severe airway obstruction. It requires multi-disciplinary comprehensive medical and surgical care. Early introduction of systemic and or intralesional bevacizumab treatment seems to be efficient and well tolerated in children. As for prevention, early inducing of the human papillomavirus vaccine to child-bearing women will significantly reduce the risk of transmission of the virus to neonates and hence reduce the risk of JoRRP and other related cancers.

EP420/#1075 | Poster Topic: AS05 SIOP Scientific Program/AS05.I  
*Rare Tumours and Histiocytosis*

#### BECKWITH-WIEDEMANN SPECTRUM (BWSP) AND ADRENOCORTICAL TUMORS: AN INSIGHT INTO CLINICAL AND MOLECULAR CHARACTERISTICS

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**Background and Aims:** Adrenocortical tumors (ACTs), including adrenocortical adenoma (ACA) and carcinoma (ACC), represent 0.3-0.4% of pediatric tumors. Beckwith-Wiedemann spectrum (BWSp) confer an increased risk of ACTs, but the prognosis, management, and molecular characteristics of these patients are still debated.

**Methods:** Data from one unpublished patient and 62 published reports of patients with BWSp and ACTs were reviewed. Patients with isolated hemihypertrophy and/or BWSp clinical score <4, with inconclusive genetic analyses, were excluded (n=17).

**Results:** Twenty patients with ACA, 30 with ACC, 5 with ACT of uncertain malignant potential (umACT) were included. Genetic analyses were available for 33 patients: 19 had uniparental disomy of chromosome 11p15.5 (*patUPD11*) (14 ACC, 2 ACA, 2 umACT), 10 imprinting Center 2 Loss-of-methylation (IC2-LoM) (5 ACC, 5 ACA), 4 other results. Mean BWSp clinical score was  $3.5 \pm 2.4$  for ACC (17 patients (56%) had a score <4) and  $3.7 \pm 2.2$  for ACA. Mean age at ACA and ACC diagnosis was 6.6 and 5.8 years respectively. Thirty-three patients were symptomatic at diagnosis, mainly virilization (n=13) and Cushing syndrome (n=13), 11 were diagnosed during follow up. Mean Wieneke's score was 0.83 for ACA, 3.33 for ACC. Six patients had metastasis at diagnosis, two of them had a Wieneke's score <2. *CTNNB1:p.S45P* and *GNAS:p.R201H* somatic mutations were found in 2 patients respectively. Six patients relapsed (11%), 8 patients died (14.5%).

**Conclusions:** Patients with BWSp and ACT mostly carried *patUPD11* and IC2-LoM. Fifty-six percent of patients with BWSp and ACC did not reach the score for BWSp clinical diagnosis, suggesting that this score might have a limited value for early diagnosis in this setting. Tumor histology (Wieneke's score <2) did not correlate with tumor aggressiveness in 2 cases, highlighting limitations of the current histopathological classification. Screening for BWSp-related tumors failed identifying ACC before metastases in two cases, indicating an urgent need to develop new strategies.

EP421/#599 | Poster Topic: AS05 SIOP Scientific Program/AS05.I  
*Rare Tumours and Histiocytosis*

#### ALK-POSITIVE NON-LANGERHANS CELL HISTIOCYTOSIS - THE GERMAN COLLECTION AND CONSULTATION SERVICE

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**Background and Aims:** Rare or Non-Langerhans cell histiocytoses (non-LCH) include many malignant and benign, localized or diffuse diseases. Recently, ALK-positive histiocytosis (ALK+H) has been defined as a separate subgroup, on a molecular basis. In many cases, conventional histologic appearance of ALK+H resembles juvenile xanthogranuloma (JXG), however, other variants have been described as well. ALK+H are especially common in early childhood - but adults are described as well, and they often show intracerebral involvement with neurological sequelae. Both single-system as well as multisystemic diseases are described.

**Methods:** In 2012, the German registry and consultation study for non-LCH - part of the International Rare Histiocytic Disease Registry - was

initiated. While meanwhile, 17 patients have been formally registered, in about 100 cases, consultation was applied.

**Results:** Meanwhile, 5 patients with ALK+H have been reported. Since molecular analysis has only been done in a small proportion of patients, other ALK+H cases might also be contained, in particular in JXG cases. The cases include a 4y old boy with large temporal tumor achieving remission by LCH-like chemotherapy, a 30y old man with spinal tumor, with ongoing stable disease by inhibitor therapy; an 8y old girl with retroauricular tumor in continuous first remission after complete resection, a 10 y old boy with large abdominal tumor, and an 18 mon. old boy with large maxillar tumor; both planned to be put on inhibitor therapy.

**Conclusions:** ALK-positive histiocytoses represent a heterogeneous disease spectrum, and diagnosis depends on molecular analysis, which should be performed in all cases of pediatric non-Langerhans cell histiocytosis. Appropriate consultation depends on international prospective data collection, which should be further propagated.

EP422/#1405 | Poster Topic: AS05 SIOP Scientific Program/AS05.I  
*Rare Tumours and Histiocytosis*

#### RETROSPECTIVE AUDIT OF PEDIATRIC GRANULAR CELL TUMOUR (PGCTS) FROM A TERTIARY CANCER CENTRE IN INDIA

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**Background and Aims:** Granular cell tumours are rare group of soft tissue neoplasms believed to be of Schwann cell in origin. They usually manifest as a solitary skin nodule. Several case reports and smaller case series have been published in the medical literature, but studies on larger cohorts of childhood GCTs are lacking. We report here the clinical profile and management Pediatric GCTs at our unit

**Methods:** We performed a retrospective audit of case records of children ( $\leq 14$  years) who were diagnosed with Granular cell tumor at Regional cancer centre, Thiruvananthapuram between January 2010 and December 2022

**Results:** A total of 5 children were diagnosed with Cutaneous Granular Cell tumor during the study period. The median age of study cohort was 6 years (range: 5-8 years) with male predominance (M:F:3:2). Eighty percentage of the patients had primary extremity lesion with one patient presented with multiple lesions over both upper limbs. Rest one patient had chest wall primary. Median duration from

symptom onset to diagnosis was 12 months (range: 6–24 months). All 5 of them underwent wide excision with subsequent clinical follow-up. One child with chest-wall primary had a recurrence 1-year post-marginal resection

**Conclusions:** Granular Cell Tumors are extremely rare in children and margin negative resection may be needed to obviate the recurrence risk.

EP423/#569 | Poster Topic: AS05 SIOP Scientific Program/AS05.I Rare Tumours and Histiocytosis

### THE USE OF BEVACIZUMAB IN THE TREATMENT OF JUVENILE-ONSET RECURRENT RESPIRATORY PAPILLOMATOSIS: A TERTIARY CARE EXPERIENCE

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**Background and Aims:** Juvenile Onset Recurrent Respiratory Papillomatosis (JORRP) is a benign neoplasm of the respiratory tract and is a therapeutic challenge due its impact on quality of life, risk of airway obstruction, and high recurrence rate. Primary management involves frequent surgical debridement. The off-label use of bevacizumab for JORRP treatment has shown promise in case studies, but there is limited data on its efficacy. We present a case series of patients with JORRP at our institution and their clinical courses before and after bevacizumab.

**Methods:** All patients with JORRP treated with bevacizumab at Aga Khan University Hospital from March 2015–February 2023 were retrospectively included. All patients received three 5 mg/kg doses of systemic bevacizumab two weeks apart.

**Results:** We identified 6 patients in our cohort. All were male with a mean age of disease onset at 4.6 (range 2–9). Presentations included hoarseness in 4 (66%), respiratory distress in 3 (50%), and aphonia in 1 (16%) patient. Sites affected included larynx in all patients, trachea in 1 (16%) patient, and nasopharynx in 1 (16%) patient. Pre-bevacizumab, the number of recurrences and surgical debridements in the previous 1 year was 5.7 (SD +/- 2.7), and recurrence occurred every 7 (SD +/- 3) weeks. Post-bevacizumab, all patients had complete response in affected areas. During 1-year follow-up, 1 patient required no further intervention, while 5 (83%) patients had recurrence. Recurrence frequency was 1.5 (SD +/- 1.37), and recurrence occurred every 19.2 (SD +/- 15.1) weeks. Two patients' recurrence was managed with bevacizumab, while 3 patients required surgical debridement. One patient experienced treatment-associated hypertension as a side-effect.

**Conclusions:** Our data indicates that bevacizumab reduces the rate of recurrence, prolongs recurrence-free period, and reduces the need for surgical debridement in patients with JORRP at our tertiary care center. It also demonstrated a strong safety profile in our cohort.

EP424/#1358 | Poster Topic: AS05 SIOP Scientific Program/AS05.I Rare Tumours and Histiocytosis

### DEVELOPING A BUSINESS PLAN FOR A RARE PEDIATRIC EYE CANCER BIOBANK

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**Background and Aims:** Rare pediatric eye cancers (R-PECs) include over 30 types of neoplastic lesions. The first R-PEC Biobank was established at The Hospital for Sick Children (SickKids, Toronto, Ontario). The R-PEC Biobank systematically collects nationally and internationally sourced biospecimens, clinical data and images. Increasingly, biobank financial and operational sustainability is found to be associated with utilization of a well-defined business plan. To this end, we aimed to develop a business plan for the R-PEC Biobank.

**Methods:** A Business Plan Working Group was formed including key leadership and staff of the R-PEC Biobank. Biobank business plan consultants were hired to advise the working group. A framework for the business plan, aligned with established guidelines and best practices, was developed. Working group members drafted sections of the business plan which were then iteratively revised until consensus was reached.

**Results:** The resultant business plan included mission, vision and objectives; key elements and guiding principles; governance; management and operations; finances and sustainability; marketing and communication; implementation; and risk mitigation. Development of the R-PEC Business Plan was uniquely complicated owing to the rarity of the conditions of interest; commitment to authentic patient engagement across all areas of the R-PEC Biobank; and the atypical milieu in which the R-PEC Biobank operates, specifically as a subset of a broader pediatric ophthalmology biobank residing within the institutional SickKids Central Biobank.

**Conclusions:** The business plan will be shared on the R-PEC Biobank website and refined by internal and external oversight entities including the R-PEC Patient Advisory Committee. The R-PEC Business Plan will be critically appraised by the Principal Investigator and R-PEC Biobank Manager after each of the first 3 years of implementation to ensure it is realistic and accurate.

EP425/#1863 | Poster Topic: AS05 SIOP Scientific Program/AS05.I Rare Tumours and Histiocytosis

### MALIGNANT EXTRA-RENAL NON-CEREBRAL RHABDOID TUMOUR IN CHILDREN: 14-YEAR EXPERIENCE IN AN ARGENTINIAN INSTITUTION

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**Background and Aims:** ERNC-MRT are rare, highly aggressive neoplasms affecting mainly infants and children younger than 3 years. Aim: To report clinical features and outcomes of patients with ERNC-MRT treated at our Institution.

**Methods:** We retrospectively analyzed 13 patients diagnosed with ERNC-MRT from January'07 to May'21, 9 treated according to EpSSG-NRSTS2005 Protocol. We used maintenance therapy (MT) with cyclophosphamide/vinorelbine after completing chemotherapy. One patient received MUV-ATRT Protocol. In 2 patients only biopsy was performed.

**Results:** Median age at diagnosis was 10 (range: 1-69) months. INI-1 expression by immunohistochemistry was negative in all patients. FISH was performed to detect 22q11.2 deletion or translocation in 9 patients (69%). Metastatic disease in 4 patients (30%), all in lungs. Primary tumour site was paraspinal in 5, thoracic 4, liver 3, cavum 1 patient. Five patients achieved complete remission (CR), and one of them died due to early relapse in the CNS. Five patients received MT after completing chemotherapy. Of them, 4 are alive, including one metastatic patient and one patient with subtotal tumor resection. One of 5 patients died 49 months after diagnosis and 11 months after disease progression on maintenance therapy. Six patients had progressive disease on treatment and died at a median of 2.76 (range: 0.07-8.09) months. Complete surgical resection was achieved in four patients, of whom three are alive. All seven patients younger than 12 months died with a median survival of 2.2 months. After a median follow-up of 4.21 (range: 0.4-155) months, the 3-year event-free survival and overall survival rate were 38.4%

**Conclusions:** ERNC-MRT is a rare disease with a poor prognosis. Age under 1 year was the main prognostic factor. All but one patient that received maintenance therapy are alive, suggesting that MT might have a role in ERNC-MRT; however, a larger number of patients with a longer follow-up is necessary to draw definite conclusions.

EP426/#1223 | Poster Topic: AS05 SIOP Scientific Program/AS05.1  
*Rare Tumours and Histiocytosis*

#### PEDIATRIC NASOPHARYNGEAL CARCINOMA - EXPERIENCE FROM A TERTIARY CANCER HOSPITAL IN NORTH EAST INDIA

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**Background and Aims:** BACKGROUND Nasopharyngeal carcinoma (NPC) arises in the lining of the nasal cavity and pharynx with a very low incidence in children younger than 10 years. Incidence rises in the adolescents. Due to rarity of the tumor in younger children there is delay in diagnosis and timely referral. Epidemiological studies that have been done to establish the etiological factors associated with this disease include genetic and environmental factors. EBV infection has been strongly associated with its occurrence. AIMS To describe the patient characteristics, symptomatology, management and outcomes of Pediatric NPC cases in a Tertiary Cancer Hospital in Northeast India.

**Methods:** Retrospective chart review of all the pediatric (0-19yr) patients with NPC diagnosed histopathologically, registered from January 2016 to December 2022 and not suffering from any other malignancy. Neoadjuvant chemotherapy (Taxane, Cisplatin/Carboplatin, 5FU, Gemcitabine based therapy) was given in 21(52%). Eighteen (45%) received Radiotherapy (upto 70Gy in 33 fractions). Three year survival was calculated using Kaplan Meier Survival Analysis.

**Results:** Forty patients of Pediatric NPC were registered from January 2016 to December 2022. Male: Female ratio was 28:12. Sixty five percent of the patients (26), were in 15-19 yr age group and 14 (35%) were less than 15 yr of age. Cervical lymphadenopathy was the commonest clinical presentation (35%). Cranial nerve involvement was found in two. The commonest histopathology was WHO type III (47%). All were stage 3 or 4 at presentation, 13 (32%) metastatic. Hearing loss was found in one. Fourteen (35%) expired, 14 alive, 12 patients - status unknown. Three year survival was 30% for the cohort.

**Conclusions:** Pediatric NPC is a rare tumor with distinct epidemiological association. Early detection and timely referral to cancer care unit can help lower morbidity and mortality associated with the disease.

EP427/#1651 | Poster Topic: AS05 SIOP Scientific Program/AS05.1  
*Rare Tumours and Histiocytosis*

#### LANGERHANS CELL HISTIOCYTOSIS WITH NEONATAL DEBUT, PRESENTATION OF A SERIES OF CASES

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**Background and Aims:** Langerhans cell histiocytosis is characterized by reactive clonal proliferation and accumulation of dendritic cells with variable clinical manifestations. Regarding the presentation in the neonatal stage there are few publications on the clinical course of this entity in this period of life, early age at the time of presentation has been associated with multisystem involvement and, therefore, with a worse prognosis, studies on this disease in the neonatal period are described almost exclusively with an isolated cutaneous presentation with a high tendency to spontaneous regression (called "Self-limited congenital histiocytosis" by "Hashimoto-Pritzker"), The lack of large series of patients excludes reliable conclusions about the real incidence

of LCH in neonates, as well as its clinical spectrum, natural history, prognosis and sequelae, so this publication aims to show the most frequent clinical findings at this stage of life, in order to reach an early diagnosis and timely management

**Methods:** Multicenter retrospective descriptive study, series of clinical cases diagnosed with neonatal Langerhans cell histiocytosis was collected, reviewed and analyzed, reporting a total of twenty-six cases with different presentations.

**Results:** From 26 patients; 9 in follow-up and treatment, 4 deceased in treatment phases, 1 without treatment, 7 spontaneous resolution, 3 with pulmonary involvement in follow-up, 3 with reactivation in treatment and follow-up,

**Conclusions:** Langerhans cell histiocytosis in the neonatal period is rare, there are few publications on the clinical course of this entity in this period of life. Course of clinical presentation of this entity, in terms of differential diagnosis should be made with viral diseases typical of neonatal age, in addition to other types of hematological neoplasms such as leukemia or transient myelodysplastic syndromes that can also occur with hematological alteration. Therefore, the disease represents a challenge and it is important to sensitize medical personnel about the need to deepen their knowledge for timely diagnosis and management.

EP428/#627 | Poster Topic: AS05 SIOP Scientific Program/AS05.I  
*Rare Tumours and Histiocytosis*

#### INFLAMMATORY MYOFIBROBLASTIC TUMORS IN CHILDREN

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**Background and Aims:** Inflammatory myofibroblastic tumors (IMT)- and epithelioid inflammatory myofibroblastic sarcoma (EIMS), a variant of IMTs- are rare in children. ALK re-arrangement can be seen in both tumors, but RANBP2-ALK fusion is seen in EIMS. Surgical resection without morbidity is the mainstay of treatment. Recently, the efficacy of crizotinib, an ALK inhibitor, has been reported in unresectable/resistant/relapse cases.

**Methods:** Files of children with IMT between 1990-2022 were retrospectively reviewed.

**Results:** The mean age of 7 patients (5 male, 2 female) was 7.5 years. Five patients had IMT and two had IMS. ALK was positive in tumor tissue of five patients, and unknown in two. Tumor localization was intestine and retroperitoneum in two patients, liver, lower extremity and scapula in one each. All were non-metastatic at diagnosis. Three of the five patients (one IMS) underwent only surgical resection had negative margins and are under follow-up without event. In other two patients who underwent surgical resection only, margin was positive, one of them underwent re-resection (IMS) and is under follow-up without event. The other patient with positive margin experienced local and

metastatic (lung, liver) recurrences and treated with chemotherapy containing vincristine, actinomycin-D, and cyclophosphamide, but the patient died due to progressive disease. A patient who underwent surgical resection at diagnosis with positive margin received crizotinib and under follow-up in complete remission. Crizotinib was started in one who was inoperable at diagnosis. Complete remission was achieved, upon local recurrence crizotinib was re-administering, she achieved complete response and is under treatment.

**Conclusions:** Surgery is the mainstay of treatment in IMTs. Detection of ALK rearrangement by FISH or RT-PCR in addition to IHC will increase the possibility of receiving targeted therapy and further confirm the diagnosis of EIMS, providing a reliable reference for ALK-targeted therapy, which is thought to increase survival.

EP429/#436 | Poster Topic: AS05 SIOP Scientific Program/AS05.I  
*Rare Tumours and Histiocytosis*

#### VEMURAFENIB EXPERIENCE IN TWO CASES WITH LANGERHANS CELL HISTIOCYTOSIS UNRESPONSIVE TO CHEMOTHERAPY

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**Background and Aims: INTRODUCTION:** There is no standard treatment protocol for refractory Langerhans Cell Histiocytosis (LCH). Here, we aimed to present our vemurafenib experience in two cases with BRAF mutation positivity unresponsive to chemotherapy.

**Methods: CASE 1:** Seven-month-old male patient, presented with the complaints of fever, discharge in both ears and skin rash. Thora-coabdominal CT revealed lymphadenopathies, pleural effusion, hepatosplenomegaly. Temporal bone CT showed lytic lesions with soft tissue components in the temporal bones, lytic lesions in occipital and parietal bones. Biopsy taken and resulted as LCH. Induction chemotherapy was started according to the LCH-IV protocol. In the evaluation, disease progression was detected, and second-line treatment was started. BRAF positivity was detected in patient's pathology blocks. Vemurafenib treatment was started due to the continued increase in swelling in the left mastoid region of the patient during the treatment. After both clinical and radiological regression were achieved in the first month of vemurafenib treatment, chemotherapy was discontinued. Complete remission was achieved and his treatment has been ongoing for 18 months.

**Results: CASE 2:** A 17-year-old male patient with the diagnosis of Type 1 DM, was referred to our center after lytic lesions were detected on the right 9th rib, T4, T12 vertebra and left iliac bone in the CT scan taken with the complaint of low back pain for 3 months. In thoracoabdominal CT, millimetric cysts in both lungs and hepatomegaly

were detected. Biopsy of T12 vertebra resulted as LCH. Induction chemotherapy was started in accordance with the LCH-IV protocol. Post-treatment imaging was evaluated as stable disease. While it was planned to switch to the Stratum-2 arm containing vincristine and ARA-C, BRAF mutation positivity detected and vemurafenib was started. Partial response was achieved in the second month of treatment. The patient was transferred to adult hematology because of his age, and we learned that he is ongoing vemurafenib, an increase in sclerosis was observed in lytic bone lesions in the first year of treatment.

**Conclusions:** COMMENT: Vemurafenib appears to be an effective and safe option in the treatment of refractory LCH cases with BRAF mutation.

EP430/#313 | **Poster Topic: AS05 SIOP Scientific Program/AS05.I Rare Tumours and Histiocytosis**

### NEONATAL CANCER 25 YEARS OF EXPERIENCE IN MULTIDISCIPLINARY MANAGEMENT OF THE REBAGLIATI NATIONAL HOSPITAL, TEZZA CLINIC AND INTERNATIONAL CLINIC LIMA PERU 1999 -2023

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**Background and Aims:** BACKGROUND: Malignant tumor present in the first 28 days of life and can be diagnosed by prenatal imaging; different etiology, incidence, histology, therapeutic response and prognosis, due to the anatomical and physiological immaturity of his age.

**Methods:** MATERIAL AND METHODS: Retrospective and descriptive study in the Pediatric Oncology Unit of the Rebagliati Hospital and two private clinics between 1999-2023. Analysis; frequency distribution, Kaplan Meier curves and Cox regression model.

**Results:** RESULTS: Thirty seven cases (1.19%) of Neonatal Cancer in 3100 pediatric cancer patients, period 1999-2023. Median age 5 days (range one prenatal month-28 days). Males 70.2%. Histology: germ cell tumor 8 cases (21.6%, 6/8 teste); 7 cases (18.9%) of Hepatoblastoma preter III, 7 neuroblastoma; group D and E retinoblastoma: 5 (13.51%), sarcomas 3 (8.10%, cervical leiomyosarcoma, vaginal rhabdomyosarcoma and renal), 2 cases (5.4%) pnet, 2 acute leukemias (lymphatic and myeloid) 2 brain (glioblastoma and grade III astrocytoma) and 1 Wilms (2.7%). Prenatal diagnosis 7 cases (19%): 2 hepatoblastomas, adrenal neuroblastoma, bladder pnet, Wilms, 1 immature teratoma and 1 mixed cervical, avoiding death by neonatal asphyxia with immediate tracheostomy. Seven with metastasis and only 2 died (paraorbital-brain neuroblastoma and Wilms tumor with lung metastasis) HR 0.22 (95% CI 0.18 to 0.48). Breastfeeding + chemotherapy 34 with a survival of 79.4% (HR 0.44), of which 31 developed neutropenia+sepsis with a survival of 77.4% (HR 0.43). Overall survival at 5 years 73% (EE 0.061), DFS 67.5% (EE 0.063).

**Conclusions:** CONCLUSIONS: Neonatal cancer occurs in advanced stages and has a varied etiology; the prognostic factors that contribute to a greater survival are breastfeeding and to a lower one neutropenia and sepsis; Despite the immaturity of their organs, they have a good tolerance to multidisciplinary surgical and chemotherapy treatment with a high survival.

EP431/#1395 | **Poster Topic: AS05 SIOP Scientific Program/AS05.I Rare Tumours and Histiocytosis**

### MULTILOCUS INHERITED NEOPLASIA ALLELE SYNDROME IN FIVE PEDIATRIC PATIENTS

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**Background and Aims:** Background. Multilocus inherited neoplasia allele syndrome (MINAS) refers to individuals who have two or more pathogenic cancer predisposing germline variants. This report presents five MINAS cases with detected germline mutations in different genes associated with increased risk of cancer. Aims: To highlight the importance of using multigene panels for diagnostics of cancer predisposition syndrome (CPS) patients demonstrating several clinical cases with MINAS.

**Methods:** Among group of 549 pediatric patients suspected to have CPS we revealed five probands with a range of tumors including scalp epidermoid cyst, Burkitt lymphoma, Wilms tumor, optic pathway glioma and pleuropulmonary blastoma type III. Some patients had phenotypic features: café au lait spots, Lisch nodules, developmental disorders of the genitourinary system, bilateral sensorineural hearing loss (SNHL) or burdened family history. We analyzed probands' DNA extracted from peripheral blood leucocytes with custom-targeted NGS-198 genes-panel, one patient had whole exome sequencing. The detected variants were checked in family members by Sanger sequencing.

**Results:** Five patients had a combination of two pathogenic germline heterozygous mutations in different genes: **APC** (de novo) and **BRCA2** (inherited from mother), **CDKN2A** (inherited from father) and **LZTR1** (unknown inheritance), **NF1** (de novo) and **BRCA2** (inherited from father), **WT1** and **CHEK2** (unknown inheritance), **DICER1** (inherited from mother) and **SPRED1** (inherited from father). One patient also had compound heterozygous mutations in **USH2A** causative for congenital SNHL.

**Conclusions:** Next generation sequencing reveals that some patients suspected to have a particular CPS may have pathogenic germline



mutations in other genes including those in the list of American College of Medical Genetics recommendations for secondary findings reporting. These results may be crucial for individual surveillance and genetic counselling in the family.

EP432/#298 | Poster Topic: AS05 SIOP Scientific Program/AS05.I  
*Rare Tumours and Histiocytosis*

#### CLINICAL CHARACTERISTICS AND TREATMENT OUTCOME OF CHILDREN AND ADOLESCENTS WITH EPITHELIAL OVARIAN NEOPLASM – A RETROSPECTIVE REVIEW FROM A TERTIARY CANCER CENTRE IN INDIA

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**Background and Aims:** Epithelial ovarian neoplasms (EON) are uncommon in the pediatric population. The data on EON in children is limited. We conducted this study to assess the clinical characteristics and outcomes of children and adolescents with EON

**Methods:** Children  $\leq 18$  years of age diagnosed with EON, registered at GCRI, Ahmedabad, India between 1<sup>st</sup> January 2010 and 31<sup>st</sup> December 2022 were included for retrospective analysis. Clinical characteristics, treatment details, and outcomes were noted.

**Results:** One-hundred-sixteen patients were diagnosed with ovarian mass, eight (0.07%) of them had EON. Median age was 17 years (range 13 – 18 years). One (12.5%) patient had family history of breast cancer in her grandmother. One (12.5%) child had borderline serous cystadenocarcinoma (stage Ia), three (37.5%) had malignant mucinous cystadenocarcinoma (two stage Ia, one stage II), and four (50%) had malignant serous adenocarcinoma (one stage II, two stage IIIc, one stage IV). One girl with borderline tumor was treated with surgery only and alive at 79 months from diagnosis. Three (two stage Ia and one stage II) patients underwent primary debulking surgery without adjuvant chemotherapy. Two patients (stage IIIc) underwent suboptimal interval debulking surgery after neoadjuvant chemotherapy. Two (stage II and IV) patients could not undergo surgery because of progressive disease after neoadjuvant chemotherapy. All patients with stage Ia are alive without evidence of disease at last follow up. One girl (12.5%) with stage IIb relapsed after 78 months of primary treatment and succumbed to disease. All three patients with stage IIIc and one with stage IVa had relapse/progression and three patients died due to disease

**Conclusions:** Malignant EONs require multimodality of treatment. Children with serous tumors and advanced disease have poor survival. Uniform treatment modalities should be rigorously adopted in children with EON. Genetic counselling is an important part of the management.

EP433/#1371 | Poster Topic: AS05 SIOP Scientific Program/AS05.I  
*Rare Tumours and Histiocytosis*

#### METASTATIC MALIGNANT MELANOTIC NERVE SHEATH TUMOR (MMNST): A RARE CASE REPORT IN A CHILD AND A SYSTEMATIC REVIEW OF PEDIATRIC AND ADULT LITERATURE

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**Background and Aims:** MMNST are rare tumors making up  $< 1\%$  of nerve sheath tumors and only around 1% of cases have been associated with distant metastasis. The aim of this study was to identify the incidence of MMNST with distant metastasis, its clinical features, the course of the disease, and its outcomes.

**Methods:** A child with MMNST presenting with multiple sites metastasis is reported. A systematic review of all reported cases of MMNST with distant metastasis (pediatric and adult) in the literature was carried out followed by a descriptive analysis.

**Results:** The web search elicited 35 case reports of metastatic MMNST but 32 cases with adequate data were included in the study. The first case was reported in the year 1973. Only 2 cases were less than 16 years of age, including the index case report. The mean age of presentation was 41.2 years  $\pm$  17.74 SD. The male-to-female ratio was 1.4:1. Most common presenting complaint was neuropathy (68%) and the median duration of symptoms was 12 (4-36) months. The primary tumor site was the peripheral nervous system in 78%, and bone and soft tissue in 22% of cases. Lumber nerve roots were the commonest primary site of involvement (31%). Metastatic sites were lungs (53%), liver (28%), bones (25%), and lymph nodes (22%). Rare metastatic sites were skin, thyroid gland, chest wall, and soft tissue. The median time to develop metastasis was 14 (0-96) months. Surgery was conducted (69%) for the primary site while radiation therapy (19%) was given for metastatic sites in the majority of cases. Seventy-eight percent of patients expired with median overall survival of 24 (1-96) months.

**Conclusions:** Metastatic MMNST is extremely rare in children and has a very poor prognosis. Targeted therapies might be a ray of hope but the small number of cases would be the biggest challenge in future clinical trials.

EP434/#247 | Poster Topic: AS05 SIOP Scientific Program/AS05.I  
*Rare Tumours and Histiocytosis*

#### PEDIATRIC PHEOCHROMOCYTOMA AND PARAGANGLIOMA: CLINICAL AND MOLECULAR CHARACTERISTICS

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**Background and Aims:** Pheochromocytoma and paraganglioma (PPGL) are very rare chromaffin cell tumors in pediatric population, in which inherited cases consists of more than 80%. The aim was to study the clinical and molecular genetic features of a cohort of patients with PPGL treated in the national pediatric oncology center in Russian Federation.

**Methods:** The study included 19 patients with PPGL diagnosed for the period 01.2012-12.2022. Histological diagnosis was confirmed by the reference pathologist in all cases. Different molecular methods (NGS, PCR) were used to assess the germline status of PPGL predisposition genes depending of clinical data. Median follow-up was 17.7 months (range 3.9-99.5).

**Results:** The median age of patients was 10.3 years (range 4.5-17.2). 13/19 were diagnosed with paraganglioma, 5/19 - pheochromocytoma, and 1/19 with synchronous paraganglioma and pheochromocytoma. Arterial hypertension was present in 10/19 of cases at the onset of the disease. A germline mutation in one of PPGL-susceptibility genes was identified in 15/19 patients: *SDHB* (n=10), *VHL* (n=3), *SDHD* (n=2). Hereditary PPGL was proven in 6/15 patients: *SDHB* (n=3), *VHL* (n=2), *SDHD* (n=1). 4/19 had synchronous tumors defined as detection within 6 months interval: *VHL* (n = 3), *SDHD* (n = 1). 5 patients experienced a new event: local/locoregional recurrences (n = 3), metastatic relapse (n = 1), combined relapse (n = 1): *SDHB* (n=4), *VHL* (n=1). Surgery was a mainstay of therapy (18/19). 3 patients received additional therapies: chemotherapy (n = 3), 131I-metaiodobenzylguanidine therapy (n = 1) and distant radiation therapy (n=1) for unresectable disease. 2-year event-free survival was 74.4 ± 13.7%, whereas the overall survival was 100%.

**Conclusions:** Genetic counseling are mandatory to improve clinical follow-up and to identify asymptomatic mutation carriers in relatives. All pediatric patients with PPGL require lifelong follow-up due to the risk of subsequent unfavorable events.

EP435/#669 | Poster Topic: AS05 SIOP Scientific Program/AS05.I Rare Tumours and Histiocytosis

## GASTROINTESTINAL NEUROENDOCRINE TUMORS IN CHILDHOOD

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**Background and Aims:** Neuroendocrine tumors (NETs) originating from neuroendocrine cells are rare in children. Its incidence is 6/100000 in adults and 2.8/million in children. Pediatric NETs are commonly located in appendix.

**Methods:** Demographic, clinical, treatment information and results of patients with NETs between 1993-2022 were evaluated.

**Results:** The median age of 14 patients (11 female, 3 male) was 13 (9-18) years. Tumor localization was appendix in 12, stomach in one and pancreas in one. Tumors of appendix were diagnosed after being operated with diagnosis of acute appendicitis and of stomach was diagnosed with endoscopic polypectomy due to dyspeptic complaints. A pancreatic mass was detected due to complaints of prolonged abdominal pain in one patient with metastatic lesions in liver. Tumor size was < 2 cm in 13 patients. Mesoappendix invasion was detected in 4 patients. Right hemicolectomy and lymph node resection (>20) were performed in two of these patients; 3 nodes were positive in one and node involvement was negative in the other. The other two patients did not undergo surgery. Chromogranin A, Urine 5-HIAA levels were high in the patient with pancreatic origin and normal postoperatively in others. On Ga68 DOTATATE PET CT after surgery, all 13 patients had no residual involvement except one with pancreatic tumor with liver metastasis. Somatostatin was given to patient with pancreatic metastatic disease and the other with gastric disease. No additional treatment was given in other patients. The median follow-up was 54 months (1-220 months). All patients are under follow-up without evidence of disease.

**Conclusions:** Pediatric NETs are most commonly located in appendix. Most of the patients presented with appendicitis, diagnosed incidentally have a good prognosis. Although NETs are rare, they should be considered in the differential diagnosis of patients with acute appendicitis. It is important to increase the awareness of pediatricians, pediatric surgeons and pathologists in this regard.

EP436/#1756 | Poster Topic: AS05 SIOP Scientific Program/AS05.I Rare Tumours and Histiocytosis

## MALIGNANT TERATOMA OF THE THYROID IN A 17-YEAR-OLD PATIENT WITH XERODERMA PIGMENTOSUM

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**Background and Aims:** Thyroid teratomas are usually of a benign nature. Primary malignant thyroid teratomas are an extremely rare form. The risk of malignancy increases with age. It's usually stumbled upon in histopathologic study of surgically resected masses of the thyroid. As fine-needle aspiration (FNA) is most frequently unreliable, diagnosis prior to surgery can be challenging. Given their heterogenous nature, the outcome varies depending on the degree of maturation of its components. But largely, its prognosis is poor. In this case we describe a patient diagnosed and treated at our department for primary thyroid teratoma.

**Methods:** We report the case of a patient diagnosed with malignant teratoma of the thyroid at the pediatric department of Salah Azaiz Institute.

**Results:** A 17-year-old female patient with medical history of Xeroderma Pigmentosum was presented with a rapidly growing cervical mass. A cervical ultrasonography revealed a multinodular thyroid goiter of the left lobe, classified EU-TIRADS 3. Fine-needle-aspiration (FNA) was inconclusive thus a total thyroidectomy with neck dissection was performed. The histopathologic analysis has shown malignant immature teratoma of the left lobe of the thyroid with lymph node metastasis of the neuroepithelial contingent. Shortly after thyroidectomy, a right cervical adenopathy appeared measuring 6cm. The patient received 3 courses of adjuvant chemotherapy based on PEI regimen: cisplatin, etoposide and ifosfamide, with excellent clinical response as proven by the disappearance of the cervical adenopathy after the first cycle. The patient then received radiotherapy given the locally aggressive nature of the tumor.

**Conclusions:** Malignant teratoma of the thyroid is a rare entity. It is usually diagnosed after pathological study following surgical excision. The administration of adjuvant chemotherapy can increase disease-free survival rates. The indications of neoadjuvant chemotherapy and post-operative radiation therapy have yet to be established.

EP437/#746 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### ADJUVANT TREATMENT OF PEDIATRIC CHOROID PLEXUS CARCINOMA; OUTCOMES AND TOXICITIES

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**Background and Aims:** **Background:** Choroid plexus carcinoma is a sporadic pediatric CNS tumor. **Aim:** To investigate the best management of pediatric choroid plexus carcinoma patients in a large pediatric oncology hospital.

**Methods:** A retrospective review of the electronic medical records of 34 pathologically proven choroid plexus carcinoma patients diagnosed at Children's Cancer Hospital, Egypt (2008-2022).

**Results:** Patients were predominantly males (64.7%) with a mean age of 3.12 years (median = 1.9). Lateral ventricles were the most frequent primary site (88%, N=30). Gross total resection (GTR) could be achieved in 55.9% of patients. The median follow-up was 26.3 months. Adjuvant Chemotherapy (6 cycles) for patients ≤ 3 years (64.7%, N= 22) and combination chemo-radiotherapy for those older than three years were adopted. The 2-year event-free survival (EFS) and overall survival (OS) were 80.8% and 90.9% for those who received radiotherapy compared to 40.4% and 63.6% for those who did not (p= 0.049, p= 0.097), respectively. Ten patients (out of 12) > three years have received 36 Gy craniospinal irradiation (CSI) plus local boost up to 54-55.8 Gy, in addition to chemotherapy, while two patients received 55.8 Gy localized radiotherapy. Those who received CSI had 2-year EFS of 88.9 % while the two patients who received localized field had 50% EFS. The extent of surgery had no significant impact on the EFS (p = 0.350). The most common adverse event reported was neutropenic sepsis (≥G3=18%). Three patients (9%) developed second malignancy. Those who received radiotherapy suffered from short stature and slow hair growth.

**Conclusions:** Patients with CPC who received multimodality treatment with adjuvant chemotherapy & radiotherapy had significantly better EFS than those who received chemotherapy alone. Although CSI seems to lead to better EFS and OS, yet not significant, as only two patients received localized radiotherapy.

EP438/#1052 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### DISRUPTIONS TO THE STRUCTURE-FUNCTION RELATIONSHIP PREDICT DECREASED EPISODIC MEMORY PERFORMANCE IN CHILDREN TREATED FOR BRAIN TUMOURS

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**Background and Aims:** The Medial Temporal, Posterior Medial, Anterior Temporal, and Medial Prefrontal Networks appear to support episodic memory in adults. However, it is unclear how these networks support episodic memory processing in children. Children and adolescents treated for brain tumours are a model of memory impairment, as they show perturbed episodic memory, neural communication, and white matter microstructure. As white matter provides axons a more efficient method of signal propagation (via structural connectivity), damage to this tissue is theorized to disrupt functional connectivity and cognition. We hypothesized that individuals treated for brain tumours, compared to controls, would show worse episodic memory performance due to disrupted synchrony between relevant networks via white matter damage.

**Methods:** 24 individuals treated for brain tumours and 23 controls were scanned with Diffusion (DTI) and T1-MRI and completed Transverse Patterning (TP) during Magnetoencephalography (MEG), and subtests from the Children's Memory Scale (CMS). Task accuracy was assessed for group differences using robust regressions. Fractional anisotropy (FA) and theta/gamma weighted phase lag indices (wPLI) were calculated (using DTI and MEG scans respectively) for all unique pairs of network regions. Task scores and FA/wPLI metrics with significant group differences (determined via Network Based Statistics) were inputted into a path model to determine the relationship between structural connectivity, functional connectivity, and episodic memory performance.

**Results:** Individuals treated for brain tumours demonstrated decreased TP, CMS Word Pairs Learning and Stories Delayed accuracy, and fifteen region pairs with increased theta wPLI and decreased FA compared to controls. Path model results showed decreased FA predicted increased theta wPLI and decreased memory task performance.

**Conclusions:** This suggests the relationship between structural and functional connectivity in these networks supports episodic memory performance in a task-specific manner. Furthermore, damaged white matter microstructure and theta hyper-synchrony may be a signature of injury in individuals treated for brain tumours.

EP439/#1041 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### NEXT GENERATION SEQUENCING FOR CNS TUMORS IN CHILDREN; DOES IT ADD VALUE IN A MIDDLE-INCOME COUNTRY SETUP?

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**Background and Aims:** Advances in molecular diagnostics led to improved targeted interventions in the treatment of pediatric brain tumors. However, the capacity to do these diagnostics is limited in LMICs, and consequently their value is questionable.

**Methods:** We reviewed our experience of Next Generation Sequencing (NGS) testing (TruSight RNA Pan-Cancer seq panel) for pediatric CNS tumors at KHCC/Jordan (July/2022- January/2023). Paraffin blocks' scrolls were shipped to Sickkids laboratory based on local MDT recommendations. We reviewed patients' clinical characteristics, tumor types and the impact on treatment.

**Results:** There were 12 boys and 14 girls; median age 8.5 years (range, 0.9-19years). Seventeen samples were sent at diagnosis and nine upon tumor progression. The main diagnoses were LGG (10), HGG (9), and other tumors (7). Reasons to do NGS were: to find a molecular target (14), and to characterize more the tumor/behavior (12). With a median laboratory processing time of 15.5 days (range, 8-39 days) and a cost of US\$1000, sixteen (62%) tumors had targetable alterations (nine by MAPK inhibitors, two FGFR inhibitors, two PI3K inhibitors, two NTRK inhibitors, one with check point inhibitors). Two rare BRAF mutations were identified (BRAFp.G469A, BRAFp.K601E). One tumor diagnosed initially as undifferentiated round cell sarcoma found to have NAB2::STAT6 fusion and was re-diagnosed as aggressive metastatic solitary fibrous tumor. Five patients received compassionate targeted therapy; Trametinib (3), Entrectinib (1), Pembrolizumab (1), while conventional radio-chemotherapy was used in the others. Three patients died from disease progression (one used Entrectinib).

**Conclusions:** Sent abroad NGS testing was feasible, however local capacity building is necessary. In this highly selected tumor cohort, high percentage of targetable alterations were identified. NGS was helpful to characterize tumors more and to offer alternative therapies. Nevertheless, interpretation of the significance of NGS results and access to those "new" therapies continues to be a challenge in LMICs.

EP440/#1057 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### BRAF/MEK INHIBITORS USE FOR PEDIATRIC LOW-GRADE GLIOMAS; REAL WORLD EXPERIENCE FROM A LIMITED RESOURCE COUNTRY

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**Background and Aims:** Most pediatric low-grade gliomas (pLGG) are cured with surgical resection, while chemotherapy is spared for progressing and difficult to resect tumors. Alterations in MAPK pathway are found in most pLGG enabling the use of BRAF/MEK inhibitors, however data on their use in LMICs are limited.

**Methods:** We retrospectively reviewed KHCC/Jordan experience with using compassionate BRAF/MEK inhibitors from Novartis to treat pLGG. We reviewed patients' clinical characteristics, tumor response on targeted therapy, and side effects encountered.

**Results:** Eight patients (3 boys, 5 girls) were identified over 5 years. Median age at diagnosis was 4.8years (1-13years) and at start of BRAF/MEK inhibitors was 11years (5.8-21.9years). Four had optic hypothalamic glioma (OPG, three BRAFv600E mutated/ one BRAF fused), one with Neurofibromatosis-1 had thalamic/ internal capsule tumor, one spinal fibrillary astrocytoma (BRAF fused), one cervico-medullary ganglioglioma (BRAFv600E mutated) and one metastatic cerebellar pilocytic astrocytoma (BRAF fused). All patients had partial tumor resection and received 2-4 chemotherapy protocols prior to using BRAF/MEK inhibitors upon tumor progression. Three patients with BRAFv600E mutated OPGs progressed on dabrafenib so trametinib was added (after 5,7,12 months) leading to two partial responses and one stable disease. The fourth had partial response, and the cervico-medullary ganglioglioma had marked response; other tumors were stable. Symptoms improved in all patients; those with OPGs had stable vision, patient with metastatic LGG stopped her multiple analgesics, seizures in one patient were controlled, and the cervico-medullary tumor symptoms of sleep apnea improved. At a median drug use of 3 years (0.7-4.6years), all patients were alive and never received radiotherapy. Six patients needed dose reduction due to acne, paronychia, fatigue, and panniculitis.

**Conclusions:** Compassionate use of BRAF/MEK inhibitors achieved good LGG control in all our patients despite dose reductions in most. Cost effectiveness analysis and patients' satisfaction assessments are needed to evaluate the practical use of these drugs in LMICs.

EP441/#266 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

## TOXICITY PROFILE OF HIGH-DOSE METHOTREXATE IN INFANTS WITH CNS TUMORS

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**Background and Aims:** High-dose methotrexate (HD-MTX) is a critical component of therapy for certain pediatric central nervous system (CNS) tumors, the second most common category of childhood malignancies. However, characterization of toxicities secondary to HD-MTX has not been thoroughly examined in this patient population, particularly in infants. Here, we characterize the frequency of delayed MTX clearance and related toxicities in 16 infants diagnosed with a CNS tumor at Texas Children's Hospital between 2010 and 2020.

**Methods:** A retrospective cohort study assessed infants with CNS tumors who were 3 years old or younger at the time of diagnosis and received at least one dose of HD-MTX between 2010 and 2020 at Texas Children's Hospital. Pertinent demographic, clinical, and treatment-related variables from electronic health records were abstracted. Toxicities examined included mucositis, neurotoxicity, neutropenia, and thrombocytopenia. All were graded using CTCAE standards. Infections present one month prior to admission through MTX clearance were noted. Delayed clearance was defined as a serum MTX concentration >0.4 μM at hour 48.

**Results:** We identified 16 infants with a CNS tumor treated with HD-MTX. The cohort consisted of 56.3% females, 62.5% white race, and 43.8% Hispanic ethnicity. The most common diagnosis was atypical teratoid rhabdoid tumor (n=9). Of the 42 cycles of HD-MTX evaluated, delayed methotrexate clearance occurred 14 times (33%) in 9 patients. CTCAE grade 3-4 neutropenia (n=28, 66.7%) and thrombocytopenia (n=17, 40.5%) were frequently observed. CTCAE grade 2-3 mucositis occurred following 14 cycles of HD-MTX (33.3%). Three instances of infection were also documented. No acute or subacute neurotoxic events were observed following HD-MTX therapy in this population.

**Conclusions:** This preliminary work characterizes the incidence of common toxicities following HD-MTX therapy in a population of pediatric patients with CNS tumors age 0-3 years. This work generally supports the use of HD-MTX in this population as safe with appropriate supportive care and monitoring.

EP442/#1179 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

## CONVENTIONAL RISK-STRATIFICATION WITHIN INDIVIDUAL MOLECULAR SUBGROUPS OF PEDIATRIC MEDULLOBLASTOMA- DOES IT IMPACT OUTCOME?

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**Background and Aims:** Molecular subgrouping is now an integral component of medulloblastoma diagnostics and has significant impact on therapeutics and clinical outcomes. In the current study, we investigated the prognostic impact of conventional risk stratification (clinic-radiological) within the four individual molecular subgroups (WNT, SHH, Group 3 & 4) of pediatric medulloblastoma.

**Methods:** Patients aged <18 years with histopathological diagnosis of medulloblastoma, treated in a single tertiary care center during 2005-2021 were screened for this retrospective analysis. Patients with known molecular subgrouping, clinical details of risk stratification (age, residual disease, metastatic disease), and survival outcomes were included. Survival analysis was done using Kaplan-Meier product limit methods, with univariate analysis done using log-rank test. A p-value of <0.05 was considered statistically significant

**Results:** From a total of 557 patients, 401 children were identified for analysis, with 68 patients aged < 3 years. Molecular subgroup was WNT (64), SHH (73), group-3(78), and group-4(98). Conventional risk stratification information was available in 329 patients, with average risk (AR) in 45% and high risk (HR) in 55%. The median follow-up was 62 months (interquartile range 24-93 months) for surviving patients, with 137 patients developing disease recurrence and 135 deaths. Five-year overall survival (OS) for the entire cohort was 80% and 56% for AR and HR, respectively ( $p<0.01$ ). The OS was not statistically significant between the two conventional risk groups in the WNT ( $p=0.89$ ) and SHH ( $p=0.43$ ) subgroups. For group 3, the 5-year OS was 66% and 36% for AR and HR, respectively, trending towards significance ( $p=0.08$ ). The 5-year OS for AR and HR disease for group 4 was 78% and 65%, respectively ( $p<0.01$ ).

**Conclusions:** The prognostic impact of conventional risk stratification remains valid primarily for non-WNT/ non-SHH medulloblastoma. Appropriate risk stratification to guide adjuvant therapy must be revisited for WNT/ SHH subgroups to optimize the balance between cure and treatment-related toxicity.

EP443/#1721 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### DIFFERENTIAL RECURRENCE KINETICS ACROSS MOLECULAR SUBGROUPS OF MEDULLOBLASTOMA

Archya Dasgupta<sup>1</sup>, Abhishek Chatterjee<sup>2</sup>, Arpita Sahu<sup>3</sup>, Rudrani Dhele<sup>4</sup>, Saranga Sawant<sup>1</sup>, Neha Mer<sup>1</sup>, Sridhar Epari<sup>5</sup>, Neelam Shirsat<sup>6</sup>, Maya Prasad<sup>7</sup>, Girish Chinnaswamy<sup>8</sup>, Ayushi Sahay<sup>5</sup>, Prakash Shetty<sup>9</sup>, Aliasgar Moiyadi<sup>9</sup>, Tejpal Gupta<sup>2</sup>

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**Background and Aims:** Medulloblastoma constitutes four molecular subgroups: wingless (WNT), sonic hedgehog (SHH), group 3, and group 4. The current study investigated the differential effect of molecular groups on annual recurrence probabilities.

**Methods:** Patients with medulloblastoma with known molecular subgroups were included in the retrospective study. Survival analysis was done by Kaplan-Meier method. The annual probabilities of recurrence were calculated for initial 5 years from diagnosis and calculated by the proportion of events for that specific year and numbers at risk.

**Results:** Of 400 patients included in the final analysis, 149 had recurrence (median time to recurrence 23 months) with a median follow-up of 58 months. The number of recurrences and total patients for individual subgroups were: WNT (5 of 74), SHH (72 of 154), group 3 (34 of 72), group 4 (38 of 100). The recurrence in WNT was rare, with <5% annual probability for initial 5 years. For SHH subgroup, a bimodal peak was seen, higher peak at 1-2 years and second between 8-10 years. The annual relapse rates ranged between 12-20% for first 5 years. Group 3 had highest risk in first year (41%), with 75% of all recurrences happening within 2<sup>nd</sup> year. Group 4 had bimodal peak, with higher peak at 1-2 years, and late relapses leading to a second peak between 6-7 years. Relapse rate in first year was less for group 4 (3%), and again dropped between 3-5 years (<5%). Of late relapses beyond 5 years, SHH (8) and group 4 (10) constituted 90% of all recurrences.

**Conclusions:** Group 3 medulloblastoma had the highest relapse probability in first year, while SHH and group 4 had bimodal patterns of relapse (likely reflecting different outcomes of the subtypes within individual subgroups). The current study depicts the differences in the kinetics of medulloblastoma subgroups, which can aid in developing appropriate surveillance protocols.

EP444/#1308 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### INVASIVE FUNGAL INFECTIONS IN PEDIATRIC PATIENTS WITH CENTRAL NERVOUS SYSTEM TUMORS: NOVEL INSIGHTS FOR PROPHYLACTIC TREATMENTS?

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**Background and Aims:** Invasive fungal diseases (IFDs) are important causes of morbimortality in pediatric patients with neoplasm and there are no data on patients with central nervous system (CNS) tumors. Considering vulnerability factors to infections such as neutropenia, corticosteroids, chemotherapy, surgery and others, the aim of this study is to evaluate the incidence of IFDs in pediatric patients

with CNS tumors, determine their characteristics and indication for prophylaxis.

**Methods:** This is a single-center, retrospective study, conducted between 2011-2022 at Pediatric Institute of Oncology (IOP-GRAACC-UNIFESP).

**Results:** Thirty-eight IFDs were diagnosed among 818 children with CNS malignancies (4,6%). Mean age was 3.5 years (0.4-28y), 22 males (57.9%). The most common CNS tumor were embryonal (18/38, 47.3%), followed by low-grade gliomas (13/38, 34.2%). All episodes met EORTC IFD criteria, 36/38 (94.7%) proven. The most common diagnosis was invasive Yeast infections (33/38, 86.8%) mostly *Candida* (30/33, 90.9%). Twenty-five (25/38, 65.8%) were under chemotherapy, 13 of whom with embryonal tumors, 11 were infants under the *Head Start* scheme, what entails a high incidence of IFD in this group (11/58, 18.9%). Thirteen (13/38, 34.2%) patients were submitted to neurosurgery, mostly ventricular peritoneal shunt (10/13, 76.9%). Nine (9/38, 23.7%) were with prolonged use of corticosteroids, eight associated with neurosurgery.

**Conclusions:** Routinely systemic antifungal prophylaxis for low-risk based on diagnosis alone is not recommend, nevertheless considering patient- and treatment-specific risk factors, as infants under high-dose chemotherapy with an anticipated duration of neutropenia and patients with prolonged use of corticosteroids and necessity of neurosurgery procedures may benefit from antifungal prophylaxis.

EP445/#1828 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### INTRACRANIAL NON-GERMINOMATOUS GERM CELL TUMORS: BRAZILIAN CONSORTIUM PROTOCOL

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**Background and Aims:** Non-germinomatous germ cell tumors (NGGCT) accounts for one third of the intracranial GCT. While the germinoma group have an excellent overall survival the standard of practice for children with NGGCT still under evaluation. Aims: Describe the results of the of the Brazilian consortium protocol.

**Methods:** Since 2013, 15 patients with a diagnosis of NGGCT by histopathology and/or serum/CSF tumor markers, bHCG >200mIU/ml and/or positive alpha-fetoprotein (AFP) were treated with neoadjuvant

chemotherapy (CT) with carboplatin, cyclophosphamide and etoposide followed by ventricular radiotherapy (RTV) of 18Gy with boost (32Gy) in the primary site. Metastatic patients underwent craniospinal irradiation (CSI) and "slow responders" to the 4 initial cycles of CT, to autologous bone marrow transplantation (ABMT) followed by CSI.

**Results:** Mean age 13.1 years. Thirteen male. Primary sites: pineal (n=12), suprasellar (n=2) and bifocal (n=1). Four patients were metastatic at diagnosis. Eight patients had CSF and/or serum AFP levels > 1000ng/ml. Tumor response after chemotherapy was complete in six cases and partial in seven, with "second-look" surgery being performed in five cases, with two patients presenting viable lesions being referred to ABMT. The main toxicity observed was hematological grade 3/4. Two patients with metastatic disease, one with Down Syndrome and AFP > 1000ng/ml and the other with choriocarcinoma and pulmonary metastasis, had progressive disease progressing to death, as well as two other patients without evidence of disease, due to endocrinological disorders. Event-free and overall at 2 and 5 years were 80% and 72.7%, respectively, with a mean follow-up time of 48 months (range, 7-107).

**Conclusions:** Despite the small number of patients, in our series, treatment with 6 cycles of QT and RTV with focal boost for localized disease (n=11) but mainly ABMT for identified slow responders (n=2) seem to be good strategies that can contribute to the overall effort to improve the outcome of this group of patients.

EP446/#1473 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### LOW GRADE GLIOMA IN A UNIVERSITY-BASED PAEDIATRIC NEURO-ONCOLOGY SERVICE IN SOUTH AFRICA 2001-2022

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**Background and Aims:** To review the management of childhood low grade gliomas (WHO grade I and II) by the combined neuro-oncology services of the University of Cape Town.

**Methods:** Real time decision-making is achieved via a weekly neuroimaging meeting, and surveillance via a combined monthly clinic attended by paediatric endocrinologists and an educational psychologist. Despite state of the art surgical and radiotherapy facilities, molecular diagnostics, monoclonal antibodies and small molecules were only available to some patients with insurance. This study was

a retrospective analysis of all patients diagnosed at Red Cross War Memorial Children's Hospital (RCWMCH) and Groote Schuur Hospital (GSH) between 2001 and 2022.

**Results:** Among 129 children, aged 0.38 to 14.58 years [median 5.36], six had Tuberous Sclerosis and 11 had Neurofibromatosis-1. The commonest sites were cerebellum (26%), hypothalamus (17%) and optic pathway (16%), and 12 patients (9%) had metastatic disease, mostly grade I supratentorial tumours. Twenty-three patients were diagnosed on imaging without histology, six of whom were biopsied subsequently, yielding a total of 96 grade I and 16 grade II tumours. Initial management was expectant in 16% (including 8 of the 11 Nf-1 tumours), surgery in the form of debulking or total resection in 53%, chemotherapy in 24% and radiotherapy in 8%. Ultimately 36% received chemotherapy and 29% radiotherapy (almost all of them focal RT), and only 16% of those treated with radiotherapy progressed. Estimated 5-year Overall Survival (OS) and Progression Free Survival (PFS) was 90.5% and 52.6% for the whole group. Patients treated with chemotherapy had an OS of 87.2% and a PFS of 39.2%. PFS and OS were inferior for metastatic disease but not for grade II tumours.

**Conclusions:** Low grade gliomas can be effectively managed in a low- and middle-income country setting. Multidisciplinary team management is crucial to achieving positive outcomes regardless of context.

EP447/#868 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### EXTENT OF RESECTION DETERMINES THE POSTOPERATIVE TUMOR GROWTH VELOCITY IN PEDIATRIC LOW-GRADE GLIOMA

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**Background and Aims:** Low-grade gliomas (LGG) are brain tumors that occur frequently in children. With excellent long-term survival rates, there is still significant variation in clinical behavior after incomplete resection (IR). This retrospective study aimed to investigate the impact of surgical extent, tumor location, and molecular BRAF status on postoperative residual tumor growth behavior and the safety of perioperative dexamethasone (DM) application.

**Methods:** This retrospective study analyzed 172 pediatric patients with LGG who underwent surgical treatment, 107 of whom had

incomplete resection (IR). Pre- and post-operative cohorts included 53 and 94 patients, respectively, and were observed over a mean follow-up time of 40.2 and 60.1 months. TGV was calculated using sequential three-dimensional MRI-based tumor volumetry of a total of 407 MRI scans. Sixty-five patients (45%) were perioperatively treated with DM in commonly used doses.

**Results:** The study observed a significant deceleration in tumor growth velocity from a mean preoperative TGV of 0.264 cm<sup>3</sup>/month to 0.085 cm<sup>3</sup>/month, 0.024 cm<sup>3</sup>/month, and -0.016 cm<sup>3</sup>/month after the first, second, and third IR, respectively. The extent of resection correlated with the postoperative reduction of TGV. A residual cut-off tumor volume > 2.0 cm<sup>3</sup> was associated with a higher risk of progression. Postoperative TGV of BRAF V600E-mutant LGG was significantly higher than of BRAF wild-type LGG. Comparison of short- and long-term postoperative tumor growth rates in patients with vs. without perioperative DM application showed no significant difference.

**Conclusions:** The extent of the surgical resection impacts pLGG growth kinetics post incomplete resection by inducing a significant deceleration of tumor growth. Resection extent showed a correlation with postoperative reduction of TGV, and a residual cut-off tumor volume >2.0 cm<sup>3</sup> was associated with a higher risk of progress post-IR. BRAF-V600E mutation is a risk factor for higher postoperative TGV. Application of dexamethasone did not affect postoperative tumor growth rates.

EP448/#1679 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### H3G34-MUTANT GLIOMAS: AN INSTITUTIONAL EXPERIENCE

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**Background and Aims:** To study the clinico-pathological features of H3G34-mutant gliomas

**Methods:** Data of patients with H3G34-mutant diffuse hemispheric gliomas, diagnosed during 2015 - 2022, were analysed.



**Results:** Twenty-one cases formed the study cohort with age-range of 6-28 years. Twelve (57.1%) were of  $\leq 18$  years. Male to female ratio -3.2:1. Twenty showed H3 p.G35R (G34R) mutation; one case showed H3 p.G35V (G34V) mutation. All cases, except one had predominantly superficial cerebral hemispheric location. One also showed involvement of thalamus. Histologically, all the cases were high-grade. Loss of ATRX-protein expression was seen in 19/21; (90.5%) cases; p53-protein over-expression was seen in 17/21 (80.9%). Six had MGMT-promoter methylation status, 3 were methylated and other 3 were unmethylated. Adjuvant treatment and follow-up details were available in 15. Nine received focal radiation with concurrent and adjuvant temozolamide. Two could receive focal radiation with concurrent temozolamide. Four did not receive any adjuvant therapy, one died within one month of surgery and rest died within 2 to 3 months of diagnosis. Of the 11 patients who received some form of adjuvant therapy, three (all  $> 18$  years) were alive at the last follow-up i.e. at 36 months, 32 months and 19 months of initial clinical presentation respectively; however all three showed progression. Rest 8 died within a period of 8 to 49 months ( $\leq 18$  years: 8-20 months;  $> 18$  years: 4-49 months) of clinical presentation. Of the three MGMT-promoter methylated cases, 2 were alive and no follow-up details available for the other case. Age-groups (children and adult) did not show significant differences with respect to gender, ATRX-loss, and p53-protein overexpression.

**Conclusions:** H3G3-mutant glioma is a disease of adolescent and young adults. Loss of ATRX-protein expression is not a universal phenomenon. Rarely non-G34R mutation can occur. Trend of relative longer survival periods was observed in adults as compared to children. **Keywords:** H3 G34-mutant; glioma; ATRX; MGMT-promoter

EP449/#1495 | **Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours**

#### TO BE OR NOT TO BE TREATED, CHALLENGES IN ELABORATING LOW-GRADE GLIOMA (LGG) ADAPTED MANAGEMENT GUIDELINES (AMG): THE ADAPTED RESOURCE IMPLEMENTATION APPLICATION (ARIA) WORKING GROUP

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**Background and Aims:** LGGs represent one of the most challenging of the six World Health Organization (WHO) Global Initiative for Childhood Cancer index cancers. Although curable, standard approaches vary based on local resources and consensus guidance in low- and middle-income countries (LMICs) is lacking. To address this gap, we report the work of the ARIA LGG AMG.

**Methods:** A multidisciplinary panel of content and context experts, nominated by SIOP, St. Jude Global and Paediatric Radiation Oncology Society formed the LGG working group. Team members met through multiple online meetings to develop consensus treatment strategies. After a strategy was formulated, a larger representative panel consisting of healthcare providers from all global WHO regions and World Bank income levels was organized to review and provide feedback. Key controversies were summarized as Delphi statements for panel review.

**Results:** 6 working group members and 38 representative panelists from 19 countries participated in the LGG AMG draft review. Through two rounds of review, 418 comments were provided by the representative panel and adjudicated by the working group. 45% (9/20) Delphi statements achieved consensus after round 1 with the rest achieving consensus after round 2. While indications for surgery were clear, thematic debates regarding indications for chemotherapy vs radiotherapy were challenging due to the lack of randomized studies comparing these two modalities. Additional key points requiring consensus included: alternative therapies given drug access limitations (targeted therapies), diagnostics access (molecular studies), delivery schedule (weekly vs monthly), heterogeneity in radiotherapy techniques (2D, 3D, IMRT, proton), supportive care availability (vision, auditory, hormonal, cognitive), optimal management of predisposition syndromes and rehabilitation.

**Conclusions:** The treatment of LGGs is evolving rapidly with precision medicine, molecular analysis, novel targeted agents and advanced radiotherapy. In this rapidly changing landscape, ARIA will provide equitable and timely access to trusted and evidence-based guidance to inform care for clinicians across all income-levels worldwide.

EP450/#500 | **Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours**

#### THE RESULT OF PROTOCOL BASED TREATMENT OF CENTRAL NERVOUS SYSTEM GERM CELL TUMOR IN KOREA-THE REPORT OF KOREAN SOCIETY OF PEDIATRIC NEURO-ONCOLOGY (KSPNO)

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**Background and Aims:** Pediatric central nervous system (CNS) nongerminomatous germ cell tumor (NGGCT) is a rare type of CNS cancer in childhood. Here we report the protocol based treatment result of Korean Society of Pediatric Neuro-Oncology (KSPNO).

**Methods:** The KSPNO developed the clinical trial for CNS NGGCT as the protocol name of G052 and G082 in 2005 and 2008. The NGGCT was defined as the histologically confirmed yolk sac tumor, choriocarcinoma, immature teratoma, embryonal carcinoma, germinoma with hCG elevation, or the tumor with increased tumor marker (bhCG or aFP) if there is no available biopsy material. The chemotherapy was composed of courses A (bleomycin, cyclophosphamide, etoposide) and B (bleomycin, carboplatin, etoposide) with a total of four courses. The 36 Gray of craniospinal radiation was given to the patients.

**Results:** Total 152 patients were treated. Among them, 92 patients were high risk (YST, CC, EC, mixed germ cell tumor and 60 were intermediate risk (IMT or germinoma with elevated hCG). In total cohort, 5 year overall survival (5Y-OS) was 90±2.4%, and 10Y-OS was 89±2.7%. For high risk, 5Y OS was 85.0±3.9% and for intermediate risk, 5Y OS was 85.3±3.9%. As for the histology, EC and YST were the poorest group v(5Y OS 78.4%±7.8%, 71.4±17.1%, respectively). AFP over 165 was the poor prognostic marker in the total cohort (p=0.013). In HR, the chemotherapy biochemical response at the end of chemotherapy showed the tendency of prognostic marker (p=0.062) and the significant at the end of protocol treatment (p<0.0001). The radiologic response was the significant prognostic factor for 5Y OS (p=0.0036). In IMT, there was a significantly increased frequency of growing teratoma syndrome (p=0.0012). The residual tumor size over 3 cm at the start of chemotherapy was the predictive marker for unexpected surgery (p=0.014).

**Conclusions:** The result of KSPNO G052/082 protocol showed favorable treatment result for CNS NGGCT

EP451/#586 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### TRENDS IN PEDIATRIC CNS TUMORS IN ARMENIA: A MULTICENTER RETROSPECTIVE STUDY

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**Background and Aims:** CNS tumors are the most common solid malignancies in children with an incidence of 1.15-5.14 cases per 100000 children in high-income countries. However, the reported incidence is relatively low in developing countries. The current study aims to analyze epidemiological data, treatment, and outcomes of children and young adults (≤25 years) with CNS tumors in Armenia during the last 26 years.

**Methods:** We have collected data from pediatric and young adult patients treated in the neurosurgery department, three major chemotherapy clinics, and the radiation therapy department from 1<sup>st</sup> January 1995 to 31<sup>st</sup> December 2020 in Armenia. Incidence by gender, age at diagnosis, the time from first complaints to diagnosis, histopathology results, treatment strategies, complications, and overall survival (OS) rates were calculated.

**Results:** The multicenter data analysis revealed 149 patients diagnosed with primary CNS tumors over 26 years. Among them 84 (56.4%) were males. The median age at diagnosis was 7 years (range, 3 months to 25 years), and the median time from initial symptoms to diagnosis was 2 months (range, 1 week to 70 months). Medulloblastomas and other embryonal tumors (31.5%), low-grade gliomas (21.5%), and high-grade gliomas (14.8%) were the most commonly diagnosed malignancies. Other CNS tumors were observed in 14.8% of patients. For 17.4% of patients, there was no documented histopathological or radiological diagnosis. During the study period, surgery, chemotherapy, and radiation therapy were performed in Armenia by 65.1%, 22.15%, and 20.8% of patients, respectively. Follow-up information was available for 98 (65.8%) patients. 5-year OS for the whole study group was 67.7%.

**Conclusions:** Embryonal tumors and gliomas were the most commonly diagnosed CNS tumors in Armenia. Considering the number of patients lost to follow-up, actual survival rates of CNS tumors may be lower in Armenia. We hope recent advances in diagnosis and treatment will help to improve the outcomes of CNS tumors.

EP452/#1208 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### TREATMENT FOR A PAEDIATRIC BRAIN TUMOUR MAY ALTER SUSTAINED ATTENTION PROCESSES VIA TRAUMATIC EXPOSURE IN CHILDREN AND ADOLESCENTS

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**Background and Aims:** Post-traumatic stress disorder (PTSD) occurs in 20-35% of children and adolescents treated for a brain tumour. Findings in child populations with PTSD suggest that treatment may be traumatic and provoke an attentional bias characterized by an initial avoidance, followed by extended fixation to traumatic stimuli. Children and adolescents treated for a brain tumour may experience similar changes in attentional control. This study uses eye-tracking technology to characterize how treatment-related scenes influence attentional control in youths treated for a brain tumour. The *hypotheses* are that children and adolescents treated for a brain tumour will express initial avoidance followed by an extended visual fixation on treatment-related scenes compared to typically developing children. These effects will be greater in youths treated with more intensive treatment protocols (surgery plus a combination of radiation and chemotherapy) than those treated with surgery only.

**Methods:** Sixty participants (40 patients, 20 typically developing children) freely viewed 12 sets of four emotion-eliciting scenes (happy, sad, fear, treatment-related) while undergoing eye-tracking. A Helmert contrast-coded mixed regression model was applied to compare between groups' eye-tracking measures of attentional control. This analysis compared all typically developing children and all children treated for a brain tumour and low-intensity (surgery only) vs high-intensity (surgery plus a combination of radiation and chemotherapy) treatment groups.

**Results:** Analysis revealed that paediatric brain tumour treatment predicted greater initial avoidance ( $\beta = 153.61, p = .029$ ) and slower attentional disengagement from ( $\beta = -21.305, p = .014$ ) treatment-related scenes, compared to typically developing children.

**Conclusions:** Children and adolescents treated for a brain tumour may suffer alterations to their sustained attention processes result of treatment-related exposure. This research uncovers how emotional processes may be impacted by paediatric brain tumour treatment. More broadly, this research highlights the potential value of using treatment protocol intensity to predict those most at risk for developing PTSD symptomology.

EP453/#1759 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### LONGITUDINAL MEASUREMENT OF HEALTH-RELATED QUALITY OF LIFE DURING THE TREATMENT OF REFRACTORY OR PROGRESSIVE PEDIATRIC BRAIN TUMORS

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**Background and Aims:** For youth with pediatric brain tumors, longer life may come at significant cost to morbidity and health-related quality

of life (HRQOL). This is especially true during treatment for refractory and progressive pediatric brain tumors where the impact of treatment across domains is less known. HRQOL measures are critical to understanding the multidimensional impact of treatment on a child's general functioning and overall well-being. Treatments that extend survival while also maintaining HRQOL are highly desirable to those tasked with difficult decision-making regarding anticipated medical care and participation in novel therapies. This ongoing study assessed changes in HRQOL of youth receiving treatment for a refractory or progressive pediatric brain tumor.

**Methods:** Utilizing a longitudinal, prospective design, pediatric patients and their parents/legal guardians completed a psychometrically robust HRQOL battery during treatment for a refractory/progressive brain tumor. Specifically, monthly HRQOL measures (Pediatric Quality of Life (PedsQL) Generic Core, Multidimensional Fatigue, and Brain Tumor modules) were administered to all participants during the first six months following treatment initiation.

**Results:** A total of 32 patients (10.9±5.1 years old; 50% female) consented to participate in the study. Preliminary data supported the initial feasibility of longitudinal HRQOL measurement (13% declined participation; 3% withdrew from study following consent). Interim analyses suggested HRQOL decreased over time across most domains. Most notably, Generic Core Total scores decreased from 56 to 48; Fatigue Total scores from 53 to 37, and Brain Tumor Pain/Hurt subscale scores from 60 to 37.

**Conclusions:** Preliminary results suggest overall declines in HRQOL following treatment initiation for a refractory/progressive pediatric brain tumor. The goal of treatment is to preserve both the quantity and quality of life. Understanding potential mechanisms for decreased HRQOL and interventions to improve HRQOL during treatment for relapsed disease would represent a significant advancement in care.

EP454/#348 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### CHILDHOOD CRANIOPHARYNGIOMA - OUTCOMES AND ABANDONMENT ANALYSIS IN SUPERSPECIALITY SETUP IN NORTHERN INDIA

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**Background and Aims:** Craniopharyngiomas are histologically benign neuroepithelial tumors involving the CNS and commonly occur in children aged 5-10 years. We describe the outcomes and abandonment analysis of craniopharyngioma at our institution.

**Methods:** A retrospective analysis of electronic health records was done from 2010 to 2020 and patients that were diagnosed with craniopharyngioma were analysed.

**Results:** A total of 13 patients were analysed. Most of the patients belonged to age group of 11.1 to 15 years of age 38.46% (5/13). Male: Female ratio was 12:1. Country of origin was India in 84.6%(11/13). Patients presented with increased intracranial pressure in 30.76%(4/13)of cases. Partial resection was feasible in 30.07%(4/13). Gross total resection was feasible in 23.07%(3/13), subtotal in 23.07%(3/13). VP shunting was done in 46.15%(6/13) of patients. One patient abandoned during the course of radiotherapy 7.6%(1/13). Total of 53.84% (7/13) received radiotherapy and 38.46% (5/13) did not require radiotherapy. A total of 46.15%(6/13) completed radiotherapy. Complete response to treatment was seen in 38.46% (5/13), stable disease occurred in 38.46%(5/13), Progressive disease occurred in 7.6%(1/13) of the patients. Number of patients that did not relapse were 38.46%(5/13) and continued to be in clinical remission. Patients that relapsed after completion of treatment was 61.5%(8/13). The 6 out of 8 patients who relapsed abandoned treatment and 2 underwent repeat radiotherapy procedure and completed it successfully. Both of the patients are doing well and continue to be in CR2 until the median follow-up of 3.54 years  $SD \pm 2.71$  years. Median survival of all the patients was 2.25 years (95%CI- 0 to 5.046).

**Conclusions:** Treatment abandonment combined is a major hurdle to improving survival in craniopharyngioma in the developing world.

EP455/#1503 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### CLINICAL PREDICTORS FOR NEUROCOGNITIVE AND PSYCHOSOCIAL TRAJECTORIES IN CHILDREN TREATED FOR A BRAIN TUMOR

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**Background and Aims:** Long-term neurocognitive and psychosocial problems in pediatric brain tumor survivors are highly prevalent. However, longitudinal studies evaluating the trajectories of these neurocognitive and psychosocial difficulties and associated risk factors, are scarce. Therefore, we investigated the evolution of neurocognition and psychosocial functioning and the impact of potential risk factors on these trajectories.

**Methods:** This study included 78 children diagnosed with a brain tumor at the University Hospitals Leuven. Children completed a comprehensive neuropsychological test battery (intelligence, memory, visuomotor functioning) on at least three consecutive time points (2-year interval). At each time point, parents completed a set of questionnaires evaluating neurocognition, psychosocial functioning and Quality of Life. Mean

age at diagnosis was 7.51 years (SD 3.95y). The most common diagnoses were pilocytic astrocytoma (47%) and medulloblastoma (18%). 41% of the children received chemotherapy, 30% focal radiotherapy and 18% received craniospinal irradiation. We evaluated relation between multiple predictors (age at diagnosis, grade, tumor type, localization, treatment, presence of hydrocephaly) and neurocognitive and psychosocial functioning, using a generalized linear mixed model with subject-specific intercepts and slopes. First, main and time interactions effects were evaluated in a univariable model for each predictor separately. Predictors significant in this first stage were then tested in a multivariable model to evaluate an interaction effect with time.

**Results:** The results demonstrate that the trajectory for general intellectual functioning is significantly predicted by age at diagnosis ( $p=0.0023$ ), tumor type ( $p=0.015$ ), grade ( $p=0.036$ ), chemotherapy ( $p=0.0241$ ) and radiotherapy ( $p<0.0001$ ). The trajectory of memory function is predicted by the number of operations ( $p=0.0148$ ). The trajectories of internal psychosocial problems and quality of life is predicted by the age at diagnosis ( $p=0.016$ ) and sex ( $p=0.0394$ ), and chemotherapy ( $p=0.0358$ ), respectively.

**Conclusions:** Our findings demonstrate that different risk factors have an impact on the neurocognitive and psychosocial trajectories of children treated for a pediatric brain tumor.

EP456/#1312 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### CANCER-RELATED FATIGUE IN SCHOOL-AGED CHILDREN, TREATED FOR BRAIN TUMORS

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**Background and Aims:** Brain tumors and treatment after causes delayed consequences that negatively affect the quality of a children's life: timing, working memory, intelligence, attention, sensorimotor functions, cognitive flexibility and other mental functions (Puhr et al., 2019). Besides, cancer patients often complain of chronically fatigue, both physical and cognitive, and emotional overload before and during treatment and after its completion (Schmidt et al., 2020). The study aimed to identify some characteristics of cancer-related fatigue in children under dynamic observation after the completion of brain tumor treatment.

**Methods:** The sample consisted of 67 school-age children (36 girls,  $12.7 \pm 2.9$  years old, and 31 boys,  $13.1 \pm 3.05$  years old) under dynamic observation for 5-139 months after the treatment was over. The "The Turkish Scale for the Assessment of Fatigue in Pediatric Oncology Patients Aged 7-18" adapted for the Russian-speaking audience (Deviaterikova et al., 2021) was used to measure fatigue symptoms, experienced by the child, according to subscales: "Fatigue associated

with daily activities", "Subjective feeling of fatigue", "Sleep related fatigue". Maximal tapping test was used to measure nervous system endurance.

**Results:** The feeling of fatigue persists in children even after the completion of treatment for brain tumor, both according to the patients themselves and to their parents' point of view. Older children and their parents more often complain of chronic fatigue, which may be a consequence and increased reflection and responsibility. Children with more severe fatigue symptoms demonstrated more pronounced slowdown of tapping frequency from the beginning to the end of 30-seconds test. Unexpectedly, parents notice sleep problems associated with fatigue in children who gradually increase their speed in the tapping test.

**Conclusions:** Maximal tapping dynamics can be potentially applied as an objective measure of subjective fatigue in cancer patients.

EP457/#187 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### MEDULLOBLASTOMA AT RELAPSE: FOR WHICH PATIENTS AND WHICH TUMORS REIRRADIATION IS THE BETTER CHOICE

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**Background and Aims:** First line therapies for medulloblastoma (MBL) are tailored to obtain higher survival-rates while decreasing late-effects, but relapse treatment is not standardized. We describe the experience with MBL re-irradiation (re-RT), its timing and outcome in different clinical settings and tumor groups.

**Methods:** Patients were firstly treated between 2002-2019, re-irradiated up to 2021: staging and treatment at diagnosis, histotypes, molecular subgroups, relapse site/s, re-treatments and outcome are reported.

**Results:** Patients were 25, male 16, median age 11.4 years, 8 had metastases, 3 large cell/anaplastic histotype (LCA). According to WHO-classification 2021 in 24/25, 14 had SHH subgroup tumors (6 with TP53 mutation, 1 +MYC amplification), 11 non-WNT/non-SHH (3/4 methylation group3 and one group4, 3 with MYC/MYCN amplification, one p53 mutated). Thirteen had received HART-CSI (median 39 Gy, boost at 60 Gy), 11 standard-CSI at 23.4 Gy plus boost at

54 Gy, one HFRT at 36 Gy plus boost at 54+8Gy; all post-radiation chemotherapy (CT), 15 also pre-RT. Median time to relapse (local-L in 9, distant-D in 14, L+D in two) was 26 months. Fourteen patients were re-operated, (in 5 excising single D-sites), thereafter 3 received CT, two after re-RT; out of 11 not re-operated patients, 4 had re-RT as first treatment and 7 after CT. Pre re-RT CT contained temozolomide in 10/12. Re-RT was administered a median 32 months after first RT: focally in 20 cases and CSI in 5, never resulting in radionecrosis. Median post-relapse-PFS and after re-RT were 16.7/8.2 months, while OS were 35.1/23.9 months, respectively. Metastatic status both at diagnosis/relapse negatively affected outcome while re-surgery was prognostically favorable. MYC, MYCN, P53 status and molecular subgroups, RT extension/fractionation, sex and age were not prognostic at univariable analysis but in the Cox multivariable model OSs were positively influenced by longer interval before re-RT, re-surgery and not-SHH subgroups (P=0.019 from recurrence and 0.004 from second RT).

**Conclusions:** Re-surgery+reRT can prolong survival, SHH-tumor-patients worse outcome is only partially justified by molecular alterations.

EP458/#713 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### ASSESSMENT OF CLINICAL AND NEUROLOGICAL ALTERATIONS BEFORE RADIATION THERAPY IN CHILDREN WITH MALIGNANT BRAIN TUMORS

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**Background and Aims:** Young patients with malignant brain tumors show neurocognitive alterations as both consequences of the tumor and of the treatments received. A prospective study of longitudinal radiation damages after focal RT for brain tumors was activated in 2017. Herein, we present the first analysis correlating tumor localization, treatments, and cognitive assessments at the time of enrollment

**Methods:** Sixty-six children eligible for focal RT were enrolled. A database included age at diagnosis, gender, histology, tumor sites,

number of surgeries, chemotherapy adopted, neurological/endocrinological conditions, symptoms duration, hydrocephalus, and rehabilitation performed. Ad-hoc scores of neurological deficits/endocrine alterations were created to describe each patient. Moreover, by applying the standardized thresholds of each performed cognitive test, a binary outcome ("impaired"/"non-impaired") was generated with the percentage of impaired tests (%ImTest) for each patient.

**Results:** Patients median age was 8 yrs (interquartile range 5-14); the most frequent tumors were Ependymoma (41%) and Germ Cell Tumors (GCT) (23%). Posterior fossa (29%), Frontal lobes (20%), Sellar region (15%), and Ventricular system (20%) were the prevalent tumor sites. All but 5 children with GCT had undergone surgery; 43 out of 66 underwent chemotherapy (32 of them before irradiation). As the cognitive evaluations are concerned, the distribution of the %ImTest had a median of 25%, with a minimum of 0% (n=11) and a maximum of 100% (n=6). Younger children[ $r11$ ] (<6 yrs), underwent a higher number of surgeries. Posterior fossa Ependymoma ependymoma and more generally infratentorial tumors showed higher %ImTest and higher neurological damage scores. Endocrine alterations were more serious in supratentorial tumors, specifically in patients with craniopharyngioma and GCT of the sellar region and ventricular system, and in children without hydrocephalus.

**Conclusions:** The analysis of baseline evaluations highlights damages preexisting to irradiations and generated by multiple factors. In light of these findings, damages over time could be better investigated by distinguishing multiple generating factors.

EP459/#1141 | Poster Topic: AS05 SIOP Scientific Program/AS05.m  
Brain Tumours

#### VERY LONG-TERM OUTCOMES OF PEDIATRIC PATIENTS TREATED FOR OPTIC PATHWAY GLIOMAS: A LONGITUDINAL COHORT STUDY

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**Background and Aims:** Optic pathway gliomas (OPG) represent 5% of childhood brain tumors. Successive relapses lead to multiple treatments exposing to late complications.

**Methods:** We included patients treated at Gustave Roussy (GR) in 01.1980-12.2015 for OPG, before 18 years and alive at 5 years post-diagnosis. Mortality and physical health conditions data were extracted from medical data files and updated thanks to the GR long-term follow-

up program and to the French national mortality registry for patients included in the FCCSS (diagnosed<2000).

**Results:** 182 5y-OPG-childhood survivors were included in this analysis (sex-ratio M/F=0.8, 35% NF1). With a median follow-up of 17.2y (range=5-41), we registered 103 events (82 relapses, 9 second malignancies including 8 second brain tumors, 15 deaths as first-events) and 34 deaths (15 OPG-related, 7 from second malignancies, 3 from cerebrovascular disease, 1 from cardiac disease; 8 not available), resulting in 20-y conditional event-free and overall survivals of 43.5% (95%CI=36-51) and 79.9% (95%CI=71-86), respectively. NF1 (HR=3, 95%CI=1.4-6.8), hypothalamic invasion (HR=3.2, 95%CI=1.4-7.3), and radiotherapy (HR=2.8, 95%CI=1.1-6.7) were significantly associated with poorer OS in multivariable analyses. Ninety-five percent of 5y-OPG-CCS suffered from any health condition, especially visual acuity<1/10" (n=109), ante-hypophyseal insufficiency (n=106) and neurocognitive impairment (n=89). Radiotherapy (HR=1.9, 95%CI=1.2-2.9) and surgery (HR=2.9, 95%CI=1.8-4.6) were significantly associated with ante-hypophyseal insufficiency whereas NF1 (HR=2.1, 95%CI=1.3-3.5) and hypothalamic invasion (HR: 2.8, 95%CI=1.7-4.7) were associated with precocious puberty. 33 cerebrovascular events were observed in 21 patients with a median time post-diagnosis of 4.2 years (range=0.3-23) leading to death in 3 patients. Memory impairment was identified in 70 patients, attention impairment in 61 and executive function trouble in 21.

**Conclusions:** Late relapses, second malignancies and cerebrovascular diseases are severe late events resulting in premature mortality. Morbidity is high and needing specific after-cancer care to improve quality of life. Risk factors should be considered to better stratify long-term follow-up.

EP460/#1038 | Poster Topic: AS05 SIOP Scientific Program/AS05.m  
Brain Tumours

#### MOLECULAR GROUPS OF MEDULLOBLASTOMA DEFINED BY GENE EXPRESSION ANALYSIS AT WESTERN MÉXICO: A PRELIMINARY STUDY

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**Background and Aims:** Medulloblastoma (MB) is the most frequent malignant brain tumor in children. The WHO classified medulloblastoma in 4 molecular groups: WNT, SHH, Group 3 and Group 4. Cruzeiro and Cols., had reported a low cost technique for analysis of gene expression to identify Medulloblastoma molecular groups (MMG).

**Methods:** Ambispective study from 2014 to 2023 to evaluate the potential gene profile expression of MB tumor tissues at "Hospital Civil de Guadalajara Juan I Menchaca" and Pediatric Hospital "Centro Médico de occidente". Paraffin embed or Fresh Frozen tissue was obtained from pathology records for their analysis. Conversion from RNA to cDNA by RT-PCR and gene expression analysis by qPCR with TaqMan probe was done in all cases as cruzeiro described. We matched the results with the demographic data obtained from the clinical records of the patients.

**Results:** Forty seven cases were included, Male: female ratio was 2.6:1 with an average of 6 years at diagnosis (range 1-17 years). The gene expression analysis showed: WNT 3 cases (7%), SHH 25 cases (53%) and No WNT/No SHH in 19 cases (40%). Histology correlated as follows: SHH group, classic in 10 cases (40%), anaplastic in 3 (12%), desmoplastic in 12 (48%), WNT group, classic 1 case (33%), desmoplastic 12 cases (67%) and No WNT/no SHH group, classic 11 cases (58%), desmoplastic/MBEN 8 (42%). At SHH group 8/25 were infants (32%), at WNT group no infants appeared, at No WNT no SHH group 6/19 were infants (32%) and 2/19 had 17 at diagnosis (11%).

**Conclusions:** This preliminary study is valuable because there are few studies in latin american population to describe MMG and we can contribute to build up the knowledge in this regards. Correlation with clinical features is in process

EP461/#1516 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### PEDIATRIC BRAIN TUMORS: A 15-YEAR EXPERIENCE AT A GENERAL HOSPITAL IN THE MEXICO-UNITED STATES BORDER REGION

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**Background and Aims:** Pediatric brain tumors (PBT) comprise 15%-20% of childhood neoplasms, are the second most common childhood cancer after leukemia, and the first cause of childhood cancer mortality globally. In low-and middle-income countries (LMIC), overall survival (OS) for children with PBT is 0-40% due to extremely limited access to multimodal management of surgery, chemotherapy, and radiotherapy. The Pediatric Oncology Unit at Hospital General-Tijuana was inaugurated in 2008 and a Cross-Border Neuro-Oncology Program (CBNOP) was established between Hospital General-Tijuana and Rady Children's

Hospital-San Diego to provide access to neurosurgical care across the Mexico-US border.

**Methods:** Clinical features of children (aged 0-18 years) diagnosed with PBT from January 2008 to December 2022 were reviewed retrospectively. Kaplan-Meier was used to estimate OS.

**Results:** Six-hundred thirty-four children were diagnosed with cancer during the study period, 263 (41%) were diagnosed with leukemia, and 99 (16%) with PBT. Of those, 49% were male and 51% female. Age ranged from 8 months-17 years (mean=6.6 years). Frequency of PBT by age was 0-4 yrs=31%, 5-9 yrs=26%, 10-14 yrs=28%, ≥15 yrs=14%. Infratentorial presentation was found in 51% and supratentorial in 49%. Most common diagnoses were low-grade glioma (25%), benign tumor (21%), medulloblastoma (19%), glioblastoma multiforme (15%), ependymoma (10%), and other (10%). Eighty-one (82%) patients participated in CBNOP: 84% (n=68) underwent surgery and 16% (n=13) underwent biopsy. Three-year OS was 52% in 2008-2017 and 58% in 2018-2022. Five-year OS was 48% (2008-2017)

**Conclusions:** Congruent with prevalence in high-income countries, PBT were the second most common cancer in our institution. Frequency was higher in children <10 years vs >10 years. Sex distribution and infratentorial vs supratentorial presentation were both proportional. Most common diagnoses were low-grade gliomas, benign tumors, and medulloblastomas. Participating in CBNOP improved survival compared to published reports in LMIC. Similar strategies are urgently needed in LMIC to improve outcomes.

EP462/#1384 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### MICRORNAS EXPRESSION IN MEDULLOBLASTOMA CELL LINES

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**Background and Aims:** MicroRNAs (miRNAs) are small non-coding RNAs of approximately 20 nucleotides that have a key function in regulation of gene expression, mostly inducing repression. One miRNA acts on various mRNAs and one specific mRNA can be repressed by different miRNAs. There is growing evidence about the importance of miRNAs in the tumorigenesis of medulloblastoma (MB). People with Down Syndrome, who are protected against the development of MB, have increased levels of hsa-miR-125-b2, hsa-miR-155 and hsa-miR-802. We aimed to study the expression of these miRNAs on two different MB cell lines: Daoy (SHH-MB) and D283 (group 3-4 MB) and in one of acute myeloblastic leukemia: HL-60.

**Methods:** Cells were cultured for over 3 months. We used the miRNeasy Mini Kit (for RNA extraction), miRCURY LNA RT Kit (for reverse transcription) and miRCURY LNA SYBR Green PCR Kit (for miRNA isolation). We tested different amounts of RNA for cDNA, and then a range of dilutions in the real-time quantitative PCR (RT-qPCR) to

set up conditions. RT-qPCR was performed. We used total brain RNA as control and hsa-miR103a-3p, U6snRNA, and SNORD68 as reference genes.

**Results:** Increased expression of hsa-miR-125b was observed in both lines of MB, compared to HL60, and it was statistically significant for D283. The same trend was observed for the hsa-miR-155-5p relative expression in the Daoy compared to D283. In our experimental conditions, hsa-miR-155-5p was never detected in D283, and hsa-miR-802 was never detected in any cell line.

**Conclusions:** miR-155 is not expressed in the D283 MB cell line (group 3-4 MB) but it is in Daoy (SHH-MB). This observation could be related with differences in tumor phenotype or the molecular characteristics of these cell lines. Further investigation is needed to confirm these preliminary results. Acknowledgments: Universidad Francisco de Vitoria, Jérôme Lejeune Foundation, Álvaro Entrecanales Foundation, HM Hospitals

EP463/#1765 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### MEK INHIBITOR (MEKi) AND BRAF INHIBITOR (BRAFi) USE IN PEDIATRIC BRAIN TUMOR PATIENTS

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**Background and Aims:** Observational survey study from multiple sites with pediatric CNS tumor patients being treated or previously treated with MEKi/BRAFi on a pharmacological study or off label.

**Methods:** Sites completed a confidential survey form via REDCap for each patient at their institution and only our site had access to the aggregate data.

**Results:** 131 patients, 71 (54.2%) male and 60 (45.8%) females. 98 children (74.8%) underwent genetic testing, 32 (24.4%) did not and one is unknown. Genetic testing for 97% (95/98) of children were reported; (. BRAF V600E 36 (27.5%), 22 (16.8%) NF1, 22 (16.8%) BRAF duplication, 12 (9.2%) other, 3 unspecified, 3 no detectable mutation. All received inhibitors as part of an ongoing clinical trial or by treating physician. Nine (6.9%) received BRAFi inhibitor only and 94 (71.8%) received MEKi inhibitor only, 28 (21.4%) received both a BRAFi and MEKi inhibitors. 24/38 (63%) received Dabrafenib, 12 (32%) Vermurafenib and 1 patient received both Dabrafenib and Vermurafenib. Of MEKi inhibitors, 105 (80%) received one type, 9 (7%) received combination of two MEKi inhibitors. Most were treated with Trametinib or Selumetinib, 85 (65%) and 22 (17%), respectively. A smaller proportion was treated with Binimetinib and Cobimetinib, 12 (9%) and 4 (3%), respectively. 9 (7%) received combined doses of Trametinib and another inhibitor. A larger proportion of patients received BRAFi

31/36 (86%) and MEKi 79/96 (82%) inhibitors outside clinical trials. Response to therapy varied, 44 (34%) SD, 34 (26%) r PR and 5 (4%) CR. 84 (64%) responded to treatment, 15 (12%) progressive disease and 32 (24%) on treatment at the time of the study. Median response time 17 months (IQR: 11 – 24.50). Duration of response 3 to 50 months. Most patients were on treatment < 24 months (61; 46.6%). No significant differences in toxicity was noted among patients treated > or < 24 months.

**Conclusions:** Understanding off label use of MEKi and BRAFi is important.

EP464/#1231 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### SPECTRUM AND OUTCOME OF CHILDHOOD BRAIN TUMOR IN THE NATIONAL REFERRAL HOSPITAL IN INDONESIA

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**Background and Aims:** Indonesia is the world's fourth-most populous country, with over 275 million people, and approximately 25% are children below 18 years of age. Data from GLOBOCAN 2020 indicates that Indonesia has a comparatively high prevalence of pediatric cancer cases within Southeast Asia. Our centre is a national referral hospital with state-of-the-art facilities and multi-disciplinary teams. Although brain tumors as a group are the most common solid tumors in the pediatric population, there is limited data available in Indonesia regarding the tumor spectrum, treatments, and outcomes. This study aims to describe the characteristics of pediatric brain tumors treated at the [PS1] National Referral Hospital in Indonesia. [PS1]See above

**Methods:** Data were obtained from the medical records of childhood brain tumor patients treated in our unit from January 2021 to December 2022. Diagnosis is based on histopathology reports using the WHO 2016 classification for CNS tumors.

**Results:** A total of 491 new pediatric oncology cases were presented during the study period, of which 72 (15%) were brain tumors. Twenty-eight percent of patients were < 5 years, 24% between 5-10 years



and 48% between 10-18years. The diagnoses were germ cell tumors (16.7%), high-grade glioma (13.9%), medulloblastoma (13.9%), pilocytic astrocytoma (12.5%), ependymoma (9.7%), DIPG (8.3%), craniopharyngioma (4.2%) and uncertain diagnosis (20.8%) due to limited pathology facilities available. Eighty-three percent of patients underwent either resection or biopsy. At the time of analysis in December 2022, 33 patients (44.4%) were still alive, 19.4% of patients died due to their primary tumor despite treatment or infectious complications, and 36.1% of patients were lost to follow-up.

**Conclusions:** Pediatric brain tumors carry a high burden of mortality in Indonesia. Uncertain diagnoses, limited treatment options and poor outcomes are significant issues despite management in a national referral hospital. Multidisciplinary strategies throughout the country must be built to improve diagnosis and standard of care.

EP465/#1387 | Poster Topic: AS05 SIOP Scientific Program/AS05.m Brain Tumours

#### CLINICO-PATHOLOGICAL FEATURES OF H3 K27-ALTERED DIFFUSE MIDLINE GLIOMAS AMONG VARIOUS AGE-GROUPS

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**Background and Aims:** Comparison of clinico-pathological features of H3 K27-altered diffuse midline gliomas among children, adolescents/young adults (AYA) and older adults.

**Methods:** Data of patients with H3 K27-altered diffuse gliomas, diagnosed between January 2015 and February 2023, were extracted retrospectively from the electronic records. The patients with age upto 14 years were considered children, between 15 and 39 years were considered AYA and  $\geq 40$  years were considered older adults.

**Results:** Total 101 cases formed the study cohort with age range of 1-56 years. Age distribution among Diffuse midline gliomas, H3 K27-altered was 40 (39.6%) children, 48 (47.5%) AYA, and 13 (12.9%) adults  $\geq 40$  years, with male to female ratio of 1.29. Of these, 14 were diagnosed on immunohistochemistry (all were positive for H3K27M, negative for EZHIP and H3K27me3) while 87 cases were diagnosed by sequencing and showed following mutations: H3F3A p.K27M mutation

in 81 cases, H3F3A p.K27E mutation in 2 cases and H3B p.K27M in 4 cases. Location was midline (55; 54.4%), cerebellar (13; 12.8%), spinal (14; 13.8%) and secondary hemispheric (19; 18.8%). Histologically, 8 (7.9%) cases were low-grade. Overall, loss of ATRX-protein expression was seen in 35/101; (34.6%) cases while p53 protein over-expression was seen in 75/101 (74.2%). The children and AYA groups did not have any significant association with gender; however, male preponderance was significantly associated with older adults group ( $p=0.025$ ). Cerebellar and spinal location was significantly associated with children than adults and AYA age-group ( $p=0.048$ ). ATRX loss was more frequent in AYA and adult age-group ( $p=0.003$ ). Type of histone mutation and p53 protein overexpression showed no significant correlation with any of the age groups.

**Conclusions:** Among patients with H3 K27-altered diffuse midline gliomas, children tend to have tumors at cerebellar and spinal location more frequently than in AYA and older adults while ATRX loss is more frequent in AYA and older adults age-group.

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#### PATTERNS OF INVOLVEMENT OF CEREBROSPINAL FLUID SPACES DURING RECURRENCE ACROSS DIFFERENT MOLECULAR SUBGROUPS OF MEDULLOBLASTOMA

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**Background and Aims:** Medulloblastoma has four distinct molecular subgroups: wingless, sonic hedgehog (SHH), group 3, and group 4. The location of relapses in relation to the cerebrospinal fluid (CSF) spaces was investigated in the current study.

**Methods:** Medulloblastoma with known molecular subgroups developing recurrent disease and available magnetic resonance imaging of brain and spine were included in the retrospective study. The imaging during first recurrence was reviewed and classified into several categories as per disease location. Statistical analysis was done using Pearson chi-square test and Fisher's exact test.

**Results:** Forty-eight patients were included in the final analysis. Median age was 8 years, with high-risk disease in 68%. Molecular profiling revealed SHH (20), group 3 (10), and group 4 (18). The

median time to recurrence was 16 months. Local and metastatic relapse was significantly different across molecular groups ( $p < 0.01$ ), with isolated tumor bed recurrences seen in SHH subgroup only. Involvement of ventricular system (inclusive of cistern and recess) was seen in 38% and significantly different across group 3 (70%), group 4 (39%), and SHH (20%) ( $p = 0.03$ ). Involvement of compartments included: lateral ventricle (6), third ventricle (2), suprasellar recess (10), periaqueductal (6), quadrigeminal cistern (10), infratentorial CSF space (8), supratentorial sulcal space (16), cerebellar extraventricular space (16), and spine (27). Disease around hippocampal region (within 1 cm) was seen in 13: group 3 (50%), group 4 (28%), and SHH (15%) ( $p = .12$ ). Nodular metastases were significantly more in group 4 (100%), while group 3 had predominantly diffuse disease (70%), ( $p < 0.01$ ).

**Conclusions:** Recurrence patterns in the ventricular system are diverse across molecular subgroups, with highest propensity for group 3. The lower rates of ventricular relapse and around hippocampus in SHH medulloblastoma provide the opportunity to explore hippocampal avoidance-craniospinal irradiation, particularly for this subgroup, while it will be unsafe for group 3/ group 4 medulloblastoma.

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#### THE ST. JUDE GLOBAL VIRTUAL PEDIATRIC NEURO-ONCOLOGY FELLOWSHIP: A NOVEL APPROACH TO INCREASING PEDIATRIC NEURO-ONCOLOGY CAPACITY IN LOW- AND MIDDLE- INCOME COUNTRIES

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**Background and Aims:** The majority of children with central nervous system (CNS) tumors reside in low- and middle- income countries (LMICs), yet one of the limiting factors in their management is the availability of trained pediatric neuro-oncologists. The St. Jude Global Virtual Pediatric Neuro-Oncology Fellowship (VPNOF) was launched in 2022 with the goal of increasing capacity of CNS tumor experts in LMICs.

**Methods:** A targeted needs assessment (TNA) was performed using semi-structured interviews with 11 international pediatric neuro-oncologists with global mentorship experience, either as mentors or mentees, to identify content and career needs relevant for the care of children with CNS tumors in LMICs.

**Results:** A two-year fellowship program was designed based on the TNA results, with a curriculum tailored for LMICs. The program structure is two-pronged. First, clinical competency facilitation via an online lecture-based learning month, monthly teaching sessions, two clinical rotations at a mentor's site, clinical discussions via bi-monthly virtual tumor boards, and case discussions with mentors. Mentorship is the second major component, consisting of matching each fellow with two mentors, one from the trainee's region and one global mentor. These formal mentorship triads allow the definition of both career and institutional goals to advance pediatric CNS tumor management. In 2022, the program's first year, 5 trainees were selected from a pool of 52 applicants, from pediatric cancer units in 5 countries: Armenia, China, Indonesia, Mexico, and Pakistan. The program aims to recruit six fellows annually, with a goal to measure the impact on patient outcomes and local capacity.

**Conclusions:** The VPNOF is an innovative approach to maximizing training resources and leveraging global mentorship to train pediatric oncologists in resource-limited settings in CNS tumor management, including the establishment of a local network, and provide mentorship in career development and multi-disciplinary care. Data on its impact on patient outcomes and local service delivery is currently being collected.

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#### NON-INVASIVE GRADING OF PEDIATRIC BRAINSTEM GLIOMA USING QUANTITATIVE SUSCEPTIBILITY MAPPING

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**Background and Aims:** Brainstem gliomas have a high incidence in children – accounting for 10%–20% of all childhood primary brain tumors with a high rate of malignancy. The treatment of gliomas depends to a large extent on their grades, which affects the survival rate. Although preoperative Magnetic Resonance Imaging (MRI) has a very important role in detection and differential diagnosis of intracranial tumors, it is inadequate for tumor characterization and grading. Besides, tumor biopsy is useful but an invasive and time-consuming procedure. In order to improve preoperative grading, various MRI techniques are being used in clinical settings. Quantitative susceptibility mapping (QSM) is a recently developed MRI technique for quantifying the spatial distribution of magnetic susceptibility (iron content) by assessing the intratumoral susceptibility signals (ITSS) caused by tumor vascularization, hemorrhage or necrosis that cannot be shown by conventional MRI. The aim of this study is to investigate the usefulness of QSM grading for preoperative tumor grading.

**Methods:** A total number of 20 children ranging from 5 to 14 years old underwent routine brain MRI and QSM examinations with histopathological diagnosis of glial tumor. QSM image processing was done and ITSS numbers for QSM grading were determined by two radiologists blinded to histopathological diagnoses. Statistical analysis including correlations between QSM and pathological grading and also inter-rater reliability of gradings were evaluated.

**Results:** There was a strong positive correlation between both pathological and QSM grading ( $r=0.85$ ,  $p<0.001$ ) and also a strong agreement between ITSS scores and pathological gradings (Kappa=0.783,  $p<0.001$ ).

**Conclusions:** ITSS scores of QSM have a promising role in non-invasive preoperative pediatric brainstem glioma grading and should be considered as complementary sequences to routine MRI studies

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#### CURRENT SITUATION OF INTRACRANIAL SARCOMAS IN A PERUVIAN HOSPITAL

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**Background and Aims:** Primary Intracranial Sarcoma (IS) are uncommon tumors, which incidence is based on few case reports worldwide,

ranging from 0.1 to 4.3%. A high incidence is observed in recent years in Peru, we present this data willing to increase the actual literature.

**Methods:** This study is a retrospective review from a Peruvian hospital, including clinical and biological characteristics, and the management of 27 patients since 2018 to 2021. The analysis was done with R and RStudio.

**Results:** Thirty patients with IS were identified; only 27 patients with complete data were analyzed. The median age was 6 years (range 4.0-8.5) and we found a higher frequency in female patients (55.6%). The main symptom at debut was related to intracranial hypertension (92.6%); 7 patients presented hydrocephalus on admission, and all of them required surgical management. We found a similar number of patients going to gross total resection (48.1%) or subtotal resection (48.1%), also 16 patients underwent surgical reintervention (including management of complications). The main chemotherapy scheme used was ifosfamide, carboplatin and etoposide (ICE), followed by focal radiotherapy, 3D conformational, dose of 59.4 Gy (54 - 66Gy); one patient received craniospinal radiotherapy because of CSF infiltration. The median follow up was 21.6 months (2-53 months). The 2-year overall survival rate was 66% (95% CI, 49%-89%) and 2-year Event-free survival rate was 70% (95% CI, 54%-91%), 7 patients presented recurrence of tumor in the surgical bed and 8 patients died during the follow up.

**Conclusions:** IS has a high incidence in Peru. Despite its aggressiveness, multimodal treatment seems to offer some benefit to these patients. We consider it is necessary a longer follow up to determine factors associated with better prognosis.

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#### PREDICTIVE VALUE OF ACQUIRED NYSTAGMUS FOR VISION IMPAIRMENT IN CHILDREN WITH A BRAIN TUMOR: A RETROSPECTIVE STUDY

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**Background and Aims:** Visual impairment (VI), which is defined as visual acuity (VA) or visual field (VF) loss, is common in children with a brain tumor, especially optic pathway tumors, and may affect their quality of life. Unfortunately, especially in younger children, there often is a delay in recognizing visual impairment. The cause of this is multifactorial, for example children's greater ability to adapt and compensate, their inability to communicate their vision loss and/or their inability to cooperate during VA/VF testing. Children with a brain tumor might concurrently have ocular motility diseases and acquired nystagmus. The aim of this retrospective cohort study is to investigate whether

acquired nystagmus is predictive of VI in children with a brain tumor, to improve early recognition and initiation of therapy to prevent further visual deterioration.

**Methods:** Data on tumor characteristics, VA, VF and orthoptical investigations were collected from medical records of 710 children. We compared clinical characteristics between children with and without nystagmus. Linear regression analyses were used to investigate the predictive value of respectively acquired nystagmus as well as other patient, tumor and ophthalmologic characteristics on vision impairment.

**Results:** The cohort consisted of 389 patients with a brain tumor and visual assessment, amongst which 95 with nystagmus (24.4%). Mean Best Corrected Visual Acuity (BCVA) was 0.10 LogMAR [CI 0.06-0.14] in control and 0.50 LogMAR [CI 0.35-0.66] in nystagmus group ( $P < 0.001$ ). A multivariate regression analysis in the nystagmus group demonstrated a reduced BCVA on LogMAR scale of 0.61 LogMAR ( $P < 0.001$ ) for suprasellar located tumor, 0.40 LogMAR ( $P = 0.024$ ) for horizontal nystagmus and 0.31 LogMAR ( $P = 0.039$ ) for mixed nystagmus, and an increased BCVA on LogMAR scale of -0.05 LogMAR ( $P = 0.002$ ) for age at diagnosis.

**Conclusions:** Acquired nystagmus and its type is an independent predictor of vision impairment in children with a brain tumor.

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#### STUDY OF THE ANTIPROLIFERATIVE EFFECT OF POLYPHENOLS FROM GRAPE MUST ON PEDIATRIC TUMORS

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**Background and Aims:** Polyphenols comprise a wide family of natural compounds present in plants that could promote anti-aging and anticancer cell responses by molecular mechanisms that are not fully understood. Grape juice of the Airén white variety, used to manufacture children food, has a polyphenol content like other grape varieties, with higher concentration of quercetin and catechin. These polyphenols, as well as resveratrol, have an antiproliferative effect on some leukemia cell lines. Leukemias are the most frequent pediatric tumors, and medulloblastoma (MB) is the most common central nervous system (CNS) malignancy in children. The main goal of our project is to analyze the antitumor properties of relevant polyphenols found in this grape must on cell lines derived from MB and leukemia.

**Methods:** Leukemia cell lines HL60 (Human promyelocytic leukemia) and Jurkat (leukemic T-cell lymphoblast), as well as the MB cell lines, DAOY and D283, were treated with different concentrations of resveratrol, quercetin and catechin for 24, 48 and 72 hours. Cell proliferation was evaluated by MTT proliferation assay.

**Results:** The polyphenols evaluated showed a distinct effect on the different cell lines. Resveratrol inhibits proliferation in every cell line, as expected. Quercetin, but not catechin, inhibited cell growth in both leukemia cell lines. Quercetin inhibited proliferation of Daoy cells but promoted cell growth on D283 cell line. Unexpectedly, catechin promotes proliferation in both MB cell lines.

**Conclusions:** The negative effect of polyphenols on proliferation could be due to an apoptotic process, but improvement in proliferation involves other pathways that are under investigation. Differences observed in the MB lines could be due to their different molecular subtypes. Natural compounds can be used as nutritional supplements which help or improve conventional therapies. Thus, their specific effects on each type of tumor must be meticulously analyzed. Acknowledgments: Universidad Francisco de Vitoria.

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#### DISCREPANCY BETWEEN THE OUTCOME OF VISUAL ACUITY AND VISUAL FIELD IN CHILDREN WITH NON-NEUROFIBROMATOSIS RELATED CHIASMATIC GLIOMAS

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**Background and Aims:** Sporadic optic pathway gliomas (OPG) typically occur in the first decade of life and pose significant risk of permanent visual loss. Chemotherapy is standard for clinical and/or radiographic progression, occasional debulking surgery, and rarely radiation. Reports on visual outcome typically focus primarily on visual acuity (VA) alone. We aim to compare the VA with the final visual field (VF).

**Methods:** Charts from all children with non-neurofibromatosis chiasmic OPG treated at Schneider Children's Medical Center from 2004 - 2023 were reviewed. Visual outcome including VA & VF were the primary outcome measures.

**Results:** 14 children (50% boys), with a mean age at presentation of  $4.9 \pm 5.0$  years, (follow-up  $7.3 \pm 5.2$  years) were included. 71% ( $n=9$ ) presented with ophthalmological abnormalities: strabismus ( $n=5$ ), nystagmus ( $n=4$ ), and poor vision ( $n=1$ ). On initial examination 57% of eyes ( $n=16$ ) had partial optic atrophy, 25% ( $n=7$  eyes) had diffuse optic atrophy and 18% ( $n=5$  eyes) had normal optic discs. At final follow-up visit VA was not different than at presentation ( $P=0.360$ ), with 57% of eyes ( $n=16$ ) having VA  $\geq 6/12$ . 21 eyes had repeat VF testing demonstrating unchanged damage in 71% ( $n=25$ ), 10% ( $n=2$ ) improvement, and 19% ( $n=4$ ) worsening. Spearman's correlation coefficient between first and last VF exams was high  $R=0.736$ ,  $P < 0.001$ . Interestingly, there was

poor correlation between VA and VF damage, with a Spearman's correlation coefficient of  $R=0.035$ ,  $P=0.433$ . 46% (13/28) had a significant VA vs. VF discrepancy demonstrating a good VA ( $>6/12$ ) but severe VF damage.

**Conclusions:** The most common visual outcome for children with chiasmatic OPG after treatment is stability. There is frequent discrepancy between VA and VF. Evaluation of VF constriction and not just VA is essential. Accurate determination of visual disability enables necessary adaptations at school and appropriate assessment for career choice & eligibility for a driving license.

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#### PEDIATRIC DIFFUSE INTRINSIC PONTINE GLIOMAS: IS THERE ANY POTENTIAL FOR BETTER SURVIVAL?

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**Background and Aims: Purpose:** The aim of this study is to assess the treatment results of patients with diffuse intrinsic pontine gliomas (DIPG) in a tertiary university hospital in Turkey.

**Methods: Materials and Methods:** All cases diagnosed with DIPG and received treatment in the Pediatric Oncology Department, between January 2008 to January 2021 were retrospectively evaluated. The recommendations of the Response Assessment in Pediatric Neuro-Oncology (RAPNO) working group were used in the diagnosis and evaluation of treatment response. All patients underwent local radiotherapy (RT). Nimotuzumab (NIM), vinorelbine (VIN), and temozolomide (TMZ) are the medications given after radiotherapy. Temozolomide was used as a single agent at a dose of 180 mg/m<sup>2</sup>/day for 5 days within a 28-day cycle. Nimotuzumab was given at a 150 mg/m<sup>2</sup>/dose intravenous administration combined with vinorelbine weekly in the first 12 weeks, then every alternate week until progression, or the end of 52 weeks (including 32 doses in total). Patients with overall survival (OS) longer than 24 months were named long-term survivors (LTSs).

**Results: Results:** The median OS for the study group is 12 months. The mean number of nimotuzumab doses was 21.6 (median 24), from 4 to 32 doses. The median OS for patients who were treated with and without nimotuzumab were 16 and 6 months, respectively ( $p < 0.05$ ). After the nimotuzumab therapy, we reported four cases with partial response (PR) (44.4%) and one patient with stable disease (SD) (11.1%). Four patients (22.2%) were LTS. The median age of LTS was 14 (range, 8 to 15) years. Median OS for DIPGs older than 10 years and  $<10$  years were 16 months and 8 months respectively ( $p=0.61$ )

**Conclusions:** In conclusion, DIPGs have poor prognosis in pediatric population and Nimotuzumab therapy could be a promising treatment option for DIPG.

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#### EXPLORING THE EFFECT OF VISUAL TELEREHABILITATION PROGRAM ON VISUAL PERCEPTION IN CHILDREN WITH HEMIANOPIA CONSECUTIVE TO A BRAIN TUMOUR, PRELIMINARY RESULTS OF A PILOT STUDY

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**Background and Aims:** Brain tumours (BT) in children often lead to visual impairment, which represents significant morbidity for long-term survivors. A recent Children Cancer Survivor Study showed that 22.5% of patients with astroglial tumours had visual impairment five years after the diagnosis. In the pediatric population with hemianopia, there are no standardized protocols for managing vision loss. In this pilot study, a 6-week home-based visual telerehabilitation program (VTP) evaluated visual changes in 10 children with hemianopia consecutive to a BT.

**Methods:** The study included 10 patients aged 8-18 years old with hemianopia consecutive to a pediatric BT. Five patients had a chiasmatic tumour (CT), other 5 had a tumour located outside of the chiasm (OCT). Patients followed a 6-week VTP on a virtual reality device at home with remote control of the device from the UHN laboratory. Visual assessments performed at baseline, 2, 4, 6 weeks, with follow-ups at 1 and 6 months to check the visual field, contrast sensitivity and reading speed. A quality-of-life (QoL) questionnaire was also filled out by patients and parents at every visit.

**Results:** The preliminary results of 8 patients have been analyzed. Four patients (3 CT, 1 OCT) showed visual field improvement with increased luminance perception in the monocular Humphrey test. Four patients (2 CT, 2 OCT) showed visual field improvement in the binocular Esterman field analysis. Reading speed improved in 6 patients (3CT, 3OCT). All patients had significant improvement in contrast sensitivity and QoL.

**Conclusions:** The preliminary results of this study showed that this VTP was feasible in children. The program was effective, especially for patients with CT in improving the visual field with an impact on contrast sensitivity, reading speed and QoL. Further studies are in development to confirm these results and identify the most appropriate schedules to optimize visual outcomes.

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### TARGETED THERAPY IN PEDIATRIC LOW-GRADE GLIOMAS; REAL WORLD DATA IN THE CONTEXT OF CONVENTIONAL TREATMENT MODALITIES

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**Background and Aims:** Treatment of progressive inoperable pediatric low-grade gliomas (pLGG) is challenging with chemotherapy providing poor long-term disease control. Majority of pLGGs harbor alterations within MAPK pathway targetable by small molecule inhibitors. We aimed to evaluate efficacy and toxicity of these inhibitors, namely dabrafenib in BRAF-V600E positive pLGG and trametinib in KIAA1549::BRAF fused or NF1-associated pLGGs.

**Methods:** Retrospective review of patients with molecularly profiled pLGGs treated with MAPK inhibitors at our institutions was performed. Response to targeted therapies was evaluated using RAPNO criteria and volumetric analysis.

**Results:** In total, 26 patients treated with BRAF/MEK inhibitor were eligible for this study. Namely, patients with BRAF-V600E pLGG were treated with dabrafenib (n=11) or KIAA1549::BRAF fused/NF1-associated pLGG treated with trametinib (n=15) outside clinical trials. Overall response rate (ORR) of the whole cohort using RAPNO criteria was 46.1% (12/26). There was a discordance observed between bidimensional and volumetric analysis in 7 patients (26.9%). ORR of patients with BRAF-V600E pLGG was 64% (median time to response 2.6 months). In trametinib cohort, 33% achieved partial response (median time to response 6.6 months). In total, 6 patients experienced progression during trametinib therapy. Six patients were treated with vinca alkaloids when trametinib was added into the combination. All 15 patients experienced trametinib-related adverse event (grade 3 in 40%) with frequent dose reductions/interruptions (73%).

**Conclusions:** Dabrafenib and trametinib represent novel treatment modality in pLGG patients with clinical benefit in proportion of patients. Nevertheless, targeted therapies alone do not represent a magic bullet to cure all patients but rather provide another therapeutic option in progressive pLGG.

EP476/#449 | Poster Topic: AS05 SIOP Scientific Program/AS05.m  
Brain Tumours

### TREATMENT OUTCOME OF RESPONSE-BASED RADIOTHERAPY IN CHILDREN AND ADOLESCENTS WITH CENTRAL NERVOUS SYSTEM NONGERMINOMATOUS GERM CELL TUMORS: RESULT OF A PROSPECTIVE STUDY

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**Background and Aims:** The optimal dose and range of radiotherapy for the central nervous system (CNS) nongerminomatous germ cell tumors (NGGCTs) have not been unified. Therefore, this study aimed to investigate the effect of individualized radiotherapy, based on the response to induction chemotherapy combined with surgery, on the prognosis of patients with NGGCTs.

**Methods:** Based on the imaging examination and tumor markers after induction chemotherapy and pathologic results of second-look surgery, patients with NGGCTs in this study received different radiotherapy strategies, including R1 (30.6 Gy whole ventricular radiotherapy and 54 Gy tumor-bed boost), R2 (30.6 Gy craniospinal irradiation and 54 Gy tumor-bed boost), R3 (36 Gy craniospinal irradiation and 54 Gy tumor-bed boost), and R4 (36 Gy craniospinal irradiation and 54 Gy tumor-bed boost with 45 Gy to metastatic spinal lesions).

**Results:** A total of 51 patients were enrolled in this study between January 2015 and March 2021, with a median age of 10.3 years. There were 34 patients who had localized NGGCTs, and 17 had metastatic NGGCTs. The 3-year event-free survival (EFS) and overall survival (OS) of the entire cohort were 70.2% ± 6.9% and 77.5% ± 6.0%, respectively. The 3-year EFS of patients with localized and metastatic NGGCTs were 75.5% ± 7.6% and 62.7% ± 12.3%, respectively. The 3-year EFS of patients achieving a complete response, partial response, stable disease, and progressive disease after induction chemotherapy was 85.7% ± 13.2% vs. 74.2% ± 11.7% vs. 57.8% ± 12.2% vs. 0% ( $P = 0.01$ ), respectively. The 3-year EFS and OS of the 18 patients receiving R1 radiotherapy were 88.9% ± 7.4% and 94.4% ± 5.4%, respectively.

**Conclusions:** This study suggests that an individualized radiotherapy strategy based on the response to induction chemotherapy and surgery is feasible, and promising results are still achieved after reducing radiation intensity in patients with good responses.

EP477/#486 | Poster Topic: AS05 SIOP Scientific Program/AS05.m  
Brain Tumours

### TREATMENT OUTCOME OF RESPONSE-BASED RADIOTHERAPY IN CHILDREN AND ADOLESCENTS WITH CENTRAL NERVOUS SYSTEM GERMINOMA: RESULT OF A PROSPECTIVE STUDY

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**Background and Aims:** The optimal dose and range of radiotherapy for central nervous system (CNS) germinoma have not been unified. This study aimed to investigate the effect of individualized radiotherapy on the prognosis of patients with CNS germinoma.

**Methods:** Based on the imaging examination and tumor markers after induction chemotherapy and pathologic results of second-look surgery, patients with germinoma in this study received different radiotherapy strategies, including R1 (24 Gy whole ventricular irradiation and 40 Gy tumor-bed boost), R2 (24-30 Gy craniospinal irradiation and 54 Gy tumor-bed boost), R3 (24 Gy craniospinal irradiation and 40 Gy tumor-bed boost), and R4 (30 Gy craniospinal irradiation and 54 Gy tumor-bed boost with 45 Gy to metastatic spinal lesions).

**Results:** A total of 77 patients were enrolled in this study between January 2015 and March 2021, with a median age of 13.1 years. There were 58 patients with localized disease and 19 patients with metastatic disease. The 3-year event-free survival (EFS) and overall survival (OS) of the whole cohort were  $94.7\% \pm 2.6\%$  and  $96.0\% \pm 2.3\%$ , respectively. The 3-year EFS for patients with localized and metastatic disease were  $96.6\% \pm 2.4\%$  and  $89.2\% \pm 7.2\%$ , respectively. There were 47% of the patients undergoing second-look surgery, all of which were proved to have achieved pathological complete response. The 3-year EFS of the patients receiving R1, R2, R3, and R4 radiotherapy were 100%,  $94.1\% \pm 5.7\%$ , 100%, and  $86.2\% \pm 9.1\%$ , respectively. Compared to previous studies, the radiotherapy intensities were decreased in selective patients with localized diseases receiving R1 radiotherapy and those with metastatic diseases receiving R3 radiotherapy without compromising the treatment outcomes.

**Conclusions:** This study suggests that an individualized radiotherapy strategy in patients with CNS germinoma based on the response to induction chemotherapy and surgery is feasible, and decreases the radiotherapy-related side effects in specific patients.

EP478/#738 | Poster Topic: AS05 SIOP Scientific Program/AS05.n  
New Drugs/Experimental Therapeutics

### ASSESSING THE IMPACT OF THE CANADIAN U-LINK. CARE WEBSITE: A NATIONAL SURVEY OF HEALTHCARE PROVIDERS' VIEWS ON EARLY PHASE CLINICAL TRIALS ACCESS FOR CHILDREN WITH CANCER

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**Background and Aims:** The Canadian U-Link.care is an online database of early phase clinical trials in Canada for children with cancer, that includes information regarding trial design, study objectives and eligibility, comprising family-friendly content with access to financial resources. U-Link.care was launched in September 2021. The objective of our survey was to assess the impact of U-Link.care on healthcare providers' (HCP) views on access to early phase clinical trials for children with cancer.

**Methods:** A RedCap survey was distributed via email to HCP including attending physicians, fellows, nurse practitioners, physician's assistants, and research nurses from Canadian paediatric oncology centres in May 2021 prior to the launch, and January 2023, 16 months post-launch. It consisted of multiple choice and short answer questions related to the website, early phase recruitment and patient referrals.

**Results:** The 2023 survey yielded relevant representation from Canadian HCP with 59 responses across 15 centres, comparable to 2021 with 53 responses across 13 centres. Most HCP felt knowledgeable (somewhat 50%, strongly 27.6%) about early phase clinical trials and comfortable counselling patients (somewhat 48.3%, extremely 36.2%). U-Link.care was in the top 3 knowledge sources (15.4%), along with clinicaltrials.gov (29.7%) and the Children's Oncology Group website (21.1%). A majority of HCP who used U-Link (n=32), declared that U-Link.care increased their knowledge of clinical trials available in Canada (87.5%) and that the website was easy to use (81.25%). Nevertheless, common barriers to referral and enrolment remained a) lack of trial availability at a given site and b) inability to travel to a study site due to distance and/or financial limitations.

**Conclusions:** U-Link.care has become an important tool to Canadian paediatric oncology HCP. Still, the lack of trial availability and high cost of travel to centres continue to be the leading obstacles to early phase clinical trials access. Further quality improvement initiatives are needed to address these barriers.

EP479/#339 | Poster Topic: *AS05 SIOP Scientific Program/AS05.n New Drugs/Experimental Therapeutics*

### LONG-TERM FOLLOW-UP OF THE EFFICACY AND SAFETY OF LAROTRECTINIB IN PAEDIATRIC PATIENTS WITH TROPOMYOSIN RECEPTOR KINASE (TRK) FUSION CANCER

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**Background and Aims:** Neurotrophic tyrosine receptor kinase (*NTRK*) gene fusions are oncogenic drivers in various tumour types. Larotrectinib is a highly selective TRK inhibitor approved for tumour-agnostic use in patients with TRK fusion cancer based on a rapid, robust and durable objective response rate (ORR) in patients with various cancers. Here, we report data on an expanded cohort of paediatric patients with non-CNS primary, TRK fusion cancer treated with larotrectinib.

**Methods:** Patients aged <18 years with TRK fusion cancer were included. Responses were independent review committee (IRC)-assessed (RECIST v1.1).

**Results:** As of July 2022, 94 patients were eligible for IRC assessment. Tumour types included infantile fibrosarcoma (52%), other soft tissue sarcoma (41%), congenital mesoblastic nephroma (2%), thyroid cancer (2%), breast cancer (1%), bone sarcoma (1%) and melanoma (1%). One

patient had known brain metastases at baseline. The ORR was 84% (95% CI 75–91): 46 (49%) complete responses (including 12 pathological complete responses), 33 partial responses (35%), 10 stable disease (11%), three progressive disease (3%) and two not evaluable (2%). Median time to response was 1.8 months. Treatment duration ranged from 1 to 75+ months. Medians for duration of response and progression-free survival were 38.4 (95% CI 26.7–not estimable) and 36.1 months (95% CI 25.5–52.5), respectively, with median follow-ups 30.9 and 32.5 months. Median overall survival (OS) was not reached at a median follow-up of 41 months; the 41-month OS rate was 89% (95% CI 83–96). Treatment-related adverse events (TRAEs) were mostly Grade 1/2. Four patients discontinued treatment due to TRAEs.

**Conclusions:** With extended follow-up, larotrectinib demonstrated remarkable and long-lasting responses, extended survival and a favourable safety profile in paediatric patients with TRK fusion cancer. This supports the wider adoption of next-generation sequencing panels, which include *NTRK* gene fusions, to identify paediatric patients who would benefit from larotrectinib therapy.

EP480/#606 | Poster Topic: *AS05 SIOP Scientific Program/AS05.n New Drugs/Experimental Therapeutics*

### DEVELOPMENT OF A NEW BIOMARKER AT THE LEVEL OF GENE CHANGE IN CISPLATIN OTOTOXICITY

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**Background and Aims:** Cisplatin is a chemotherapeutic agent used in the treatment of many childhood cancers. The most important side effects of this alkylating agent, which is effective through DNA platinization, are nephrotoxicity, ototoxicity and neurotoxicity. Cisplatin ototoxicity commonly causes sensorineural, bilateral, irreversible and progressive hearing loss. Cisplatin-induced hearing loss is particularly important in very young children, as it leads to impaired language acquisition, difficulties in learning and psychological development, and reduced social functioning that will affect them for the rest of their lives. The aim of this study is to investigate biomarkers that can predict cisplatin ototoxicity in childhood cancers.

**Methods:** In our previous study; we found that ADAM6, SIX3, GNAS, NDUFV1, H19, DEFA4, ZIM2 genes were mutant in 5 patients with severe hearing loss by comparative genomic hybridization analysis. In line with these data, we aimed to detect the proliferation of 7 mutated genes in a larger patient population. DNAs were isolated from mononuclear cells separated from the peripheral blood of 82 patients who received cisplatin therapy, and then RT-PCR analysis was performed



for 7 genes. Patients' diagnoses, cumulative cisplatin doses, Brock and Muenster scores, severity of ototoxicity were evaluated.

**Results:** Of the 82 patients included in the study; 44 were boys and 38 were girls. Diagnostic distribution: Neuroblastoma 42.7%, CNS tumor 14.6%, germ cell tumor 11%, hepatoblastoma 11%, nasopharyngeal carcinoma 6.1%, osteosarcoma 4.9%, other tumors 9.7%. The median cumulative dose of cisplatin was 400 mg/m<sup>2</sup>. 28% patients had ototoxicity. A correlation was found between the presence of ototoxicity and the amplification of the ZIM2 gene (correlation coefficient 0.461,  $p=0.003$ ). Especially the patients with severe hearing loss and the group with ZIM2 gene amplification were correlated (correlation coefficient 0.38,  $p=0.017$ ).

**Conclusions:** New biomarkers are needed to predict ototoxicity. The ZIM2 gene has been identified as a candidate biomarker that needs to be studied in more detail in our study.

EP481/#575 | Poster Topic: AS05 SIOP Scientific Program/AS05.n  
New Drugs/Experimental Therapeutics

#### FACTORS INFLUENCING UPTAKE OF INDIVIDUALISED PRECISION MEDICINE TREATMENT RECOMMENDATIONS FOR HIGH-RISK PAEDIATRIC ONCOLOGY PATIENTS: RESULTS FROM THE PRISM ENGAGEMENT WITH CLINICIANS (PRE-CLIN) STUDY

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**Background and Aims:** The determinants of clinician decision-making in the application of precision medicine (PM)-derived therapies for paediatric high-risk cancer remain poorly defined. PRE-CLIN aims to determine the factors associated with clinician uptake of individual treatment recommendations, inform the approach to future recommendation delivery, and assist with rationalising pre-clinical experiments for individual patient use.

**Methods:** PRE-CLIN is a retrospective analysis of the PRECISION Medicine for Children with Cancer (PRISM) cohort. Patients enrolled in PRISM from 2017-2020 were reviewed for patient-, disease- and recommendation-related factors associated with uptake of treatment recommendations.

**Results:** PM-derived treatments were recommended to 291/403 (72.2%) patients. A total of 504 individual recommendations were made, some patients received >1 recommendation. Patients lost to follow-up or deceased prior to recommendations (43/291) were excluded. Clinicians decided to take up <sup>3</sup>1 recommendation in 114/248 (45.9%) patients. There were 307 individual decisions made about recommendations, 128/307 decisions (41.7%) were for treatment

uptake. Progressive disease was associated with decisions for treatment uptake (OR 4.49, 95% Confidence Interval 2.74-7.34,  $p<0.01$ ). Only 15/179 (8.4%) decisions to not follow a recommendation were due to inability to access medications. Decisions to pursue recommended therapy were more likely in central nervous system (CNS) tumours (61/128) compared to solid (57/128) or haematological malignancies (10/128) ( $p=0.05$ ). More patients with stable CNS tumours (30/81; 37%) received recommended therapies compared to those with solid (21/82; 25.6%) or haematological malignancies (1/21; 4.8%) in stable disease ( $p=0.01$ ). Decisions regarding recommendations were not associated with the size of centre, oncologist experience, enrolment age, timepoint of enrolment (diagnosis/relapse), or availability of preclinical experiment results.

**Conclusions:** Uptake of PM-derived therapy recommendations appears to be linked with disease type and state. Relationships between tier of recommended therapy and route of administration will also be examined. Future studies in PRECLIN will further inform a framework to understand and support clinician decision-making in high-risk paediatric cancers.

EP482/#270 | Poster Topic: AS05 SIOP Scientific Program/AS05.n  
New Drugs/Experimental Therapeutics

#### THE NATIONWIDE PEDIATRIC CANCER GENOME PROFILING PROJECT: A REPORT FROM THE JCCG-TOP2 STUDY

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**Background and Aims:** Pediatric cancer encompasses a wide and heterogeneous range of rare cancers for which comprehensive genomic profiling has immense potential to provide novel diagnostic and therapeutic solutions. To establish the platform for pediatric cancer-optimized genomic medicine, we commenced a nationwide cancer genome screening project in January 2022, in collaboration with Japan Children's Cancer Group (JCCG).

**Methods:** In this prospective observational study, FFPE tumor and matched blood samples are collected from patients aged 0-29 years with solid tumor. The sequencing analysis uses the TOP2 system to analyze 737 and 456 genes in the DNA and RNA panels, respectively, along with the assessment of genome-wide copy number variations and allelic imbalances. Central pathology review is conducted in parallel, and the multidisciplinary team discusses the clinical significance of genomic alterations.

**Results:** As of February 10, 2023, a total of 207 patients have been enrolled from the 50 institutes across Japan. The patients were enrolled: during the initial diagnosis in 34 (16%) patients, after the first-line treatment in 117 (57%) patients, and upon either disease progression or relapse in 56 (27%) patients. Thus far, the results have been returned in 147 patients. The tumor types include central nervous system (CNS) tumors 47 (32%) and non-CNS tumors 100 (68%). Oncogenic driver fusion genes were identified in 27 (18%) patients. Two (1%) patients had high tumor mutation burden of  $\geq 10$  mutations per megabase. The potentially actionable findings were identified in 93 of 147 (63%) patients [Diagnosis: 64 (44%), Prognosis: 34 (23%), and Treatment: 40 (27%)].

**Conclusions:** These interim results suggest promising evidence in genomic medicine for pediatric cancers, and its incorporation into standard clinical practice would have substantial impact for all pediatric and adolescent/young adult patients, both at diagnosis and at relapse. The feasibility and clinical utility of this platform will be further evaluated.

EP483/#376 | Poster Topic: AS05 SIOP Scientific Program/AS05.n New Drugs/Experimental Therapeutics

#### RESISTANCE TO ALK TYROSINE KINASE INHIBITORS IN PAEDIATRIC CANCER IS MEDIATED THROUGH ACTIVATION OF BYPASS SIGNALLING TRACKS INCLUDING IL10R/STAT3, RAS/MAP KINASE AND FGFR

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**Background and Aims:** One of the most prominent therapeutic targets for childhood cancers is the anaplastic lymphoma kinase (ALK), aberrantly activated in anaplastic large cell lymphoma (ALCL), neuroblastoma (NB) and inflammatory myofibroblastic tumours (IMT). Multi-generation ALK inhibitors have been used successfully in the treatment of adults, but as expected, resistance is a clinical problem and research is underway to determine how and why this occurs to facilitate the development of strategies to circumvent or treat ALK TKI resistant disease. In our lab, we have identified both on-target and bypass mechanisms of resistance to ALK TKIs which highlight therapeutic strategies that help to prevent/delay the development of resistance.

**Methods:** CRISPR activation screens of both NB and ALCL were conducted detecting genes whose overexpression enables cells to survive in the presence of ALK inhibitors. Cell lines rendered resistant to ALK inhibitors through chronic exposure to increasing concentrations of the drug, as well as biopsies from ALK inhibitor resistant patients were also examined for expression of the identified genes.

**Results:** A number of bypass resistance mechanisms were identified including activation of FGFRs, STAT3/IL10R and Ras/MAPK. It follows that inhibition of these pathways induced tumour regression in models of ALK inhibitor resistant disease but furthermore, we show that inhibitors of these pathways act in synergy with ALK TKIs in a strategy that is predicted to prevent the emergence of resistance via these routes.

**Conclusions:** Based on these data, we propose that use of single targeted agents is more likely to lead to resistance than clinical application of combinations of these drugs. In addition, due to the synergistic activity of the identified drug combinations, their use as upfront therapeutic approaches will allow a reduction in the individual doses used, which may not only reduce the side-effects associated with these agents, but also delay or prevent the emergence of resistance.

EP484/#412 | Poster Topic: AS05 SIOP Scientific Program/AS05.n New Drugs/Experimental Therapeutics

#### WHAT IS THE BEST WAY TO ADMINISTER TARGETED THERAPEUTIC AGENTS TO INDUCE REMISSION AND PREVENT RESISTANCE FROM DEVELOPING?

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**Background and Aims:** Targetted therapeutic agents are gradually being introduced into routine clinical practice for the treatment of children with cancer. While they hold much promise

inducing remission with minimal side-effects, it is increasingly becoming apparent that chronic exposure is required whereby either disease can rapidly return on cessation of therapy or resistance can develop. This is particularly the case for inhibitors of anaplastic lymphoma kinase (ALK) which is aberrantly activated in ALCL and neuroblastoma. We have investigated different schedules of drug administration and combinations of agents with the aim of identifying the best therapeutic approach that allows safe cessation of treatment and/or delays/prevents the emergence of resistant disease.

**Methods:** Cell lines and patient derived xenografts (PDX) were exposed to different therapeutic agents given by various schedules, and time taken to development of resistance was assessed.

**Results:** Our data show that time taken for resistance to ALK inhibitors to develop can be increased by altering not only the administration schedule but also the order in which generations of ALK inhibitors are given. In particular, if the third generation ALK inhibitor lorlatinib is given prior to first or second generation inhibitors, specifically crizotinib, or if third and first generation inhibitors are given together, the time to resistance development is significantly increased. Furthermore, drug holidays or metronomic dosing of the ALK inhibitors were superior to continuous dosing whereby time to development of resistance was significantly higher.

**Conclusions:** We propose that the schedules by which ALK inhibitors are administered to patients can significantly alter treatment outcomes. In particular, improved outcomes may be seen with metronomic dosing or the use of combinations of synergistically acting drugs.

EP485/#1730 | Poster Topic: AS05 SIOP Scientific Program/AS05.o  
*Tumor Biology, Immunology and Immunotherapy*

#### LIQUID BIOPSIES MULTI-MODAL ANALYSIS CORRELATES WITH DISEASE BURDEN AND RESPONSE TO TREATMENT IN PAEDIATRIC CANCER

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**Background and Aims:** The analysis of cell-free DNA (cfDNA) from liquid biopsies for the detection of circulating tumor-derived DNA (ctDNA) offers a powerful, minimally invasive tool for diagnosis, and emerging technologies offer the capability for significantly increased sensitivity, including detection of emerging mutations not otherwise detectable by routine biopsy. Whilst detection of somatic copy number aberrations (SCNAs) and single nucleotide variants (SNV) is currently translating into standard of care, new technologies provide additional capabilities for detection of ultra-low template reads, methylation profiles and nucleosome signatures. We compared results by multi-modal analysis of plasma cfDNA, and correlated with clinical information from pediatric cancer patients.

**Methods:** Between September 2020 and March 2023 more than 250 cases were enrolled in a dual institution protocol for collection of serial, longitudinal, clinically annotated blood samples in paediatric oncology patients, and more than 600 samples were collected. The most frequent diagnoses were neuroblastoma and sarcoma. Samples were analysed by standard of care Illumina panel and whole-genome sequencing, and results were correlated with Oxford Nanopore long-read sequencing, nucleosome signature (Volition H3.1 nucleosome assay) and disease burden (standard Imaging scores).

**Results:** Nanopore and Illumina were highly concordant in detecting clinically relevant somatic SNV and SCNAs, whilst Nanopore sequencing disclosed methylation profiles from as few as 20-50 ng of cfDNA. Longitudinal monitoring using both Nanopore and Volition assays correlated with disease burden in neuroblastoma patients and were predictive of disease recurrence.

**Conclusions:** Our results suggest that application of highly sensitive emerging technologies for detection of ctDNA offer a platform for higher throughput and increased sensitivity of detection of disease allowing accurate diagnosis of disease burden, efficient serial monitoring of disease progression, and early detection of relapse.

EP486/#1117 | Poster Topic: AS05 SIOP Scientific Program/AS05.o  
*Tumor Biology, Immunology and Immunotherapy*

#### COULD EARLY AGE AT DIAGNOSIS BE A POSSIBLE HALLMARK OF CANCER PREDISPOSING SYNDROMES (CPS) IN PEDIATRIC SOLID TUMORS?

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**Background and Aims:** Genetic factors, as cancer predisposing syndromes (CPS), seem to play a major role in childhood malignancies' development. Younger age at diagnosis (AaD) has been previously correlated to CPS in few pediatric solid tumors histotypes, but it has not considered a criterion for genetic testing yet.

**Methods:** Patients (0-18 years) diagnosed with solid cancer from 2013 to 2022, who underwent germline genetic analysis were included in this monocentric, retrospective study, with the aim to explore how AaD distributes according to genetic results.

**Results:** Ninety-seven patients were included, 33% with brain tumors, 30% with rare tumors, 20.6% with Wilms tumors, 12.5% with sarcomas, 4.4% with other single diseases. Sixty-nine patients (61.6%) underwent next-generation-sequencing gene panel testing, 17 patients (15.2%) single gene sequencing. We identified 33 (34%) pathogenic/likely pathogenic variants (PV/LPV), 11 (11.3%) variants of uncertain significance (VUS), and 53 (54.6%) negative results. Among PV/LPV *TP53*, *PTPN11* mutations were the most frequent ones, with a high heterogeneity among the remaining cases. Globally, mean and median AaD were 7.3 years (CI95% 6.13-8.4) and 4.9 years (IQR 10.1). A significant difference in median AaD was found among PV/LPV, VUS and negative results (3.4, 9.2, 7 years respectively, Kruskal-Wallis 7.42,  $p=0.01$ ). At pairwise comparison, median age in PV/LPV group was significantly different from the negative group (Dunn's 16.2,  $p=0.02$  Bonferroni's adjustment). At cumulative incidence analysis on 18-years time frame, cancer diagnosis occurs earlier in PV/LPV group compared to negative and VUS [Median *time-to-diagnosis* 3.3, 7, 9.2 years (Breslow test 9.2,  $p=.010$ )]. At ROC analysis plotting AaD of PV/LPV versus negative results, we obtained a discriminant value of 6.7 years (sensitivity 71%, specificity 56.5%; overall AUC 0.67 CI95%[0.55-0.78];  $p=0.03$ ).

**Conclusions:** We identified a statistically significant correlation between PV/LPV results and early AaD in solid tumors. These findings suggest that AaD might be explored as a criterion for genetic testing in larger studies.

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#### EMAPALUMAB FOR THE TREATMENT OF CRS AND OTHER CYTOKINE STORM SYNDROMES IN PEDIATRIC PATIENTS

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**Background and Aims:** Neutralization of interferon gamma (IFN $\gamma$ ) with the monoclonal antibody emapalumab is FDA-approved for the treatment of relapsed or refractory primary hemophagocytic lymphohistiocytosis (HLH). IFN $\gamma$  may drive the pathophysiology of other cytokine storm syndromes (CSS), including cytokine release syndrome (CRS) and macrophage activation syndrome (MAS). We report on the use of emapalumab at our center for the treatment of CSS.

**Methods:** A retrospective review of all patients treated with emapalumab at the Children's Hospital of Philadelphia (CHOP) between 20NOV2018 and 08MAR2023 was performed. Data, including cytokine panels, were extracted from the medical record into a REDCap database and analyzed in GraphPad Prism 9.

**Results:** Twenty-one patients between 0 and 27 years were treated with emapalumab for the following indications: HLH (N=13; 5 primary, 5 secondary, 3 MAS), CRS (N=6), inflammatory pulmonary disease (N=1), and Crohn's disease (N=1). All patients who received emapalumab for refractory CRS had received CD19-directed chimeric antigen receptor T cells (CART19) for relapsed B-cell acute lymphoblastic leukemia (B-ALL). Patients developed severe CRS (Grade 4) requiring intensive care within six days (range 2-6 days), and received IL6-blockade with tocilizumab (N=6) and/or siltuximab (N=1), steroids, and anakinra (N=3). In four patients CRS resolved; one patient subsequently received dasatinib, and one patient who required ECMO prior to emapalumab for cardiac decompensation progressed and died of cerebral edema. Four patients had bone marrow aspirates/biopsies at day 28, and one patient was lost to follow up. Three patients were in a morphologic and minimal residual disease (MRD) negative remission, and one patient was in a morphologic remission with MRD non-evaluable due to aplasia.

**Conclusions:** Emapalumab has been safely utilized at our center for indications beyond primary HLH, including CRS and MAS. The impact of emapalumab on the short- and long-term efficacy of CART19 should be evaluated in clinical trials.

EP488/#1770 | Poster Topic: AS05 SIOP Scientific Program/AS05.o  
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#### LIQUID BIOPSY FOR CHILDREN AND ADOLESCENTS WITH MALIGNANCIES: EXPERIENCE IN URUGUAY

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**Background and Aims:** Liquid biopsies (LB) from blood samples are non-invasive alternative options for diagnosis, monitoring treatment response, detection of minimal residual disease, and post-therapy surveillance. There is little evidence reported outside major centers in high income countries or cooperative groups; the aim of this study is to report on its use in a referral center in Uruguay.

**Methods:** Retrospective study, including every patient in whom LB was performed using FoundationOne®liquidCDx by Roche®, from 2021 to 2022.

**Results:** Sixty-nine patients (34 boys and 35 girls) were included; median age of 8 years. Underlying malignancies: Soft tissue tumors 18, CNS tumors 11, neuroblastoma 10, osteosarcoma 7, Ewing sarcoma 7, renal tumors 5, others 11. In 65 cases, LB was taken at diagnosis and in 15 (25%) of them, it revealed clinically meaningful information: 3/8 neuroblastomas showing MYCN-amplification; 7/7 patients with Ewing sarcoma EWSR1 fusions. In one soft tissue sarcoma, BCOR alteration was found prompting the categorization of this subtype. In one case with medulloblastoma, alterations in MSH3-ATM-SOX9 helped in molecular characterization and PTCH1-B949fs\*3 in other. In two patients, findings in LB suggested a germline mutation, including a child with a choroidal plexus tumor with TP53 mutation and one patient with pseudopapillary tumor of pancreas, in whom a mutation in MUTYH was reported. In 2/4 patients studied at relapse, potentially targetable alterations were found (ALK, PIK3CA in a child with neuroblastoma and NTRK1 in a child with small clear cell sarcoma). However, patients progressed before access to targeted therapy.

**Conclusions:** LB provided useful data for molecular characterization in a high proportion of patients at diagnosis. Mutations associated to cancer predisposition could be inferred. Actionable targets were found in patients with relapse, however they could not access to treatment. In settings with limited access to molecular characterization of tumors, LB may be a useful tool.

EP489/#724 | Poster Topic: AS05 SIOP Scientific Program/AS05.o  
*Tumor Biology, Immunology and Immunotherapy*

#### CHARACTERIZING DENDRITIC CELL SUBPOPULATIONS FOR CANCER IMMUNOTHERAPY

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**Background and Aims:** Dendritic cells (DCs) are a lineage of hematopoietic stem cells that originate from CD34<sup>+</sup> cells in the bone marrow and have been recognized as effective antigen-presenting cells (APCs) in the immune system. Current principles for DC-based cancer immunotherapy include isolating DCs from blood, activation and

antigen-loading, and reinfusion into patients for antigen-specific T-cell responses. Cancer is a leading cause of death among children, therefore, specific DC-based immunotherapy can play an important role in pediatric patients. Here, we highlight our efforts to characterize DC subpopulations using umbilical cord blood as a reliable source of DCs in their nascent state.

**Methods:** We used fluorescence-activated cell sorting (FACS) to sort DCs from umbilical cord blood using cell surface markers for each DC subpopulation. We used bulk ATAC-Seq and scRNA-Seq for verification of sorted populations and differential expression analysis.

**Results:** We demonstrated that common DC precursors can differentiate into three lineage and unique transcriptional trajectories: plasmacytoid DCs, classical dendritic cells 1 (cDC1) that activate CD8<sup>+</sup> T cells, and cDC2 that activate CD4<sup>+</sup> T cells. Using scRNA-Seq, we further demonstrated differential expression among these three branches that phenotype DC subpopulations, uniquely characterized by the TIM3 marker of T-cell exhaustion.

**Conclusions:** We identified specific DC subpopulations that carry the inhibitory TIM3 and further identified markers that can enhance DC-mediated activation of antigen-specific T cells. These markers include inhibitory sialic acid-binding immunoglobulin-like lectin (Siglec) receptors, which are features of specific DCs from cancer patient samples. Our goal is to further delineate the complex character of these DC subpopulations using a multi-omics approach.

EP490/#437 | Poster Topic: AS05 SIOP Scientific Program/AS05.o  
*Tumor Biology, Immunology and Immunotherapy*

#### ROUTINE WHOLE GENOME SEQUENCING IN CHILDREN WITH SOLID TUMOURS IS FEASIBLE AND DELIVERS CLINICAL BENEFIT

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**Background and Aims:** With the growing utility of whole genome sequencing (WGS) NHS England has commissioned paired (germline and tumour) WGS for children with suspected malignancies, but its clinical impact has not been assessed. After establishing feasibility, WGS was made available to all patients aged 0-15 years inclusive with newly diagnosed or relapsed malignancy at Cambridge University Hospitals (CUH), UK. We assessed the clinical impact of WGS in children with solid malignancies in the programme's first 18 months.

**Methods:** Data was collected from all patients presenting to the CUH Paediatric Haematology/Oncology department, including WGS uptake and turnaround time (TAT). Clinical impact was defined by alterations to diagnosis, treatment, or prognosis as a direct result of WGS.

**Results:** Between 18/3/21 and 17/9/22, of 143 new/relapsed presentations, 98 (68.5%) had sufficient fresh-frozen tissue available for WGS, 87 (60.8%) were offered and all accepted. Median TAT from DNA extraction to clinically available data was 27 days (13-69 days). Including the feasibility phase, 111 tumours were sequenced from 110 patients. WGS revealed clinically relevant findings in 27 patients (24.3%), with eight (7.3%) germline and 19 (17.1%) somatic findings not detected by standard-of-care (SOC) testing. Diagnosis was modified in 10 patients and significantly changed in two, whilst seven patients had findings that meaningfully impacted prognosis. Treatment was changed in six patients as a direct result of WGS, with a further nine patients having novel therapeutic opportunities identified.

**Conclusions:** Whole genome sequencing was successfully implemented in our unit, showing WGS can be utilised for sequential patients as part of their routine care. WGS impacts patient management in a substantial proportion of patients and their families. Furthermore, opportunities to investigate and target novel molecular subgroups and cancer predisposition are considerable. WGS also has the potential to replace multiple SOC investigations, which are currently inconsistently utilised across centres.

EP491/#1393 | Poster Topic: AS05 SIOP Scientific Program/AS05.0  
*Tumor Biology, Immunology and Immunotherapy*

#### EXPLOITING GLYCOSPHINGOLIPIDS FOR THE CLASSIFICATION AND TREATMENT OF PAEDIATRIC TUMOURS OF THE PERIPHERAL AND CENTRAL NERVOUS SYSTEM

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**Background and Aims:** The classification of tumours has the potential to identify subtypes of prognostic, diagnostic and therapeutic relevance. Genomic and methylation data have been intensively

investigated for this purpose in the past years. Lipids have not been considered for tumour classification so far, even though the profile of lipids and particularly glycosphingolipids (GSL) is altered in cancer. GSLs are especially abundant in the nervous system. Here we analysed the potential of GSL profiles to identify subgroups in neuroblastoma and in three paediatric CNS tumor entities

**Methods:** GSL were extracted from frozen tissues of 14 Neuroblastoma (NB), 9 Medulloblastoma (MB), 9 Pilocytic astrocytoma (PA), and 2 CNS BCOR ITD and analysed by thin layer chromatography.

**Results:** NB can be divided in four major GSL groups: GD2<sup>high</sup>, GD2<sup>low</sup>/GD1a<sup>high</sup>, GD2<sup>high</sup>/GT1b<sup>high</sup>, GD2<sup>intermediate</sup>/GD1d<sup>high</sup>. GD2<sup>high</sup> samples were also MYCN amplified. GD2<sup>low</sup>/GD1a<sup>high</sup> samples were more differentiated. 4S NB had a GD2<sup>intermediate</sup>/GD1d<sup>high</sup> profile. MB have a subtype-dependent GSL profile, with Group 3 containing two GSL groups, GM3<sup>high</sup>/GD2<sup>negative</sup> and GD2<sup>positive</sup>/GM3<sup>negative</sup> respectively. PA can be divided in galactosylceramide (galcer)<sup>high</sup> and galcer<sup>low</sup>, which seems to be related to the age of the patient. All PA samples were GD2 positive. With regard to CNS BCOR ITD, the profile was different between the primary tumour (Gb4Cer<sup>negative</sup>/GD2<sup>positive</sup>) and an inoculation metastasis on the skullcap of the same patient (Gb4Cer<sup>positive</sup>/GD2<sup>negative</sup>).

**Conclusions:** In conclusion, GSL profiles are tumor entity specific. GSL profiling allows to define subtypes within paediatric tumours of the nervous system. This has consequences for therapy options e.g. anti-GD2 therapies for CNS BCOR ITD, PA and some subgroups of MB. Moreover, GSL profiles can be used to define subtypes within heterogeneous subgroups such as MB group 3. We are currently investigating the GSL composition of other paediatric tumours and the association between GSL profiles and prognosis and resistance to therapy.

EP492/#98 | Poster Topic: AS05 SIOP Scientific Program/AS05.0  
*Tumor Biology, Immunology and Immunotherapy*

#### REACTIVE OXYGEN SPECIES, PROTEIN TRAPPING AND CANCER: NOVEL INSIGHTS FROM IN VITRO STUDIES

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**Background and Aims:** Telomere maintenance is a hallmark of cancer and, in many malignancies, this is attained through the telomerase-independent alternative lengthening of telomeres (ALT) pathway. ALT is particularly prevalent in solid tumours affecting children and adolescents (e.g. osteosarcoma, glioma). Recently published work suggested that in addition to loss of the *ATRAX* gene, the central driving event

in ALT-pathway initiation was formation of DNA-protein complexes (DPCs).

**Methods:** The work was a basic science study, involving both bioinformatic and in vitro assays.

**Results:** Bioinformatic analysis of RNA-sequencing data from glioma revealed a role for excessive reactive oxygen species (ROS) in *ATRX*-mutant tumours. Consequently, cell lines were exposed to conditions of elevated ROS (hydrogen peroxide/silencing of superoxide dismutase/cellular hypoxia/*SETD2* loss). This led to strong ALT-induction in *ATRX*-mutant (but not *ATRX*-wildtype) cells. The induction of ALT by elevated ROS was mediated through the formation of R-loops (abnormal RNA:DNA structures). R-loops were found to trap TOP1 protein and form DPCs - and enzymatic degradation of R-loops prevented ROS-mediated ALT-induction. Whilst elevated ROS levels were found to be the driving force underpinning ALT-induction, it was also observed that *ATRX*-mutant cells were exquisitely sensitive to further elevation of ROS, with resulting genetic instability and cell death.

**Conclusions:** This work provides the first complete, cogent model of ALT-cancer biology: re-framing the evolution of ALT-telomere maintenance as a complex interplay between genetic causation (*ATRX*-loss) and tumour microenvironment (elevated ROS levels). Excessive ROS led to R-loops and subsequent formation of DPCs - this providing the genetic substrate for ALT-telomere elongation. However, further elevation of ROS beyond the level required for ALT-induction lead to DNA damage and cell death: ALT-cells live in a "Goldilocks zone", where the level of ROS must be *just right*. These novel insights highlight new therapeutic approaches to exploit cellular vulnerabilities in these difficult-to-treat cancer types and future work will explore the translational potential.

EP493/#1329 | Poster Topic: AS05 SIOP Scientific Program/AS05.o Tumor Biology, Immunology and Immunotherapy

### PIK3CA-RELATED OVERGROWTH SPECTRUM: TARGETED THERAPY

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**Background and Aims:** PIK3CA-related overgrowth spectrum (PROS) it is a broad-ranging spectrum of disorders that leads to overgrowth of various body parts due to PIK3CA gene mutations. The aim of the study was to analyze clinicopathologic features, molecular genetic characteristics of patients with PROS spectrum disorders and to present the first Russian experience of the therapy with PIK3 inhibitor -alpelisib

**Methods:** Twenty-four patients with PROS were analyzed from 2020 to 2023. In 24/24 cases samples of tissue or blood were investigated for PIK3CA mutations using different methods: RT-PCR, NGS. Alpelisib therapy was administered in 71% (17/24) cases in dose 50 mg. Children under 24 months were prescribed therapy every 48 hours and the patients older 24 months - daily. Toxicity assessment carried out according to the International Toxicity Criteria (Common Terminology Criteria for Adverse Events) version 5

**Results:** The median age at diagnosis was 23 months (range 0 - 213) with equal gender distribution. Most patients (79.2%, 19/24) presented with combined overgrowth, 20.8% (5/24) with isolated overgrowth. The most frequent *PIK3CA* mutations: 8 - H1047R, 6 - E545K, 3-E542K, 2-Glu110del and 1 case each with H1047L, G106V, E545G, Asn345Lys, C420R. The median therapy duration was 6 months (range 1-26). At 12 and 24 weeks of therapy, all patients had no signs of disease progression. Reduction in the volume of lesions more than 20% were detected in 4 cases and less than 20% - in 5 cases. The most common adverse effect - skin toxicity (grade 1-2) which manifested in 41.2% (7) patients, diarrheal syndrome (grade 1-2) - 35.3% (6), fever (grade 2) 1, alopecia (grade 1) 1, aphtha 1. No acute or late grade 4-5 toxicity was observed

**Conclusions:** This study showed that Alpelisib is a promising targeted treatment in patients with PROS. Treatment was well

tolerated. Our data deserves confirmation in larger cohorts with longer follow-up

EP494/#331 | Poster Topic: AS05 SIOP Scientific Program/AS05.o  
*Tumor Biology, Immunology and Immunotherapy*

### CLUSTERIN OVEREXPRESSION INDUCES RESISTANCE TO EXHAUSTION IN TCR-TRANSGENIC T CELLS TARGETING AN EPIOTOPE DERIVED FROM THE EWING SARCOMA METASTATIC DRIVER CHM1

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**Background and Aims:** Previously we have shown that CHM1<sup>319-327</sup> specific T cell receptor (TCR) transgenic T cells (ChoTCR-T cells) show significant cytotoxicity against Ewing Sarcoma (EwS) in vitro and in vivo; both in preclinical models and the clinic. EwS is characterized by an immunosuppressive tumor microenvironment inducing T cell exhaustion, e.g. by hypoxia. An exhausted T-cell phenotype is characterized by a reduction in proliferation and cytokine secretion and finally, loss of cytotoxicity. Thus, induction of resistance to exhaustion is a major endeavour in immunotherapy research. Clusterin (CLU) increases resistance to various stresses in tumor cells. It is therefore an interesting candidate to prevent T cells exhaustion. Our objective is to assess the effects of CLU overexpression on TCR-transgenic T cells.

**Methods:** Following overexpression of CLU in ChoTCR-T cells (ChoTCR<sup>CLU</sup>-T cells), we performed co-culture studies with A673 EwS cells for up to 9 days. Several exhaustion markers and the cytotoxic function were evaluated. Furthermore, we used an EwS spheroid model to elaborate the impact of CLU overexpression under hypoxia.

**Results:** We observed a reduced expression of CLU in various therapeutic T cell models. Overexpressing CLU in engineered T cells reduced expression of exhaustion markers PD-1, LAG-3 and TOX in long co-cultures. Proliferation and persistence of ChoTCR<sup>CLU</sup>-T cells were increased, while their functional capacities and activation

profile remained comparable to ChoTCR-T cells. In co-culture with tumor spheroids, CLU overexpressing cells showed a better infiltration into the hypoxic core of the spheroid. Moreover, under hypoxic culture conditions (1.5% O<sub>2</sub>) the ChoTCR<sup>CLU</sup>-T cells showed increased functionality.

**Conclusions:** CLU protects TCR transgenic T cells from exhaustion and hypoxia and increases their persistence in the tumor microenvironment. Therefore, CLU is an interesting candidate for protecting therapeutic T cells from exhaustion, a hallmark of low therapeutic efficacy in both engineered TCR- and CAR-transgenic T cells.

EP495/#1056 | Poster Topic: AS05 SIOP Scientific Program/AS05.p  
*Supportive Care and Palliative Care*

### IMPACT OF EARLY PHASE STUDY ENROLLMENT FOR PEDIATRIC ONCOLOGY PATIENTS ON SYMPTOM BURDEN AND QUALITY OF LIFE

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**Background and Aims:** Pediatric patients with relapsed or refractory malignancy have limited options for therapy. The primary aim is to determine if those enrolled in a phase I or II trial have better QoL compared to those not enrolled in a trial.

**Methods:** QoL is measured using the Symptom Screening in Pediatrics Tool (SSPedi) comparing score from baseline, 4 weeks and 8 weeks of those enrolled on an early phase trial to those who do not enroll in these trials. Scores are compared for patient reports for 8-18 years and parent-proxy reports for 2-7 years. The total SSPedi score is the sum of 15 items' 4 Likert scale scores, for score ranges from 0 to 60 (worst possible).

**Results:** Of the 18 patients recruited thus far, 9 (50%) patients are enrolled in an early phase trial and 9 (50%) patients are not enrolled in a study. For those enrolled in the study at baseline (enrollment time), 4 weeks and 8 weeks time points, the total score for the participant mean is 10.5 (SD 5.3), 10.0 (SD 8.7) and 14.0 (SD 11.3) respectively compared



to those not enrolled in a study with mean scores at the same time points of 13.9 (SD 10.5), 14.3 (SD 10.2), and 18.3 (SD 12.6). At present, there are too few patients to statistically compare scores.

**Conclusions:** The data provided demonstrates that over the time period studied, patients enrolled in a phase I or II trial may have improved quality of life compared to non-enrolled patients as per the SSPedi. The study experience to date suggests that investigation of this question is feasible. Further efforts will focus on more recruitment and using the PedsQL 3.0 Acute Cancer Module to further define differences in QoL. This research is supported through granting from the C17 and Kindred foundations.

EP496/#549 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### DENGUE IN PEDIATRIC HEMATOLOGY AND ONCOLOGY PATIENT - A MUTIREGIONAL EXPERIENCE

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**Background and Aims:** Dengue Viral Infection (DVI) is caused by four flavivirus serotypes (DEN-1, DEN-2, DEN-3, and DEN-4), transmitted by mosquito bite and could be asymptomatic, symptomatic with or without warning signs and severe dengue. Eighty percent of children with Hematology and Oncology diseases (HMD) live in low middle income countries and also tropical countries where the incidence of DVI is highest. We sought to describe the incidence and outcomes of DVI in children with HMD in 4 institutions of four countries in three world regions.

**Methods:** A working group was created of experts in pediatric oncology, hematology, and infectious diseases working in Indonesia, Greece, Brazil, Paraguay, Pakistan, and the USA. Data collected between 01/01/2018 and 31/12/2022 and included institutional characteristics and DVI diagnostic capacity, availability of care guidelines, number DVI in children with HMD. Descriptive were statistics to report the results of our study.

**Results:** Participants consist of one children hospital and three referral General Hospital. All had pediatric cancer units and three of it had transplant units. The number of beds ranged from 46 to 600. During 2018-2022, a total of 643 cases of DVI in the pediatric, and 48 cases occurs in pediatric HMD patient, incidence per years is between 1 to

6 per 1000 admissions. diagnosis was done by serology mainly and frequently available, confirmation diagnosis using PCR only available in central government lab in three countries, National care guidelines were present in the three hospitals. None of them had guidelines for DVI for HMD patients

**Conclusions:** DVI is an important burden for LMICs institutions. while incidence in pediatric population is high, incidence is low and rarely reported in the pediatric Hematology/Oncology patients, availability of specific serology test to confirm DVI frequently available and could benefit to overcome the challenges to diagnosis DVI in this special population in endemic countries.

EP497/#1625 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### THE PERSPECTIVE OF PEDIATRIC FAMILIAL CANCERS IN A LOW-MIDDLE-INCOME COUNTRY

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**Background and Aims:** Familial Cancers are not uncommon among the pediatric population. Therefore, the identification of such syndromes and families is important for active screening and early detection of cancer among those at risk of developing cancer

**Methods:** A retrospective cohort study was done at Children's Hospital Lahore Pakistan to explore the Familial cancer syndromes being treated in the Oncology Department from June 2016 to June 2022. These families were divided into five groups: Retinoblastoma Families, HLH/Chediak-Higashi Syndrome Families, CMMRD/Li-Fraumeni Syndrome, Parents and Children, Siblings only group, and others like Ataxia-Telangiectasia family, Fanconi Anemia families

**Results:** Among **RB families** of 25 cases, children presented early, and despite family history present multiple children expired before, during, or after treatment and many of them refused curative treatment. Among **7 CMMRD families**, these children had brain tumors, colorectal carcinomas, and lymphoblastic Lymphomas with poor prognosis and most of them expired during treatment. Children presenting with **familial HLH** and others having Chediak-Higashi Syndrome of 15 families with more than 30 children, most of the siblings expired due to the non-availability of stem cell transplantation. **The sibling group** had 10 families where siblings had Wilms tumor, Rhabdomyosarcoma, Neuroblastoma, Acute Lymphoblastic Leukaemia/Lymphoma, Hodgkin Lymphoma, Burkitt Lymphoma, and brain tumors with variable prognosis. **Parent and Child group** of 5 families having leukemia, lymphoma, Neuroblastoma, and CRC and only one parent alive and the rest expired due to CA Breast, Lymphoma, AML, and brain tumor. Two siblings of the Li-Fraumeni family expired from choroid plexus tumor grade II and CRC with two young aunts from CA Breast and CRC. Other families included

Fanconi Anemia and Ataxia Telangiectasia with malignancies having a grave prognosis despite treatment

**Conclusions:** These families require extensive psychosocial support, genetic counseling, and better surveillance means for early diagnosis and better management of all the index cases and at-risk family members in LMIC.

EP498/#908 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### MAPPING THE QUALITY OF LIFE AND UNMET CARE NEEDS OF CAREGIVERS OF CHILDREN WITH CANCER IN NIGERIA

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**Background and Aims:** Caregivers play a crucial role in the care of childhood cancer survivors by providing physical, emotional, and practical support. They also contribute significantly to the decision-making process in the treatment of these survivors. To improve the quality of cancer care and health outcomes, it is imperative to identify and address any unmet needs among caregivers.

**Methods:** This study was conducted at Lagos University Teaching Hospital and involved 50 childhood cancer caregivers. The study utilized the Comprehensive Needs Assessment Tool in cancer for Caregivers (CNAT-C) and the World Health Organization Quality of life (WHOQOL-BREF) tool to assess the comprehensive needs and quality of life of cancer caregivers. The data collected was analyzed using the descriptive analyses, independent student t-tests, and Pearson's correlation analyses.

**Results:** The average age of the caregivers included in the study was  $42.74 \pm 7.254$ . The most prominent areas of unmet needs for caregivers were healthcare services, information needs, and practical support needs. The majority of the caregivers were females (64%) and the most common cancer type was leukemia (26%). The mean scores (standard deviations) for unmet needs and quality of life (QOL) were 54.88 (24.43) and 72.7 (8.83) respectively. There was a negative correlation ( $r = -0.354, p < 0.05$ ) between the unmet needs of the caregivers and their QOL. Hospitalization of the child and the absence of insurance were significantly associated with poor quality of life.

**Conclusions:** Caregivers of childhood cancer survivors often have unmet needs that can impact their quality of life. Demographic factors of caregivers also affect their quality of life, and addressing these

factors alongside their needs can result in holistic care for patients and their caregivers, ultimately increasing their quality of life.

EP499/#1660 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### USING PROFILE QUALITY IMPROVEMENT TRACK TO DEVELOP AN ACTION PLAN TO DECREASE TIME TO ANTIBIOTIC ADMINISTRATION IN THE EMERGENCY ROOM AT THE PHILIPPINE GENERAL HOSPITAL

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**Background and Aims:** Quality improvement (QI) and Patient Safety (PS) training are not readily available in LMICs. The St. Jude ProFILE implementation process incorporates a QI track that provides multiple stakeholders with a comprehensive, modular, and guided QI experience, including free licenses to the Institute for Healthcare Improvement (IHI) Open School and six QI exercises. We present the problem assessment and action planning on delayed time to antibiotics (TTA) among febrile neutropenia patients in the emergency room (ER) using the ProFILE exercises.

**Methods:** We implemented ProFILE from August 2022 to May 2023. During the preparation phase, the site coordinator (SC) and physician lead (PL) recruited a 12-member multidisciplinary team. The ProFILE Champions (PL, SC, and SC assistant) completed the 13-module IHI QI & PS Basic Certificate and six QI exercises instructional packages (video tutorial, facilitator guide, and PowerPoint Presentation) via Cure4Kids. Profile Champions led the QI exercises using previously shipped posters.

**Results:** We held four TTA QI sessions. The average attendance was 13 (range 10-18). The audience included ER nurses, pharmacists, doctors, trainees, administrators, and the ProFILE team. First, the Block Diagram exercise illustrated the patient experience with the significant delay between physician order to medication release (250 minutes). The Cause-and-Effect exercise highlighted issues in the ordering process (unstable internet, additional paper request forms), plus lack of staffing and knowledge of the medical staff. In the Affinity Diagram, participants brainstormed interventions, grouped these into five

themes, and prioritized them. In the Impact Effort Matrix, the creation of febrile neutropenia clinical pathways and the provision of antibiotic kits were voted as the most impactful interventions requiring the least effort.

**Conclusions:** Education and empowerment of medical team on systems thinking, teamwork brainstorming techniques, and consensus building enabled systematic gap assessment and action planning. PrOFiLE QI track provides an excellent foundation to tackle the problems revealed during the institutional assessment.

EP500/#1708 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

### KNOWLEDGE, ATTITUDE, AND PRACTICES AMONG BANGLADESHI NURSES TOWARD PEDIATRIC PALLIATIVE CARE: A QUALITATIVE STUDY

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**Background and Aims:** Access to palliative care for children suffering from malignancy is quite meager in underdeveloped or developing nations such as Bangladesh. Social stigma, poor infrastructure, and lack of awareness from the side of patients and caregivers may delay palliative consultation. Since oncology nurses build a close bonding with patients and parents, their insights and technical abilities also greatly influence the effectiveness of Pediatric Palliative Care (PPC) services. In this study, oncology nurses' perceived knowledge, attitude toward needs, and barriers to implementing palliative care were viewed and their insights were traced. We further, explored their insights on the barriers to implementing PPC in Bangladesh and ways to overcome these obstacles.

**Methods:** The qualitative study used purposive, convenience sampling to select ten oncology nurses (N=10) from different tertiary-level hospitals. They were all invited to a central location for a Focus Group Discussion (FGD). The discussion guide was made by one pediatric oncologist and two clinical psychologists. We used thematic content analysis for analyzing the data. Main Research Variables: definitions of palliative care, beliefs about palliative care decision-making and its implementation barriers in Bangladesh.

**Results:** Nurses' perceptions of palliative care focused on physical symptoms and stress management mostly in the late stage of life. Most of them could not draw a difference between palliative care services and end-of-life care. Furthermore, nurses believed that their role in making decisions regarding palliative care was not welcomed even if they are concerned about their responsibility. Regarding

implementation barriers, lack of monitoring, guidance, skill training, and proper guidelines on counseling, communication, symptom management, limited recourse, and less cooperation from physicians were mostly highlighted.

**Conclusions:** In this study, oncology nurses' perceived knowledge, attitude, needs, and barriersto palliative care were viewed and insights were traced. For the structured PPC changes in policy and administration, awareness and training of professional care providers are required.

EP501/#1264 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

### THE EFFECT OF NUTRITIONAL STATUS ON OUTCOME OF CANCER IN CHILDREN

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**Background and Aims:** Malnutrition among children with cancer is reported between 6-50%. Malnutrition may have adverse effect on survival by reducing doses, widening interval of courses and increasing side effects. There are few tools for the diagnosis and management of malnutrition in childhood cancer. In this study the anthropometric indices and nutritional status of newly diagnosed children with cancer were measured with different screening tools and the effect of these indices and tools on cancer outcome were evaluated.

**Methods:** The weight, height, body mass index (BMI), mid-upper arm circumference (MUAC), and triceps skinfold thickness (TSFT) of newly diagnosed 163 consecutive children with cancer were measured and STRONGkids, Pediatric PG-SGA and SCAN tools were applied to each child. The disease status and outcome data were recorded.

**Results:** Median age of 94 boys and 54 girls was 6.6 years (2-14.9). The most frequent diagnoses were CNS tumors in 23.3%, lymphomas in 21.4%, and soft tissue tumors in 15.3%. Mean z-scores of height-for-age and BMI-for-age were  $0.1 \pm 1.3$  (-3.5-3.4) and  $0.0 \pm 1.5$  (-3.8-4.1). The mean percentiles of MUAC and TSTF were  $42.0 \pm 30.0$  (0.0-100.0) and  $50.0 \pm 29.0$  (5.3-100.0). The percentage of patients with chronic malnutrition (below -2SD) according to height-for-age z-scores was 7.4%, and the percentage of acute malnutrition according to BMI-for-Age z-scores was 10.4%. Malnutrition risks were 73%, 53% and 48% according to SCAN, Pediatric PG-SGA and STRONGkids tools. Patients were followed-up median 21 months (0.4-39mo). The 2-y OS rates for children with and without malnutrition risk were as follows: with SCAN tool 66% vs 85% (p=0.03), with STRONGkids tool 77% vs 90% (p=0.03) and with PG-SGA tool 79% vs 88% (p=0.065).

**Conclusions:** STRONGkids, Pediatric PG-SGA and SCAN are reliable tools to determine the risk of malnutrition in children with cancer. STRONGkids and SCAN tools might be useful for selecting the children at high risk for malnutrition and altered outcome.

EP502/#578 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### INCIDENCE AND REASONS FOR DELAY IN THE ADMINISTRATION OF HIGH-DOSE METHOTREXATE IN CHILDREN, ADOLESCENTS, AND ADULTS: A RETROSPECTIVE STUDY OF 1,922 CYCLES

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**Background and Aims:** High-dose methotrexate (HDMTX) is a vital component of the treatment of acute lymphoblastic leukemia (ALL) and non-Hodgkin lymphoma (NHL). We investigated the incidence and reasons for the delayed administration of HDMTX at the Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India.

**Methods:** This retrospective study reports outcomes from a single center participating in the Resonance global retrospective registry of HDMTX. Patients with ALL and NHL from 2012-2021 at PGIMER were included. HDMTX was administered without measuring methotrexate levels using extended hydration and additional leucovorin doses. We defined clinically relevant treatment delay as  $\geq 7$  days from the 14-day interval specified by protocols. The incidence of delay and its reasons were noted.

**Results:** The analysis included 511 patients and 1,922 cycles; 332 patients with B-ALL, 124 T-ALL, and 55 T-NHL. The median age at diagnosis was 7.0 years (range 15 days - 42 years), and 119 (23.3%) were female. The dose of HDMTX was 3 and 5 gm/m<sup>2</sup> in 65.9% and 32.7% of the cycles, respectively. The median duration to the next HDMTX cycle was 18.5 days (IQR 16-23); 523 (27.2%) cycles had a clinically relevant delay. The reasons for the delay included toxicity of the preceding cycle 306 (58.5%), lack of inpatient beds 35 (6.7%), and financial barriers 25 (4.8%). The reasons were unclear from records in 156 (29.8%) cycles. Febrile neutropenia (OR 4.59, CI95 2.66-7.90,  $p < 0.001$ ), increasing age (OR 1.04, CI95 1.02-1.05,  $p < 0.001$ ) and female sex (OR 1.58, CI95 1.22-2.40,  $p < 0.001$ ) were associated with increased odds of delay.

**Conclusions:** Over 1 in 4 cycles of HDMTX had a clinically relevant delay. The most common (58.5%) cause was toxicity resulting from the preceding cycle. Corrective reasons, including lack of inpatient beds and financial barriers, contributed to 11.5% of the delayed cycles.

EP503/#120 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### DETECTION OF ABNORMAL COVICYTES IN THE PERIPHERAL BLOOD OF COVID-19 CANCER PATIENTS: DIAGNOSTIC AND PROGNOSTIC POSSIBILITY

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**Background and Aims:** Peripheral morphological abnormalities play important roles in the early diagnosis and prognosis of the COVID-19 infection. The aim of the present study was to assess the morphological alterations in the peripheral blood (PB) cells in patients with COVID-19 infection, with special attention to a different group of atypical lymphocytes that had been observed in the PB of COVID-19 cancer and non-cancer patients.

**Methods:** The PB cells were examined in 84 COVID-19 positive cancer patients, and 20 COVID19 positive non-cancer patients, compared to 30 healthy normal controls. The data were correlated to the disease severity, patients' clinicopathological features, and outcomes.

**Results:** There was an increased incidence of giant platelets, neutrophils shifting left, and abnormal monocytes in the COVID-19 positive cancer and non-cancer patients compared to the control group ( $P < .001$ ,  $P < .001$  and  $P = .014$ ; respectively). Neutrophils with abnormal toxic granulations, Pseudo Pelger-Heut abnormality, and reactive lymphocytes were significantly increased in COVID-19 cancer patients compared to COVID-19 non-cancer patients and the control group ( $P = .001$ ,  $P < .001$ , and  $P < .001$ ; respectively). An abnormal form of lymphocytes' morphological changes (Covicytes) was significantly detected in COVID-19 cancer patients [60.7% (51/84)], and in COVID-19 non-cancer patients [55% (11/ 20)], while it was absent in the normal controls [0.0% (0/30),  $P < 0.001$ ]. The presence of the Covicytes is associated significantly with a better prognosis in cancer and non-cancer COVID-19 patients.

**Conclusions:** Covicytes could be a useful marker supporting the diagnosis of SARS-COV-2 infection, and it is associated with a favorable prognosis. Undergoing investigations of the peripheral blood for other respiratory viruses prognostic prediction without the need to undergo expensive diagnostic tools detecting morphological changes in peripheral blood specially in pediatric cancer patients. Covicytes Is a simple tool to detect in COVID19 infected children with cancer.

EP504/#1810 | Poster Topic: AS05 SIOP Scientific Program/AS05.p  
Supportive Care and Palliative Care

### IMPLEMENTING A LONGITUDINAL PROSPECTIVE STUDY OF FINANCIAL DISTRESS IN PARENTS OF CHILDREN WITH NEWLY DIAGNOSED ACUTE LYMPHOBLASTIC LEUKEMIA: A REPORT FROM CHILDREN'S ONCOLOGY GROUP

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**Background and Aims:** Parents may come to their child's pediatric cancer diagnosis with characteristics that heighten risk for financial distress (money worries). No study has prospectively examined trajectories of financial distress in this population. The purpose of ACCL20N1CD (NCT04928599): *Financial distress during treatment of acute lymphoblastic leukemia (ALL) in the United States* is to describe trajectories of financial distress for parents of children (ages 1-15 years) with newly diagnosed ALL. We describe implementation of this study that uses multiple modes to collect parent-reported data.

**Methods:** ACCL20N1CD uses a longitudinal prospective cohort design and mixed methods. Settings are Children's Oncology Group (COG) institutions in the National Cancer Institute Community Oncology Research Program (NCORP). Eligible participants are English- and/or Spanish-speaking parents or legal guardians ("parents") of index children. Parents are asked to complete a survey at 3 time points using unique REDCap® links sent to their preferred contact mode (text or email), or a paper form from which their responses are entered into REDCap®. We report a preliminary analysis of participating parents' preferred mode of contact and completion mode by language and contact method, completion rates for the first survey, and number of messages sent before completion.

**Results:** ACCL20N1CD was activated in March, 2022. As of March 8, 2023, 33/47 (70%) of eligible COG NCORP institutions have opened the study, and 48 parents enrolled, 44 of whom completed a survey (92%) to date. Of 48 parents, n=42 (95%) preferred English, and n=6 (14%), Spanish. More than half (n=27, 61%) chose to be contacted by text; all Spanish-preferring parents chose text (n=6, 100%). Only 39% of parents chose paper surveys (n=17). On average, 3 messages (email: 3.33 vs text: 2.77) were sent prior to survey completion.

**Conclusions:** Monitoring study implementation may optimize data quality and application of study findings to future interventional research.

EP505/#547 | Poster Topic: AS05 SIOP Scientific Program/AS05.p  
Supportive Care and Palliative Care

### PEDIATRIC CANCER PAIN MANAGEMENT AT BSMMU BANGLADESH: IMPLEMENTATION OF WHO ANALGESIC LADDER

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**Background and Aims:** Pain is the frequently reported symptoms of cancer in children. About 70% of Children experience cancer-related pain at diagnosis or during the active treatment phases. This pain not only from the cancer itself but also from medical treatments and procedures related. **Aim:** To recognizes the various types of cancer pain and to implement the WHO Analgesic Ladder in the management of pain in Pediatric cancer.

**Methods:** One hundred twenty (120) pediatric patients (age 4-18 years) suffering of cancer pain were studied during the period 2021-2022. Pain intensity assess by Faces pain scale and Numerical rating scale (0=no pain, 10=severe pain). Pain management was given in accordance with the two steps WHO Analgesic Ladder for cancer pain. Analgesic use is acetaminophen, morphine, gabapentin and adjuvant. Patients were followed up to two weeks for response to analgesic and side effect.

**Results:** Among 120 pediatric children with cancer, nociceptive pain was in 56 (46.66%), neuropathic in 10 (8.33%) and mixed in 54 (45%). According to assessment scale mild pain was 48(40%) and moderate to severe pain was 72(60%). 50(41.66 %) children took Acetaminophen only, 12(10 %) Acetaminophen and gabapentin, 60(50%) need morphine only and 13(10.83%) need combination of morphine and gabapentin, 7(5.83%) took adjuvant treatment. 10(16.66%) patients develop mild itching and 12(20%) develop morphine induced constipation.

**Conclusions:** By WHO Analgesic Ladder Cancer pain in pediatric age group can be well managed without any significant side effect. So successful implementation of WHO Analgesic Ladder is essential to manage pain in children with cancer.

EP506/#639 | Poster Topic: AS05 SIOP Scientific Program/AS05.p  
Supportive Care and Palliative Care

### METRONOMIC CHEMOTHERAPY IN LOW- AND MIDDLE-INCOME COUNTRY; IS A NEW CONCEPT IN PEDIATRIC ONCOLOGY

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**Background and Aims:** Metronomic chemotherapy (MC) is defined as the frequent administration of chemotherapy at doses below the maximal tolerated dose (MTD) and no prolonged drug-free break. The aim of this study was to describe the use of MC and assess the safety of MC

drugs given to children with refractory, relapse and advance cancer of various tumor types.

**Methods:** This prospective observational study was conducted in the Department of Pediatric Hematology and Oncology, Bangabandhu Sheikh Mujib Medical University, Bangladesh from January 2016 to January 2019. In this study drugs used was Cyclophosphamide (50mg/m<sup>2</sup>/dose) and Etoposide (50mg/m<sup>2</sup>/dose) and Sodium Valproate (Valproic acid)- 10-15mg/kg/day for 21 days followed by 1-week break. This treatment was given to children with advance stage diseases (stage-IV), relapse and refractory cancer. Adverse events were determined through laboratory analyses and investigator observations.

**Results:** Total 21 children (median age- 4y; range, 6 m to14y) were included. Among 21 patients 2 patients lost to follow-up. 19 patients included in this study. The most frequent diagnoses were Neuroblastoma (14). At 8 weeks 13(68.42%) patients experienced disease stabilization and progressive disease 06(31.57%). 11(57.89%) patients achieved partial remission. Complete remission achieved 9(47.36%) patients at 28 weeks and 2(10.52%) patients up to last follow-up at 150weeks and continued their treatment for 37.5 months. After a median follow-up of 24 weeks (range:2-96wk) 8 patients (42%) were alive. During treatment period only one patient developed mild neutropenia.

**Conclusions:** The MC that we used was safe, well tolerated and represents good value for patients with advance diseases that are eligible for palliative care. Children achieved disease stabilization, partial and complete remission without any complication. The use of MC in children in low and middle-income countries is safe and effect.

EP507/#992 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### CENTRAL-LINE-ASSOCIATED BLOODSTREAM INFECTIONS IN A PEDIATRIC ONCOLOGY AND HEMATOLOGY HOSPITAL AT HOME PROGRAM

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**Background and Aims:** Central-line-associated bloodstream infections (CLABSIs) are associated with significant morbidity among pediatric oncology/hematology patients, and risk factors remain largely unknown in the setting of hospital at home (HAH). Children in HAH receive intensive treatment (eg, chemotherapy and parenteral nutrition), with frequent central-line handling; thus, they may be at higher risk for CLABSI.

**Methods:** We conducted a monocentric retrospective study of patients with a central line included in our HAH program from January 1 to December 31, 2016. HAH patient characteristics for children developing CLABSIs were compared to those who did not, based on blood cultures positive for infection and clinical data of all patients included.

**Results:** Overall, 492 HAH stays were analyzed, with 144 patients. The overall CLABSI rate in these patients was 2.6 per 1,000 central-line days. Children who developed CLABSIs were younger (median age, 2.5 vs 8.8 years;  $P < .001$ ), suffered more from hematological pathologies (malignant or nonmalignant, 75% vs 52%;  $P = .02$ ), and had more frequently undergone hematopoietic stem-cell transplantation (30.8% vs 6.5%;  $P = .01$ ). In addition, these patients often had a tunneled externalized catheter as the central line and were more frequently given parenteral nutrition at home (46% vs 8%;  $P < .001$ )

**Conclusions:** CLABSI rates for children in HAH were more similar to those of inpatients than to rates previously reported for ambulatory patients. The factors associated with infection identified herein should be further validated in multicentric studies and considered to improve HAH practices, parallel to prevention measures used in the inpatient setting.

EP508/#812 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### ASSESSMENT OF INCIDENCE AND SEVERITY OF CHEMOTHERAPY INDUCED NAUSEA AND VOMITING IN CHILDREN WITH CANCER ON ANTIEMETICS: A PROSPECTIVE SURVEY AT A TERTIARY CANCER CENTRE

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**Background and Aims:** Chemotherapy induced nausea and vomiting or CINV is a common and undesirable side effect of chemotherapeutic treatment in cancer patients. It has numerous and far-reaching implications on the treatment of cancer, as it is often highly unpleasant particularly for pediatric patients and is a common cause of treatment abandonment or noncompliance. The primary objective of our study was to assess the incidence and severity of CINV in children treated with appropriate chemotherapy and antiemetics.

**Methods:** A total of 105 chemotherapy courses on antiemetic prophylaxis as recommended by COG were assessed in a prospective cross-sectional study approved by the IEC which was carried out through an oral survey, utilising a prevalidated questionnaire. Patients and/or their caregivers were asked to grade the severity of nausea & vomiting and its various effects on their daily lives on a scale that ranged from 1 to 7, with a score of 1 indicating minimal severity and a score of 7 indicating maximal severity after obtaining consent.

**Results:** Among 105 courses of chemotherapy with antiemetic prophylaxis, nausea was observed in 47 courses (44.8%) and vomiting was seen in 26 courses (24.8%). The mean score in those having nausea was 3.967 and in those with vomiting was 4.166. Of the 105 courses, the emetogenic risk was classified as high for 62 (59.04%), moderate for 36 (34.28%), low for 5 (4.76%), and minimal for 2 (1.90%).

**Conclusions:** Our survey highlights that even with optimum antiemetic prophylaxis, 1/4<sup>th</sup> of the chemotherapy courses induced vomiting in children with cancer in our study population. The higher incidence of nausea and vomiting in this population could be due to the different rate of metabolism of antiemetics and appropriate changes need to be made in the existing global guidelines to better suit this population incorporating genetic polymorphism studies.

EP509/#16 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

### INFECTIONS PROFILE IN CHILDREN UNDERGOING CHEMOTHERAPY BEFORE AND DURING COVID 19. WHAT IS THE PANDEMIC IMPACT? A REPORT FROM A SINGLE INSTITUTION IN ALGERIA

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**Background and Aims:** Due to its severity, Covid 19 pandemic has imposed rigorous preventive measures both in the general population and in those treated for cancer because of major morbidity and mortality risks. Evaluate the impact of these measures on reducing infection risks among children undergoing chemotherapy.

**Methods:** A retrospective study is conducted in the pediatric oncology unit of CHU Béni Messous, involving children aged 1 to 16 years, treated for acute lymphoblastic or myeloid leukemia. The study has two periods, the 1st from January 1st, 2018 to December 31, 2019, the 2nd, from January 1st, 2020 to December 31, 2021. Data are collected from hospitalized patient records.

**Results:** We identified 92 patients (34 vs 48), with a majority presenting with ALL (79.4% vs 75%), AML is present in 20.6% vs 25%. The number of identified infectious episodes is 81 vs 121 with an average of 2.5 vs 2.4 per patient. Proportion of infectious episodes without neutropenia is 25% vs 14.8%. ORL infections are identified in 24% vs 11.6%, respiratory infections in 9% vs 14.8% while digestive infections are observed in 5% vs 12%. Blood cultures are performed in 37% vs 32.3%, they are positive in 13.4% vs 33.3%. During the second period, 50% of documented infections are due to Covid 19. Proportion of hospitalized patients was 92% vs 94.2%.

**Conclusions:** Although our study is limited due to sample size, the frequency of infectious episodes apart from neutropenia appears to be reduced most likely due to prophylactic measures. However, respiratory and digestive infections appear to be more frequent given specific manifestations at this age.

EP510/#1261 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

### EARLY INTEGRATION OF PALLIATIVE CARE INTO CHILDHOOD CANCER TREATMENT – LESSONS FROM A MODEL IN VIETNAM

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**Background and Aims:** While more than 97% of children in need of palliative care (PC) live in low- and middle-income countries (LMICs), the scarcity of pediatric palliative care (PPC) programs in LMICs highlights the unmet need for PC in children with life-threatening illnesses. Establishing the first PPC Department in a pediatric hospital in Vietnam, we aimed to build a model to facilitate the early integration of PC into pediatric cancer treatment.

**Methods:** Interdisciplinary champions including hospital leaders, pediatric oncologists, and PC professionals were involved in establishing a model to 1) provide PC for children with cancer, and 2) integrate PC early into cancer treatment.

**Results:** This model has gone through an iterative process over the years to meet our aims. In the first model, we provided PC consultation requested by the hematology-oncology (Hem-Onc) physicians. Our PC intervention included pain and physical symptom management, psycho-social support, and serious illness communication. During this period of four years (2018-2022), the PC team consulted 41 patients with cancer and 188 individual patient visits. Even though we had some success in relieving patients' suffering, the "end-of-life team" taboo was a noticeable challenge. To adjust the model, one PC physician was embedded in the Hem-Onc Department, sharing the daily work in the morning. As a result, the number of patients and visits increased remarkably. In the last nine months, we have provided PC intervention for 20 patients with cancer and 178 visits. Additionally, a psychologist was also assigned to provide art therapy and early psycho-social support.

**Conclusions:** PC needs identification and network building improve when one PC physician is assigned to the Hem-Onc Department. Also, art therapy and psycho-social support can be a simple and easy way to integrate PC earlier in the treatment of children with cancer.

EP511/#1589 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### GLOBAL INFECTIOUS DISEASES NETWORK OF ST. JUDE CHILDREN'S RESEARCH HOSPITAL (ST. JUDE): A STRATEGY FOR SUSTAINING COLLABORATION FOR INFECTION CARE AND PREVENTION

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**Background and Aims:** The Global Infectious Diseases (Global ID) program at St. Jude Children's Research Hospital established the Global ID Network to support the dissemination of best practices in infection care and prevention at pediatric cancer units worldwide. This network coalesces established regional networks (PRINCIPAL of Latin America and LOTUS of Asia Pacific-China-India), and nascent collaboration in the Eastern Mediterranean and Africa regions. Here, we describe processes and outcomes of establishing network governance.

**Methods:** Since formation of the PRINCIPAL (2017) and LOTUS (2020) networks, the St. Jude Global ID program and network members followed steps to build a sustainable global network: (1) Conceptualization of leadership structure and responsibilities. (2) Needs assessment for working group (WG)-led initiatives. (3) Agreement of network members to establish an Advisory Committee (AC). (4) Call for applications for AC members. (5) Description of the AC's charge.

**Results:** St. Jude Global ID program members built a leadership concept. Network members identified needs and interests and established an AC comprising nine geographically representative members and members of the Global ID Program. The AC drafted roles, responsibilities, and processes for WG projects and approved three pilot projects in clinical care capacity, education, and research to test the structure,

namely: 1) a febrile neutropenia care pathway 2) a surgical infections textbook chapter and 3) a bacteremia retrospective study. The AC members and projects' leaders presented early results at the 2023 Global ID Net annual meeting, attended by 72 participants from 30 countries and 58 institutions. Attendees engaged in a project brainstorming workshop resulting in 11 project ideas to be reviewed by the AC.

**Conclusions:** A network of infection care and prevention healthcare professionals guided by a representative AC provides an inclusive and diverse global perspective on priorities to improve the survival of children with cancer worldwide.

EP512/#937 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### USE OF QUALITY IMPROVEMENT METHODOLOGY TO ADAPT IN-PERSON TO VIRTUAL TRAINING DURING THE COVID-19 PANDEMIC: LESSONS LEARNED FROM A MULTICENTER PEWS COLLABORATIVE IN LATIN AMERICA

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**Background and Aims:** Proyecto EVAT is a quality improvement collaborative for PEWS (Pediatric Early Warning System) implementation in resource-limited pediatric oncology centers structured in 3 phases. The second phase consists of three train-the-trainer workshops leading to local PEWS pilot and implementation. In March 2020, in-person trainings were adapted to virtual due to the COVID pandemic. This work describes the adaptation experience and lessons learned.

**Methods:** In response to the COVID pandemic, the Proyecto EVAT leadership team used quality improvement methodology (Plan, Do, Study, Act -PDSA cycles) to 1) conduct a comprehensive review trainings; 2) restructure training content based on feedback; 3) adapt training curriculum for virtual delivery; 4) pilot with two centers; 5) make additional improvements to align with learning objectives, and 6) provide training to experts using new content and methodology to train centers. Based on lessons learned from the virtual format, trainings were changed to hybrid for the 2022 cohort.

**Results:** After training modality adaptation for virtual delivery, PEWS training was successfully delivered to 33 centers from 13 countries. Of these, 88% (29 centers) completed training exclusively virtually and 66% (19 centers) successfully implemented PEWS (9 additional centers



are currently implementing and 1 left the project). An unexpected positive result was the opportunity to have experts from multiple centers in each training, thus enriching discussion, and simpler training content for clarity and learning alignment. When travel was again possible, advantages and disadvantages of virtual and in person training were compared to develop a hybrid training strategy to optimize resources and improve learning.

**Conclusions:** The adaptation of PEWS training to virtual allowed Proyecto EVAT to continue despite the COVID-19 pandemic. The virtual modality facilitated PEWS implementation while more efficiently using resources. However, in-person training can better support engagement and connection, especially high-barrier centers, and a hybrid model may be optimal in the post-pandemic era.

EP513/#1175 | Poster Topic: *AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care*

### PHARMACOGENOMICS OF B-LACTAM ANTIBIOTIC-INDUCED SEVERE CUTANEOUS ADVERSE REACTIONS

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**Background and Aims:** Children with cancer are at a higher risk of developing infections due to cancer itself and the intensive treatments they receive.  $\beta$ -lactam antibiotics are widely prescribed and are one of the most common drug classes to induce unexpected serious adverse reactions, particularly severe cutaneous adverse reactions (SCARs). SCARs, including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), are life-threatening events with mortality rates up to 70%. There are known genetic predispositions to SCAR from several drugs, but it is unclear whether this exists in  $\beta$ -lactam antibiotics.

**Methods:** 196  $\beta$ -lactam exposed patients, including 30 SCAR cases and 166 tolerant controls, were recruited across nine Canadian Academic Health Centres between 2005 and 2022. The phenotypes of SCARs were classified according to the consensus definitions of the RegiSCAR study criteria. Relevant demographic characteristics, including age, sex, and antibiotic regimens, were identified. All patients were genotyped using a custom Illumina Global Screening Array (GSA version 3.0) plus Multi-Disease add-on content. Genome-wide analysis was then performed using allelic association tests.

**Results:** Genome-wide analysis demonstrated two genetic variants that were significantly associated with  $\beta$ -lactam antibiotics-induced SCARs. One variant near the *WDR11* gene was found in 20% of cases ( $n=6$ ) compared with only one out of 166 controls (0.6%) with an odds ratio (OR) of 43.7 (95%CI: 5.3-362.5;  $P$ -value:  $1.0 \times 10^{-8}$ ). Another variant near the *CDIN1* gene was present in 12 out of 30 cases (40%)

compared to 9 out of 166 controls (5.4%) (OR (95% CI): 8.97 (3.6-22.4);  $P$ -value:  $4.1 \times 10^{-8}$ ).

**Conclusions:** The *WDR11* gene is involved in the Hedgehog signaling pathway and contributes to epidermal development and repair. The *CDIN1* gene is part of keratinocyte expression clusters with a role in epithelial cell function. These findings suggest a role of these genes in the biology underlying  $\beta$ -lactam antibiotics-induced severe skin adverse reactions.

EP514/#1163 | Poster Topic: *AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care*

### PEWS IMPLEMENTATIONS AS A TOOL FOR IMPROVING ONCOLOGIC OUTCOMES IN A TERTIARY PEDIATRIC CENTER WITH LIMITED RESOURCES

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**Background and Aims:** Pediatric Early Warning Systems (PEWS) aid in early identification of deterioration in pediatric oncology patients. EVAT, a multicenter quality improvement collaborative project based in PEWS, has been translated and implemented in Hospital Martagão Gesteira (HMG), a tertiary pediatric center in Bahia/Brazil, since 2019. The aim of this study is to describe the characteristics, outcomes and interventions of patients who deteriorated in the HMG Pediatric Oncology Ward, comparing before and after the implementation of PEWS.

**Methods:** A descriptive prospective study, comparing the results of pediatric oncology patients (POP) admitted at HMG from April 2019 to December 2021, before and after the implementation of Pews. Age, oncology diagnostic, PEWS score and PIM2 score, deterioration events, ICU admissions and mortality were evaluated.

**Results:** Total of 155 events of deterioration were identified. The average age was 8,7 years, the most common oncology diagnosis was Acute Leukemia (40%) and the most common deterioration event was need of PICU transfer. Forty six events occurred before Pews implementation, of these 4,3% required vasopressors, 2,1% received cardiopulmonary resuscitation (RCP), 2,1% required orotracheal intubation (OTI) and two patients (4,3%) died, all of them on the ward. After PEWS implementation, 109 patients suffered deterioration with 0,9% requiring OTI, 1,8% receiving RCP and 9,1% needed vasopressors on the ward. No deaths occurred on the ward. The Pews score ranged from 0 to 10 with an average of 5.6. The Pim2 score was 15,7% and 7,8% and the

total mortality was 34% and 22% pre and post PEWS implementation, respectively.

**Conclusions:** PEWS identified deterioration earlier with more interventions made still on the ward. No deaths occurred on the ward after implementation. Besides, an expressive reduction in morbidity and total mortality was shown. These results indicate that PEWS implementation is essential, especially in a limited resource scenario.

EP515/#916 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

## ESAPP - A DIGITAL TOOL FOR A BETTER PEWS IMPLEMENTATION

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**Background and Aims:** Pediatric Early Warning Systems (PEWS) aids in early identification of deterioration in pediatric oncology patients. EVAT is a multicenter quality improvement collaborative project based in PEWS, supported by St Jude Children Research Hospital, developed in 45 Oncologic Centers in Latin America. In routine, however, there is a risk of human errors in the use of EVAT scales. To support nurses in order to reduce these errors, optimize time and to ensure predictive capacity of the PEWS scales, we developed a mobile application called EsApp.

**Methods:** The first prototype was developed at the Universidade Federal da Bahia (UFBA) and presented to health professionals for suggestions. As it was well received, an IT Tech startup started the development of the EsApp application, on a voluntary basis, in a 24-hour Hackathon. After the homologation, improvements and adjustments it was launched.

**Results:** The App exists in two versions, one compatible with Android and the other in PWA (Progressive Web App) that supports multi-platforms and multiple operational systems. Data science knowledge was used to define the diagnosis accumulated in the information sent to the App, processed with a pre-existing base of scenarios created in the medical scale. All information is anonymized. The data of the vital signs of each patient is entered, with their date of birth. EsApp makes the calculations at each stage and gives the color and the final score. EsApp was presented to the project leaders, nurses and pediatricians of the Martagão Gesteira Hospital in Salvador Bahia, Brazil, in 2021.

**Conclusions:** This application is now a daily hospital tool and we are intending to implement it in all others Centers participating in the EVAT Program in Brazil. It is important to continue in the constant search to minimize errors in order to guarantee the quality of the processes.

EP516/#950 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

## THE ROLE OF INFECTIOUS COMPLICATIONS ON CLINICAL DETERIORATION MORTALITY IN CHILDREN WITH CANCER IN RESOURCE-VARIABLE HOSPITALS IN LATIN AMERICA

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**Background and Aims:** Pediatric oncology patients are at higher risk of infectious complications resulting in frequent clinical deterioration and high mortality. This is particularly true in resource-limited hospitals who experience higher deterioration-related deaths due to delays in care, limited supportive care resources, and hospital practices. This study explores the relationship between infectious complications and clinical deterioration event (CDE) mortality in pediatric oncology patients hospitalized in Latin America.

**Methods:** A secondary analysis was conducted using a de-identified quality improvement registry of clinical deterioration collected from May 2019 to September 2022 at 69 pediatric hematology-oncology centers in Latin America. This analysis assessed association of patient (age, sex, oncologic diagnosis) and event (presence of a confirmed or suspected infection, neutropenia) characteristics with the primary outcome of a death during deterioration. A CDE was defined as: transfer to the ICU, use of an ICU-level intervention (vasoactive infusion, mechanical ventilation, or CPR) on the ward, or ward non-palliative death. Deterioration death was defined as death in the ICU or within 24 hours of ICU discharge or end of ward-based ICU intervention.

**Results:** Among 2423 CDE's, 1861 (77%) of events had a confirmed or suspected infection. Suspected infections were most common (respiratory infection (9.35%), mucositis (8.76%), bacteremia (3.39%)) with 961 (51.64%) confirmed with culture or laboratory evaluation. Mortality differed among CDEs without infection, with suspected, and confirmed infection (22.42%, 24.61%, 29.27%, respectively,  $p=0.037$ ). Among events associated with confirmed or suspected infection, those with neutropenia ( $ANC < 500$ ) were more likely to result in deterioration death (26.38% vs 6.23%,  $p=0.031$ ). Additionally, oncological diagnosis is associated with deterioration death, with hematologic malignancies having highest mortality (26.11%,  $p=0.001$ ).

**Conclusions:** Clinical deterioration in pediatric patients with cancer is frequently associated with infection, which carries a higher rate of mortality. Early identification and treatment of infections may improve outcomes in these high-risk patients.

EP517/#1744 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

### SLEEP IN A PEDIATRIC ONCO-CRITICAL CARE UNIT

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**Background and Aims:** Sleep promotes healing and helps prevent adverse health outcomes in pediatric intensive care units (PICUs), including onco-critical care (Calandriello et al., 2018; Kudchadkar et al., 2014). Unfortunately, PICUs can have environments that are not conducive to sleep. This quality improvement (QI) project aims to improve sleep in the pediatric onco-critical care unit.

**Methods:** Twenty-seven patients ages 2-20 years (mean age = 12.37 ± 5.58) in the pediatric onco-critical care unit had at least two nights of data collected. Rooms were equipped with sound meters (Noise Dose Meter PCE-SLD 10; n = 20) and light meters (Reed Instruments Light Meter; n = 26), and 15 patients ages 8-20 years wore actigraphy (mean age = 14.47 ± 3.31).

**Results:** At baseline, sound levels remained consistent throughout days and nights with 99.93% of days and nights recording conversation-level sound (35 - 85 dB) and no time with quiet (<35 dB) intervals. Patient rooms were dark (<30 lux) throughout the days (81.82%) and nights (95.61%). The remainder of the days were spent under dim light (39-199 lux; 14.86%) with minimal time spent in typical daytime light (200+ lux; 3.32%). Mean total sleep time per actigraphy was 314.27 ± 116.49 minutes, mean sleep efficiency was 72.78 ± 14.0%, and average wake after sleep onset (WASO) was 116.23 ± 59.12 minutes.

**Conclusions:** Baseline data revealed little variation in sound across 24-hour periods, with conversation-level sound at almost all time. Light remained dim throughout the day and night, with only 3% of days spent in typical daytime lighting. Limited variation in light and sound across the days and nights could contribute to disrupted sleep in these patients. Total sleep time and WASO could be improved with increased light and noise during the day and reduced sound at night. We plan to measure outcomes of environmental interventions to determine impact on sleep quality.

EP518/#1670 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

### WHAT'S THE RISK? UPDATE ON THE SAFE USE OF MEDICATIONS IN PATIENTS WITH G6PD DEFICIENCY IN A PEDIATRIC ONCOLOGY POPULATION

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**Background and Aims:** Glucose-6-phosphate dehydrogenase (G6PD) deficiency predisposes individuals to develop hemolytic anemia when exposed to certain medications. Regulatory agencies warn against the use of some medications in the setting of G6PD deficiency, but information may be conflicting. The expanded 2022 Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for medication use in the context of G6PD genotype systematically reviewed the evidence for 48 medications cited as being potentially unsafe in the setting of G6PD deficiency. Medications were classified as high, medium, or low-to-no risk based on a systematic review of the published evidence and regulatory warnings. High-risk medications that should be avoided include dapsone, methylene blue, pegloticase, standard-or-high-dose primaquine, rasburicase, tafenoquine, and toluidine blue. Medium risk medications should be used with caution, and low-to-no risk medications can be used without regard to G6PD phenotype. Here we describe the implementation of the guideline in a pediatric hematology/oncology population.

**Methods:** At St. Jude Children's Research Hospital (St. Jude), clinical G6PD genotype results are integrated into the electronic health record (EHR) and clinical decision support alerts guide pharmacotherapy for patients with G6PD deficiency.

**Results:** Many drugs previously labeled as potentially hazardous in G6PD deficiency lack published evidence supporting those labeled hazards. For a pediatric hematology/oncology population, the most relevant practice-changing reclassifications are the downgrading of trimethoprim-sulfamethoxazole to a low-to-no risk medication, and nitrofurantoin to a medium risk medication. To date, 2466 patients were genotyped for G6PD; 2% (n = 49) were G6PD deficient and should avoid high-risk medications due to the risk of hemolysis.

**Conclusions:** G6PD-guided medication therapy has the potential to prevent drug-induced hemolytic anemia. The updated CPIC guideline provides evidence-based recommendations for personalizing patients' therapy in the context of G6PD deficiency. St. Jude's clinical pharmacogenomics implementation program serves as a model for other institutions that are considering integrating G6PD genotype into the EHR to improve patient outcomes.

EP519/#718 | Poster Topic: AS05 SIOP Scientific Program/AS05.p  
Supportive Care and Palliative Care

### DETERMINANTS OF SUFFERING IN PAEDIATRIC PALLIATIVE CARE

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**Background and Aims:** For children receiving paediatric palliative care (PPC), significant suffering from physical and psychosocial symptoms continue to be reported, which is distressing and harmful to children, parents and clinicians. The aim of this work was to understand how suffering is experienced by children, families and clinicians, as well as what factors impact reports of suffering.

**Methods:** An integrative literature review was carried out. A search in CINAHL, Medline and AMED focused on suffering in children, excluding sudden or unexpected deaths and neonates, resulted in 828 records, with 99 full texts reviewed and a total of 18 papers included. Extraction focused on most frequently reported symptoms related to suffering, and factors influencing suffering.

**Results:** Predominantly, child suffering has been assessed by parents or health professionals and may not capture the direct experience of the child. Pain, dyspnoea and fatigue were most frequently associated with child suffering. Factors which impact child suffering were identified as the following: preparedness, prognostic understanding, effective symptom management, PPC, early introduction of PPC, home as place of care and continuity of care. Several studies found that parents were willing to accept significant child suffering in hope for their child's survival.

**Conclusions:** Symptom and suffering assessment should combine patient, parent and clinician report wherever possible. Suffering is still widespread and associated with adequate symptom management, involvement of PPC teams, but also centred around clinician-family relationships and communication issues, such as preparedness, and prognostic understanding. This points to the importance of communication around goals of care and a focus on quality of life, in order to avoid regret related to suffering in pursuit of increased chances of survival. Further research into more effective symptom management of dyspnoea and fatigue is required and would likely benefit from utilising prospective study designs.

EP520/#1101 | Poster Topic: AS05 SIOP Scientific Program/AS05.p  
Supportive Care and Palliative Care

### THE SCOPE OF PRACTICE OF AN OUTPATIENT PEDIATRIC PALLIATIVE CARE - ONCOLOGY CLINIC

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**Background and Aims:** Pediatric palliative care (PPC) improves end-of-life outcomes for children with cancer. Though PPC visits are the 'intervention' in studies focused on end-of-life care, the content of PPC visits within pediatric oncology is poorly understood. This study aimed to understand the scope of PPC practice that occurs during PPC visits for children with cancer.

**Methods:** This was a retrospective cohort study of patients 0-27 years with cancer seen in PPC clinic within an academic pediatric oncology center between 2017-2022. During each PPC visit, documenting providers chose the domains discussed or managed (Goals of Care, Symptom Management, and Care Coordination with respective subdomains). Data was abstracted from the electronic health record, PPC clinic database and Cancer Registry. The differences in frequency and type of domains addressed were analyzed by visit type, diagnosis group, proximity to the end-of-life, and year of clinic (2017-2022).

**Results:** There were 1,911 outpatient PPC visits across 351 patients. The mean domains discussed per visit (10.2) did not differ between initial visits (10.2) and follow-ups (10.2) or from 2017-2022. Mean domains were higher in visits <90 days compared to visits 91+ days from end-of-life (12.4 vs. 10.5,  $p < 0.0001$ ). Compared to brain tumor or leukemia/lymphoma visits, solid tumor visits addressed more symptom management domains including pain (80.1%;  $p < 0.0001$ ), depression (18.9%;  $p < 0.001$ ), and fatigue (33.6%;  $p < 0.0001$ ). Goals of care subdomains were more frequently discussed in follow-ups compared to initial visits, notably around accommodating to the disease (93.7% vs. 87.4%;  $p < 0.0001$ ), advance care planning (16.4% vs. 8.9%;  $p < 0.0001$ ), and code status (6.0% vs. 3%;  $p = 0.01$ ).

**Conclusions:** The scope of PPC practice is wide and each visit encompasses many domains with the most common being care coordination with oncology teams, accommodating to the disease, and discussion of symptoms. More domains were addressed in solid tumor visits and at the end-of-life.

EP521/#394 | Poster Topic: AS05 SIOP Scientific Program/AS05.p  
Supportive Care and Palliative Care

### PILOT OF A TELEHEALTH HOSPICE-TRANSITION INTERVENTION FOR CHILDREN AND YOUNG ADULTS WITH CANCER

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**Background and Aims:** Telehealth presents a unique opportunity to improve care for patients with progressive cancer enrolling in hospice. Coordinated telehealth visits (patient/family, hospital, and hospice teams) may improve communication, satisfaction, and interdisciplinary collaboration. This study pilots three coordinated telehealth visits during the first month of hospice enrollment.

**Methods:** This is a single-arm prospective pilot study of 0-29 year-old patients with cancer initiating hospice care between 2021-2023. Patients, caregivers, oncology and palliative care providers, hospice nurses and administrators were enrolled and surveyed about feasibility, acceptability, and satisfaction with telehealth (Technology Acceptance Model 2) after the first and third telehealth visits. Healthcare professionals also completed the Assessment of Interprofessional Team Collaboration Scale II. Data were abstracted from the electronic health record and cancer registry. Participant survey responses were summarized and differences in scores were analyzed.

**Results:** As of March 2023, 23 patients enrolled (56% male, 48% Non-Hispanic, 43% solid tumor, 43% brain tumor, median age at diagnosis 9.5 years (IQR 3.5-14.7)). Median days between enrollment and death was 35.3 days. Nineteen and 13 patients completed visit 1 and 3, respectively. Fourteen caregivers and two adult patients completed visit 1 surveys. Nine caregivers and two adult patients completed visit 3 surveys. Thirty-seven healthcare professionals enrolled (13 hospital providers, 15 hospice nurses, 8 hospice administrators); twenty-nine and 22 completed visit 1 and 3 surveys, respectively. Hospital providers and hospice clinicians reported excellent interprofessional collaboration (Median: 99/115 points, 111/115 points, respectively). Using a 5-point Likert scale, most participants highly rated the acceptability and feasibility of telehealth after visit 1 (Mean 4.4, range 3-5) and 3 (4.3, range: 1-5).

**Conclusions:** Patients and caregivers are receptive to telehealth services during the typically stressful first month of hospice. Preliminary findings suggest that telehealth may be utilized as an acceptable alternative to in-person services and fosters hospital-hospice collaboration.

EP522/#1608 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### SINGLE NUCLEOTIDE POLYMORPHISMS AFFECTING TOXICITIES OF 6-MERCAPTOPYRINE AND METHOTREXATE- A SINGLE CENTRE EXPERIENCE

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pital, Clinical Pharmacology, Mumbai, India, <sup>6</sup>Tata Memorial Centre, Pediatric Oncology, Mumbai, India

**Background and Aims:** 6-mercaptopurine (6MP) and methotrexate are essential components of treatment of acute lymphoblastic leukemia (ALL). Single nucleotide polymorphisms (SNPs) in certain genes have been associated with increased risk of toxicities with these agents.

**Methods:** Children upto 15 years diagnosed with ALL undergoing treatment at our hospital between January 2017-December 2021 were enrolled and data was retrieved from electronic medical record. Patients receiving 6-MP during any phase of treatment were tested for TPMT\*2 238G>C, TPMT\*3B-460G>A, TPMT\*3C-719A>G and NUDT15\*3-415C>T SNPs if they had persistent unexplained cytopenia (UC), defined as absolute neutrophil count<0.75\*10<sup>9</sup>/L and/or platelet count<75\*10<sup>9</sup>/L for more than two weeks after omitting the drug. MTFHR 677C>T, MTHFR 1298A>C and RFC1G80A SNPs were tested in patients with unexplained hepatotoxicity (Serum bilirubin>2 gm/dl and/or SGOT/ SGPT>5 times ULN) or UC after receiving methotrexate at any dose and route. Genomic DNA was extracted using the phenol chloroform method and SNPs detected by TaqMan genotyping assays using real-time polymerase chain reaction.

**Results:** Of sixty-three patients fulfilling the clinical criteria, 54(85.71%) had atleast 1 SNP. The prevalence of clinically manifesting SNPs in ALL in our cohort was 2.56%(54/2111). Sixty-percent (31/54) patients were symptomatic during maintenance phase with most common indication for testing being UC (90.74%,49/54). Frequency of various SNPs detected was-MTFHR 677C>T-16(29.62%), MTHFR 1298A>C-41(75.93%), TPMT\*2 238G>C- 2(3.7%), NUDT15\*3 415C>T-14(25.93%) and RFC1G80A- 7(12.96%). Proportion of patients with UC was significantly higher in patients with NUDT15\*3 415C>T (p=0.042). Treatment was interrupted in 47(87.03%) patients with median duration of therapy interruption being 22 days (Range 7-143 days). Twelve patients (22.22%) required blood product support while 23(42.59%) needed chemotherapy dose modifications. The 3-year EFS and OS of patients with clinically manifesting SNPs was 71.6% and 82.8% respectively, comparable to outcomes of ALL in our cohort.

**Conclusions:** In resource-limited setting where uniform screening is not feasible, SNPs should be looked for in patients meeting the clinical criteria. If detected, modifying doses can help prevent therapy interruptions.

EP523/#928 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### A RETROSPECTIVE EVALUATION OF OTOTOXICITY MONITORING IN A COHORT OF PEDIATRIC PATIENTS WITH SOLID TUMORS, TREATED IN A NATIONAL CANCER CENTER

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**Background and Aims:** Ototoxicity is an adverse effect of childhood cancer treatment with a negative impact on speech-language development and quality of life. The aim of this study was to retrospectively evaluate ototoxicity monitoring in a national cohort of solid tumor patients treated in the Princess Máxima Center for Pediatric Oncology (PMC). Additionally, the frequency of, and determinants associated with ototoxicity were determined.

**Methods:** We included all patients with a solid tumor who started treatment between 2015-2020 in the PMC and were receiving platinum agents, cranial irradiation and/or ear-nose-throat (ENT)-surgery. Demographic, clinical and audiological data were extracted from the electronic patient files. Associations between patient characteristics and hearing loss (HL) occurrence were analysed by using logistic regression analysis. HL was defined as Muenster grade  $\geq 2b$  in case of an audiogram, or if an audiologist considered the otoacoustic-emissions and/or visual reinforcement audiometry as abnormal.

**Results:** Three hundred five patients were included (median age at diagnosis 4.0 years, range 0-18). Audiological monitoring was performed at baseline in 191 patients (62.6%), and at the end of treatment in 209 patients (68.5%). Of them, 109 (109/209, 52.2%) suffered from HL, which appeared most often in neuroblastoma (60/74, 81.1%) and liver tumor (15/20, 75.0%) patients. Univariate analyses showed that age at diagnosis (OR=0.93, 95%CI 0.9-1.0), total cumulative cisplatin dose per 100 mg/m<sup>2</sup> (OR=1.3, 95%CI 1.1-1.6), vincristine (OR=2.3, 95%CI 1.3-4.1), gentamicin (OR=2.3, 95%CI 1.1-4.7), vancomycin (OR=2.7, 95%CI 1.5-4.8) and spironolactone (OR=2.9, 95%CI 1.3-6.5) were associated with HL. Multivariable analyses revealed that total cumulative cisplatin dose per 100 mg/m<sup>2</sup> (OR=1.3, 95%CI 1.1-1.6) and vincristine (OR=3.3, 95%CI 1.3-8.0) treatment were significantly associated with HL occurrence.

**Conclusions:** Despite the high frequency of HL in this national patient cohort, about one-third of treated children did not receive audiological monitoring at the end of treatment. There is an unmet need for prevention of this serious irreversible side effect.

EP524/#1764 | **Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care**

#### IMPLEMENTATION OF THE GOLDEN CODE IN AN IMSS CENTER PARTICIPATING IN THE 2ND MAS COLLABORATIVE

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**Background and Aims:** Fever and Neutropenia is the leading cause of admission due to complications associated with treatment; causing a mortality of 10-30%. In HGR 251, an average of 40-60 cases per year are diagnosed, with 30 annual admissions for fever and neutropenia, causing 30% of deaths. Achieving that  $\geq 70\%$  of febrile hemato-oncological patients (P-HOPf) who present to the emergency room receive the first dose of antibiotic in  $\leq 60$  minutes, reducing mortality associated with septic shock.

**Methods:** As part of the 2nd MAS Collaborative, our center uses a shared theory of change from which we select and test through PHEA cycles ideas to generate change in our context. During the last 12 months, we have been supported by a coach from the collaborative, who gave us guidance and support to analyze data and made adjustments to continuously improve existing processes.

**Results:** In a period from January 2022 to January 2023, 28 cases were attended, of which 18 cases met the objective (64%), in the first 6 months of implementation 8 cases were attended, only 50% met the goal; while the second half of the year increased to 70%, with a current median of 87.5%. Additionally, the intervention allowed the reduction of patients who developed sepsis (11%), patients who required intensive therapy (7%) and the reduction of mortality to 3.5% (before 30%).

**Conclusions:** The implementation of the Gold Code reduced admissions to the intensive care unit and mortality in PHO-f in our hospital. To achieve these results, we tested ideas mainly focused on increasing clinical reliability, early identification of fever, ensuring effective access and availability of supplies in the patient care area. All the support and guidance provided by the collaborative were essential to achieve these results within the first year of work.

EP525/#1505 | **Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care**

#### ANALYSING DATA FROM CHILDHOOD CANCER CLINICAL TRIALS - A DIGITAL APPROACH

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**Background and Aims:** In recent years, digital tools have increasingly found their way into various areas of medicine and research. Accelerated by the ongoing COVID-19 pandemic, the shift towards remote patient care has highlighted the need for effective digital tools for data evaluation and analysis, including in clinical trials. Digital tools can offer several advantages over traditional paper-based data collection methods, including increased accuracy, efficiency and accessibility. In addition, digital tools can help ensure compliance with trial protocols and reduce the burden on the vulnerable patient population of childhood cancer patients and their families by allowing them to participate in trials independent of hospital visits. At the same time, it can reduce the burden on trial staff by automating processes, standardising data collection and making data easily accessible.

**Methods:** There are a number of factors that need to be considered when implementing such a digital solution for data analysis, such as cross-system availability, stability and ease of use, as well as data protection and data standardisation.

**Results:** We have implemented a browser-based application that can be accessed via a web browser from any internet-enabled device. The system is then able to encrypt the responses entered and send them to a central database where they are stored in encrypted form. Automated allocation of appropriate questionnaires based on participant and study progress reduces the burden on study staff. In addition, the data entered by the participant is automatically transferred to the database in the correct data format, eliminating the need for data entry by study staff.

**Conclusions:** The implementation of digital tools for data analysis in clinical trials may hold great promise for ensuring the success of these trials, improving outcomes and reducing the burden on vulnerable patients.

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EP526/#1535 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### RATE OF SUPERBUGS COLONIZATION IN CHILDREN WITH CANCER AT SHEFA AL-ORMAN CHILDREN CANCER HOSPITAL

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**Background and Aims:** Infections represent a major cause for morbidity and mortality in children with cancer. Children with cancer

represent a particularly vulnerable patient population at high risk for drug-resistant infections due to several risk factors such as immune dysfunction, high rates of empiric antimicrobial prescription, and exposure to antiseptic agents. We aim to assess the prevalence of superbugs in children with cancer who were treated in pediatric oncology department at Shefa Al Orman Children Cancer hospital from January 2022 to December 2022

**Methods:** A retrospective observational descriptive analysis-based study on children with cancers who were treated at Shefa Al-Orman Children Cancer Hospital from January 2022 to December 2022. During the study period eligible participants were screened for rectal and nasal colonization at the time of first hospital admission

**Results:** During the study period, 191 patients were screened by rectal swab and 133 patients were screened by nasal swab. Patient screened for rectal colonization had solid tumors in 64 (33.5%), hematological malignancies in 127 patients. 63 (32.9%) patients had rectal swab colonized with normal sensitive E.coli (26 with solid cancers and 37 with hematological malignancies). 77 (40.3%) patients colonized with extended spectrum B-lactamase (ESBL) (25 with solid cancers and 52 with hematological malignancies). 2 patients colonized with carbapenem resistant enterobacterae (CRE) (1 with solid cancers and 1 with hematological malignancies). 49 (25.6%) patients colonized with both ESBL and CRE (12 with solid cancers and 37 with hematological malignancies). 119 (89.4%) children had normal nasal swab (44 with solid cancers and 75 with hematological malignancies). 14 (10.6%) patients colonized with MRSA (8 with solid cancers and 6 with hematological malignancies)

**Conclusions:** Our study sheds light on the high incidence of Superbugs colonization in children with cancer thus formulation of optimal infection prevention strategies is an urgent need especially in developing countries

EP527/#24 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### SEROPREVALENCE OF HEPATITIS A, B, AND C IN SYRIAN REFUGEE CHILDREN NEWLY DIAGNOSED WITH CANCER

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**Background and Aims:** Nearly 80% of children diagnosed with cancer are long-term survivors. However, decreased immunity due to chemotherapy and the disease itself and frequent blood transfusions increase the risk of hepatitis in those children. War is a significant cause of a dysfunctional healthcare system with a negative impact on vaccine-preventable diseases. In this study, we aimed to evaluate Hepatitis A, B, and C serological status in Syrian immigrant children newly diagnosed with cancer.



**Methods:** This retrospective study included Syrian immigrant children diagnosed with cancer between 2014-2021. The age, gender, tumor type, and results of immunoglobulin G and M levels for Hepatitis A, B, and anti-HCV status at the time of diagnosis were collected from patient files. The control group was composed of age, gender, and disease-matched Turkish children diagnosed with cancer.

**Results:** Fifty-eight boys and 38 girls, with a median age of 4.8 years were included. There were 42 patients with hematological malignancies, 20 with central nervous tumors, and 34 with other solid tumors. The Hepatitis A seroprevalence was not statistically different between Syrian and Turkish patients, whereas Hepatitis B seroprotectivity was found to be significantly lower in Syrian children with cancer than in Turkish children. Two Syrian patients were HCV-positive. Thirty-seven percent and 45% of all patients were seronegative for Hepatitis B and Hepatitis A, respectively.

**Conclusions:** This is the first study to investigate HAV, HBV, and HCV seroprevalence of Syrian pediatric cancer patients. We found that Hepatitis B seroprotectivity in Syrian children with cancer is significantly lower than in Turkish children. However, the results provided one extrapolation that may be more important: 45% and 37% of all pediatric cancer patients, respectively, do not have protective antibody levels for HAV and HBV during the initial diagnosis. Our findings support the need for Hepatitis screening and, if necessary, vaccination of this vulnerable population prior to chemotherapy.

EP528/#1626 | Poster Topic: *AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care*

#### DEVELOPMENT OF A QUESTIONNAIRE ABOUT BLOOD AND PRODUCTS USAGE BY HEALTHCARE PROVIDERS OF PEDIATRIC ONCOLOGY SERVICES IN LATIN AMERICA - A PILOT TEST

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**Background and Aims:** Oncology treatment requires consistent access to blood products (BBP). Healthcare workers (HCW) knowledge, attitude, and practices (KAP) are essential for the appropriate usage of this medical product. As a first step in improving HCWs capabilities, we built a questionnaire to assess KAP in BBP. Here, we report the steps we followed in building the questionnaire as a tool to evaluation the educational needs of HCWs in Argentina

**Methods:** We conformed a working group made of experts in transfusion medicine, pediatric oncology, hematology, and infectious diseases

working in Argentina, Uruguay, Pakistan, and the USA. We met periodically, via internet, to review and report the progress. We identified 15 studies in English, then, we built a list of all such questions. Following, we grouped the questions in the domains of knowledge, attitude, and practices. We, then, finalized the questionnaire and validated the questions by conducting a pilot testing with 10 nurses and 42 physicians. We used the results of the pilot testing to improve the questions

**Results:** The 40 questions were organized in demographics of the respondents (3Q), institutional resources for BBP transfusion (23Q), and knowledge, attitude, and practices (14Q). The responses used multiple choice (12Q), all that apply (9Q), yes/no (9Q), and Likert scale (7Q). We piloted with 10 nurses and 42 physicians working in an oncology unit. We found that areas of needs for improvement were educational, technical and legal implications

**Conclusions:** Experts from multiple regions of the world built a tool for assessing KAP of HCWs for blood safety. This tool could be useful to assess local KAP and conduct educational interventions to improve the safety of BBP. The next step will be conducting a wider participants survey and construct and educational intervention.

EP529/#1827 | Poster Topic: *AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care*

#### TIME OF REFERENCE TO PALLIATIVE CARE OF CHILDREN AND ADOLESCENTS WITH OSTEOSARCOMA: EXPERIENCE IN A PEDIATRIC CANCER CENTER IN MEXICO

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**Background and Aims:** Previous studies show benefits in quality of life when there is an early integration of palliative care.

The objective of this study was: to determine the moment of integration into palliative care and the reason for referral of patients diagnosed with osteosarcoma.

**Methods:** Retrospective study. Seventy-four patients diagnosed with osteosarcoma were included.(From 2007 to 2022). Timing of referral was classified as early (>12 months from referral to death), intermediate (>6 months to death), or late (≤6 months from referral to death).

**Results:** The median age was 13 years, male predominance was 63.5%, the most affected anatomical site was the femur 52.7%, and the most frequent osteoblastic histological subtype was 70.3%. Metastatic disease was 35%.

Local control performed: amputation 44.8%, disarticulation 37.9%, limb salvage 12.1%. Of the total patients who underwent amputation and disarticulation, 51% had phantom limbs and 29% had phantom limb pain syndrome.

Palliative care was integrated into cancer management in 74.3%. The median time from diagnosis to palliative care referral was 2 months (range 1-40 months); the reason for referral was uncontrolled pain in 78%, followed by progressive disease and relapse in 22%. About the time of referral: 78% were made early, 11% intermediate and 11% late. The Edmonton Assessment System was used to assess the prevalence of symptoms, reporting higher scores for pain (29%), anxiety (19%), depression (14%), and dyspnea (12%).

Twelve patients were referred for progression and relapse. Metronomic chemotherapy was administered to 9 patients. There were 21 deaths (34%), with palliative sedation administered at the end of life in 7 patients (11%).

**Conclusions:** Palliative care is a tool that improves the quality of life of patients. Although in our study more than 50% had an early referral; this aspect should continue to be strengthened.

EP530/#1084 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### HOW DO CHILDREN WITH CANCER DIE? THE CONTEXT OF DEATH AND END-OF-LIFE DECISION-MAKING

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**Background and Aims:** Approximately, 25% of children with cancer die due to their disease. The aim of this study is to describe the context of death and end-of-life decision-making.

**Methods:** Single-centre, retrospective, observational study of deaths in children diagnosed with cancer in a tertiary hospital. We analysed deaths from 2011 to 2021 and compared them with the cohort we studied between 2005 and 2010.

**Results:** 52 patients died from 2011 to 2021, average age at death was 7,8 years. 55 children died from 2005 to 2010, average age at death was 9,8 years. The most common tumours from 2011 to 2021 were: brain tumour (40%), solid tumour (37%), leukaemia (21%) and lymphoma (2%). Death occurred within the first 6 months after diagnosis (33%), between 6-24 months (44%), between 2-5 years (15%) and after 5 years (8%). One third of patients died after tumour relapse. The causes of death were progression (73%), infection (17%) and others (10%). Most of them died in Oncology unit (46%), 29% at home, 23% in Intensive Care Unit and 2% in the operating room. The 93% of deaths

at home were due to tumour progression. Deaths at home increased from 34% between 2005 and 2010 to 50% between 2017 and 2021. The 52% of patients were followed by palliative care (PC) teams and 65% had an advanced care plan (ACP) recorded. Life-sustaining treatment was withheld in 9/10 patients. Palliative sedation was recorded in 56%.

**Conclusions:** Death of paediatric patients with cancer occurred mainly due to tumour progression, in context of withholding life-sustaining treatment and palliative sedation. We observed a decrease in the number of deaths per year between the two cohorts and an increase in the percentage of patients who died at home. Follow-up by PC could facilitate end-of-life decision making through ACP and ensure symptom control in patients with oncologic pathology.

EP531/#573 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### EVALUATING THE MEASUREMENT PROPERTIES AND FEASIBILITY OF PHYSICAL ACTIVITY AND PHYSICAL FUNCTION ASSESSMENTS FOR CHILDREN UNDERGOING ACUTE CANCER TREATMENT

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**Background and Aims:** As physical function and physical activity are often compromised among children and adolescents undergoing acute cancer treatment, psychometrically robust and feasible assessment tools are needed to assess these outcomes. The objective of this study was to evaluate the criterion validity, responsiveness, and feasibility of one physical activity assessment tool (Fitbit Inspire, criterion Actigraph); and construct validity, responsiveness and feasibility of six physical function assessment tools (Movement ABC-2, Timed Up and Go, 30-second Chair Stand, Timed Rise from the Floor, Timed Up and Down Stairs, Six-minute Walk Test) for children with cancer.

**Methods:** A prospectively-registered, mixed methods, longitudinal, single-group study evaluated measurement properties using the Consensus-based Standards for the selection of health status Measurement Instruments (COSMIN) framework. Assessment was performed at two time-points. Feasibility was assessed quantitatively, and qualitatively with semi-structured interviews (children/adolescents/parents) and focus-groups (clinical staff).

**Results:** Twenty children/adolescents (median age 13yrs, range 5-16, various cancer diagnoses), 20 parents, and 16 clinicians participated. There was evidence of criterion validity and responsiveness for the Fitbit compared to the Actigraph, with a tendency to overestimate step count. The 30-second Chair Stand, 6-minute Walk Test and Timed Up and Go were feasible and showed evidence of construct validity and

responsiveness. Consideration of timing and intent of assessment are crucial to maximise feasibility.

**Conclusions:** We recommend Fitbit to assess physical activity and the 30-second Chair Stand, 6-minute Walk Test and Timed Up and Go to assess physical function in children undergoing acute cancer treatment.

EP532/#574 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

### A FEASIBILITY STUDY OF 'CANMOVE' TO PROMOTE POSITIVE PHYSICAL ACTIVITY BEHAVIOURS IN CHILDREN AND ADOLESCENTS UNDERGOING ACUTE CANCER TREATMENT

Sarah Grimshaw<sup>1</sup>, Nicholas Taylor<sup>2</sup>, Rachel Conyers<sup>1</sup>, Nora Shields<sup>3</sup>  
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**Background and Aims:** Supporting children and adolescents with cancer to be physically active can improve medium and long-term health outcomes. The objective of this study was to assess the feasibility of CanMOVE, a 10-week complex, theoretically-informed, behaviour change intervention to promote physical activity for children and adolescents undergoing acute cancer treatment.

**Methods:** A feasibility study using a single-group, repeated measures, mixed methods design. Participants completed CanMOVE, which included provision of a Fitbit (child and carer) and structured support from a physiotherapist. Feasibility domains of demand, acceptability, implementation, practicality, limited efficacy, and integration were evaluated. Data sources included service level data, objective assessment of physical activity, physical function, and health-related quality of life; and qualitative data collected via semi-structured interviews with participants and focus groups with staff.

**Results:** Twenty children/adolescents (median age 13yrs, range 5-16) with a mix of cancer diagnoses, 20 parents, and 16 clinicians participated. There was high *demand* with 95% enrolment rate. CanMOVE was *acceptable* for participants. All feasibility thresholds set for *implementation* were met. Under *practicality*, there were no serious adverse events related to the intervention. *Limited efficacy* data indicated CanMOVE showed positive estimates of effect in influencing child and adolescent physical activity behaviour, physical function, and quality of life. Positive impacts were also seen in parent and staff attitudes towards physical activity promotion. To improve *integration* into the clinical setting, it was suggested the duration and scope of CanMOVE could be expanded.

**Conclusions:** CanMOVE was feasible to implement in a paediatric cancer setting and is appropriate to be tested in a large-scale trial. Findings can be used to inform services in the paediatric cancer setting to promote physical activity participation.

EP533/#1519 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

### DO NOT HARM: PRACTICE FIRST; SIMULATION TRAINING CENTER FOR PROCEDURES IN PEDIATRIC ONCOLOGY

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**Background and Aims:** Determine the impact of learning lumbar puncture (LP) and administration of intrathecal chemotherapy (IT) based on theoretical-practical training in a Simulation Training Center.

**Methods:** Prospective experimental study. Pediatric residents participated in a 2-hour theoretical-practical course in the Simulation Center (SC). Full material for LP and IT administration was used. All procedures were practiced on simulation models (IIA-Kyoto-Kagaku). The SC is a 236 m<sup>2</sup> facility: classroom, 2 multipurpose rooms, 2 control rooms, a debriefing room, a multifunctional room, an outpatient clinic room. Theoretical knowledge was assessed with a five-question questionnaire on the technique. Data was collected about previous experience (number of LP), previous knowledge self-assessment (1-10scale), confidence self-assessment (1-10scale) and course satisfaction survey. A 4-month follow-up was carried out. Skills on information to patients and family and safety were evaluated.

**Results:** 43 residents participated. Theoretical knowledge, 61% obtained a score >7/over10 points, 9% <5/10 and 30% between 5-7/10. 78% had completed <10 LP. Self-assessment: 61% adequate knowledge of the technique and 65% adequate confidence. Of the latter, 43% had performed <than 10 PL. At 4 months, 65% performed 1-4 lumbar punctures, 22% 5-9 and 13% none. 48% of the participants performed 100% of the LP successfully. In 9%, less than 50% of the LPs were satisfactory. 48% improved their perception of knowledge, 9% worsened and 43% did not change. 48% improved confidence, 9% worsened and 43% did not change. 100% considered this course useful. All considered its implementation necessary prior to practice with patients. 83% would repeat it.

**Conclusions:** Evaluation of the course was very positive. Many participants improved their level of confidence and knowledge and all considered this training mandatory. Data suggests that one course is insufficient, since the success rate of the technique continues to be low. We propose continuous training based on simulation to improve patient safety.

EP534/#1267 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

### PEDIATRIC PALLIATIVE CARE (PPC) EXPERIENCE AT A TERTIARY CARE HOSPITAL OF A LOW AND MIDDLE-INCOME COUNTRY

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**Background and Aims:** Children and adolescents with cancers in low to middle-income countries commonly face delays in access to facilities resulting in advanced disease and huge tumor volumes. Along with advanced solid and CNS tumors, many children with leukemia and lymphoma also relapse, transferring to palliative care. Due to constrained resources in LMICs, due attention is often not given to children placed on treatment with palliative intent.

**Methods:** A retrospective chart review was done of pediatric cancer patients aged 2 months to 16 years presenting to Indus Hospital and Health Network (IHHN) from 2018 to 2022. Children with progressive disease, those who had relapsed, and those who had received upfront palliative treatment were included. To improve awareness and capacity, a virtual and in-person 10-week Palliative care course was also organized by the team at IHHN in collaboration with national and international faculty.

**Results:** A total of 1100 patients were placed on palliative care, with an average annual burden of 200(+/-14). The highest disease frequency was leukemia, 534 (49.8%), with the majority of patients from outside Karachi, 803(74.9%) exhibiting an increased probability of advanced disease in patients residing at longer distances from specialized facilities. As of now, 168 (15.3%) expired, 46(2.1%) are alive and the outcomes of remaining 886(82.6%) are unknown due to loss to follow-up. Over 150 people from IHHN and other oncology teams registered and completed the palliative care course. On feedback, 87% of participants reported an increased understanding of palliative care and tools to improve communication with families.

**Conclusions:** There are utmost needs for PPC in LMIC. We need to strategize provision of PPC by increasing awareness, capacity building, shared care, reduction in abandonment, and allocation of dedicated PPC teams. IHHN has established focused pediatric palliative care clinics and capacity-building courses to address the holistic needs of pediatric palliative patients.

EP535/#262 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### OCTREOTIDE AS PROPHYLAXIS AGAINST ASPARAGINASE-ASSOCIATED PANCREATITIS

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**Background and Aims:** Asparaginase is one of the key drugs in the treatment of acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LBL). Asparaginase associated pancreatitis (AAP) occurs in 7-11% of ALL patients, and 44-63% of patients who are re-exposed to asparaginase experience relapse of AAP. Octreotide, which inhibits secretion of pancreatic enzyme, has been suggested to decrease the risk of AAP recurrence following asparaginase re-exposure in several case reports. The aim of this study was to assess the efficacy of octreotide for preventing AAP recurrence who developed AAP.

**Methods:** This retrospective, single center cohort study was performed at Tokyo Metropolitan Children's Medical Center (TMCMC), a tertiary children's hospital. ALL/LBL patients who were treated with asparaginase in TMCMC between April 2010 and August 2021 were eligible. Treatment courses containing asparaginase administration after first AAP episode were included. Then, the selected courses were divided into two groups depending on whether octreotide was administered prior to relapse of AAP during each course (prophylactic octreotide group) or not (control group).

**Results:** Between April 2010 and August 2021, 184 patients diagnosed with ALL or LBL were treated with combination chemotherapy including asparaginase. Of these, 18 patients developed AAP, and 13 patients were re-exposed to asparaginase. Fifty-three courses with asparaginase administration subsequent to first AAP episode were analyzed. The prophylactic octreotide group included 48 courses, and the control group included 5 courses. The recurrence rate of AAP was not statistically different between prophylactic octreotide group and the control group (22.9% vs. 40.0%; p=0.586). However, prophylactic octreotide group had higher proportion of completing scheduled number of asparaginase (89.6% vs. 40.0%; p=0.02).

**Conclusions:** Octreotide may have prophylactic effect for AAP relapse, thus enabling completion of asparaginase administration in ALL/LBL patients. Among those who developed AAP, administration of octreotide prior to subsequent treatment including asparaginase is worth considering.

EP536/#1861 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### EVALUATION OF THE UNDERSTANDING OF DOCTORS FROM A STATE OF BRAZIL THROUGH CLINICAL CASES ABOUT PALLIATIVE CARE

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**Background and Aims:** The Palliative Care approach is still relatively new in Brazil, it had its recent implementation, characterizing a subject to be more valued, studied and updated.

**Methods:** Descriptive cross-sectional study, through a questionnaire applied to physicians in the state of Paraná, via Google Forms, containing 6 clinical cases referring to Palliative Care. After participating, the physicians received a commented answer sheet for all the questions and a folder with essential information for the improvement of the study by e-mail.

**Results:** 239 participants; 63.59% female. Age ranging from 23 years to 71 years, median of 38. Training time ranged from 1 to 48 years with median of 10. Of the professionals, 48.9% considered their understanding of the theme. 38.91% reported having already participated in Continuing Medical Education on the subject. The rate of correct answers for clinical cases ranged from 61.22% to 92.24%.

**Conclusions:** The understanding of Palliative Care by doctors in Paraná is still limited and needs to be expanded. It was verified that the professionals who declared to have a good/very good level of knowledge about PC had a better rate of correct answers, revealing a self-perception of the professional regarding the subject consistent with their knowledge on the subject. However, it was found that professionals with longer training have less knowledge about the subject, as well as those who declared not having participated in events/medical education courses on PC. In the study, the questions that addressed patients with chronic diseases and with a formal indication of the beginning of care had low assertiveness. Thus, the development of medical training that addresses the correct indications of this care has an important role and implication for health policy. Future studies on planning events and lectures are proposed, focusing not only on graduation, but mainly on the form of Continuing Medical Education on the subject.

EP537/#655 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### AUDITORY OUTCOME FOLLOWING PRENATAL EXPOSURE TO MATERNAL MALIGNANCIES TREATED WITH PLATINUM BASED CHEMOTHERAPY

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**Background and Aims:** Antenatal cancer complicates 1 in 1000-2000 pregnancies a year. Ototoxic platinum-based chemotherapy is commonly used to treat antenatal gynaecological cancers. However, limited evidence is available on the effects of prenatal exposure to platinum-based chemotherapy on the auditory development of the offspring. The aim of the current study was to determine the occurrence of hearing loss in these children.

**Methods:** A retrospective international multicentre (n=3) descriptive cohort study (the Netherlands, Belgium, Czech Republic) was performed, by using oncological and neonatal data from the International Network of Cancer Infertility and Pregnancy (INCIP) registry. Auditory outcomes of children prenatally exposed to platinum were assessed using pure tone audiometry. Hearing loss was graded according to the Muenster criteria and International Society for Paediatric Oncology (SIOP) classification.

**Results:** Overall, 25 children were included. Median gestational age at start maternal treatment was 22 weeks (range 13-31). During pregnancy, 17 children (68%) were exposed to cisplatin and 8 (32%) to carboplatin. Median gestational age at delivery was 35 weeks (range 17-39), and median birth weight was 2345 grams (range 1526 - 3360). Neonatal hearing screening was normal in 10 of 25 children (40%). At a median age of 6.0 years (range, 4.0 - 28.0 years), 8 children (32%) revealed moderate to severe hearing loss (Muenster grade  $\geq 2b$  and SIOP grade  $> 2$ ). When mild hearing loss (Muenster  $\geq 2a$  and SIOP  $\geq 1$ ) is also included, normal hearing capacity could not be confirmed in 19 (76%) children. In those exposed to carboplatin, only mild hearing losses were observed (SIOP  $\leq 1$ , Muenster  $\leq 2a$ ; 47%), whereas most cisplatin-exposed children suffered from moderate to severe hearing loss (SIOP  $\geq 2$ , Muenster  $\geq 2b$ ; 63%).

**Conclusions:** Children exposed to maternal platinum-based chemotherapy seem to be at risk of hearing loss. Hence, prospective longitudinal standardized surveillance of auditory function in children prenatally exposed to platinum is advised.

EP538/#1299 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### TO ASSESS THE IMPACT OF EDUCATIONAL INITIATIVES ON HAIS AMONG PEDIATRIC ONCOLOGY PATIENTS

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**Background and Aims:** Background Paediatric cancer patients are at higher risk of HAIs. Due to their underlying diseases and aggressive anticancer therapy, paediatric cancer patients are more likely to

develop potentially fatal infection complications as well as treatment cost AIM Study focuses primarily on paediatric cancer patients, their families, HCWS, educational activities, and how infection prevention training affects HAI rates

**Methods:** Prospective single center surveillance for HAI with standardized surveillance methods were conducted at the Pead's Oncology Ward of IHHN.

**Results:** The pediatric complex participated from January 1, 2020, to December 31, 2021. 163 HAIs were observed out of 312 pediatric cancer patients during 37262 days of inpatient surveillance, which suggests that pediatric cancer patients are at higher risk of potentially life-threatening infectious complications because of their underlying illness. Consequently, infection control decided to raise awareness of cancer, requiring oncology training and education. HAI rate decreased significantly between January 01, 2022, and March 21, 2023, as a result of training for healthcare workers, midwives, patients, and their families. There were 120 HAIs reported out of 503 patients during 43164 days. The mean knowledge level score of patients and relatives before and after training was  $20.07 \pm 46.76$  and  $97.35 \pm 12.86$ , respectively. Infection control training significantly increased patient and their family's knowledge and compliance and also helps in the reduction of HAIs in paediatric oncology's patients ( $p < 0.05$ ). Of all the midwives/nurses who responded to the survey, 87.5% said teaching patients and relatives about infection control measures improved treatment and healthcare. Overall, 95.99% of midwives/nurses believe such education contributed to patient and relative observance of infection control measures

**Conclusions:** The risk of HAIs decreased by offering patients knowledge, sanitizing the environment, and educating patients and their families about infection control procedures. To take appropriate actions, more research needs to be conducted to identify the risk factors associated with greater mortality

EP539/#1615 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### IMPACT OF ENVIRONMENTAL CLEANING AND DISINFECTION PRACTICES ON THE ERADICATION OF MULTI-DRUG RESISTANCE ORGANISM AT PEDIATRIC ONCOLOGY UNIT OF INDUS HOSPITAL & HEALTH NETWORK KARACHI

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**Background and Aims:** Background The cleanliness of the patient's environment is a significant component in facilitating rehabilitation. Cleaning efforts in hospitals have recently been brought into question, revealing that cleaning efforts are frequently insufficient, leaving microbiological contamination on surfaces. **OBJECTIVE** The main aim of the study is to minimize the infection rate of

MDR organisms in immunocompromised patients in pediatric oncology

**Methods:** We conducted an Observational and interventional study from Oct 2021 to March 2023. Data was collected from daily surveillance and medical record and 5539 patients were enrolled in this study. Education was provided to nurses and housekeeping staff regarding practices of hand hygiene, environmental cleaning, and disinfection protocols through the campaign.

**Results:** The total number of patient admission days prior to the intervention was 2711. 37 hospital-acquired MDR pathogens from various cultures were present in the infected patient population. The total number of patient admission days after the campaign launch was 2828. In a new culture, the number of hospital acquired MDR organisms per infected patient decreased from 37 to 18. The outcome demonstrated the decreasing rate of MDR organisms acquired in hospitals.

**Conclusions:** The hospital environment can be a reservoir of HAIs, and cleaning procedures can only minimize this risk to a limited extent. However, it is unknown how much the environment plays a role in infection transmission and what level of cleanliness is required to avoid acquiring organisms from the environment.

EP540/#1680 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### IMPACT OF PEDIATRIC PALLIATIVE CARE IN MOROCCO: FROM YESTERDAY TO TOMORROW

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**Background and Aims:** Pediatric palliative medicine is so differently organized to adult palliative medicine. The objective of our work, is to share the experience of our center, in order to study the impact and contribution of palliative care on all those who are involved, from near and far: the sick child, their relatives, health workers who accompany them, and society at large.

**Methods:** We carried out an analytical descriptive retrospective study, between october 2014 and december 2022, about 94 cases, studying the characteristics of the patients followed in our palliative care unit and evaluating the different aspects of their care.

**Results:** Ninety-four of our patients were cared for in palliative care with an average age of 11.22 years and a male predominance. Brain tumors are the most common (38%), followed by bone tumor locations (23.65%). Pain was the most reported symptom (75.26%). Morphine was prescribed for (64.51%) of patients. The assistance period for our patients is 128 days on average, (13.82%) gained in terms of overall survival and (86.17%) of our patients have died. About sixteen of our patients subscribed to palliative care accompanied by their families. The lack of knowledge of pediatric palliative care and the fact of

sending patients at advanced stages of their illnesses, concerned 60% of our health workers.

**Conclusions:** The illness or death of the child remains an unbearable reality for those who face it: parents, siblings and medical staff. The pediatric palliative approach was born to make the suffering less invasive, it is an active and total approach to care, embracing physical, emotional, social, and spiritual elements.

EP541/#677 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

### IMPACT OF A NUTRITION ASSESSMENT AND REHABILITATION PROGRAM FOR CHILDREN TREATED FOR CANCER IN A SUB-SAHARA AFRICA SINGLE CENTER

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**Background and Aims:** Malnutrition is common among children with cancer in Sub-Sahara Africa (SSA) and negatively impacts cancer outcomes. The mechanisms of malnutrition in these children include pre-existing malnutrition due to lack of access to nutritious food, catabolic state from cancer, mechanical obstruction of the GI tract due to tumors, and treatment side effects such mucositis and vomiting. At the Mulago National Referral Hospital (MNRH)/Global HOPE Center in Uganda we designed and implemented a nutritional rehabilitation program improve the survival and promote health of the children during cancer treatment. We describe the program and its impact.

**Methods:** From October 2019 to April 2020, we enrolled and prospectively followed children ages 0.5 to 18 years. We measured their Mid Upper Arm circumference (MUAC), height and weight. Nutritional status was categorized using the WHO Integrated Management of Acute Malnutrition Guidelines. Children with malnutrition received nutritional rehabilitation with high calorie milk (F75) or ready to use therapeutic feed (RUTF), with twice weekly for inpatients, every two weeks for outpatients and monthly for children with normal nutritional status for the period of 3 months.

**Results:** A total of 124 children (median age7) were enrolled. Of these, 43/124 (35%) were malnourished, with 36/124(29%) severely malnourished. Males and children younger than 6 years had higher rates of malnutrition (65% and 28%respectively). Children with stage 3 and 4 solid tumors, High risk leukemia, abdominal distention, and those treated on high-risk protocols were more likely to be malnourished. Of the children with severe malnutrition, 29/36(81%) received ready to use therapeutic feeds (plumpynut), and 7/36(19%) received high calorie therapeutic milk (F75). Post intervention, rates of severe malnutrition reduced from 84% to 56% in 104 children evaluated.

**Conclusions:** There is a high prevalence of malnutrition among children treated for cancer. Routine nutritional assessment and intervention is feasible and effective in a LMIC setting.

EP542/#43 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

### CANCER ABANDONMENT PATIENTS' STATUS AT THE DEPARTMENT OF PAEDIATRIC HAEMATOLOGY AND ONCOLOGY, BSMMU IN BANGLADESH DURING THE COVID-19

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**Background and Aims:** Childhood cancer is curable. About 13000 children get affected every year in Bangladesh. About 20% refused treatment due to treatment cost, poverty, lack of logistic support, family disruption, and doubt of durability. The significant challenges to be overcome are professional and public awareness, late diagnosis, perceptions of incurability, treatment refusal and abandonment, toxic deaths, and drug costs/inconsistent availability.

**Methods:** In 2021, the population was estimated to be 168 million with 47% under 15 years. There is no national population-based cancer registry but using worldwide incidence rates of between 80 and 150/million children we would expect 10-13000 new cases/per year in Bangladesh. Only about 25% of those numbers are actually currently diagnosed. About 80% of children reaching tertiary hospitals can be offered potentially curative therapy, and many families cannot afford to pay for complete treatment.

**Results:** The incidence of malignancies at BSMMU in 2021 was: ALL 54%, NHL12%, AML13%, Neuroblastoma 5%, Wilms tumour2%, Hepatoblastoma 3%, Hodgkin lymphoma 3%, Retinoblastoma 2%, Germ cell tumors 2%, Histocytosis 2%, CNS tumors 1%, Osteosarcoma 1%. In 2021, the Department of PHO found that 80% of pediatric patients coming from a lower socioeconomic background, about 60% of the parents were illiterate and almost 85% traveled long distances for treatment. Of the 402 pediatric patients in 2021, over 35% had abandoned treatment. But the 2019 abandonment rate was 21%. Telephonic audit of families, who left treatment, revealed that lack of shelter in Dhaka, travel from long distances, cost of food and local

travel, loss of income, faith in alternative medicine, and a sense of hopelessness regarding the curability of cancers.

**Conclusions:** Childhood cancer is mostly curable. Concerted efforts are being made to raise public and professional awareness, reduce diagnostic delays, and shelter and subsidies drug and travel costs. Appropriate national policy can be introduced to improve the survival of abandoned patients.

EP543/#1318 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

### STRIVING TO IMPROVE SURVIVAL IN LMICS; A DEDICATED TASKFORCE TO COMBAT INFECTION-RELATED MORTALITY IN PAEDIATRIC ONCOLOGY

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**Background and Aims:** Childhood cancer is the second leading cause of death in children aged 1 to 14 globally, a major contributor to which is infection related mortality. Children with cancer are at an additional disadvantage of contracting infections due to prolonged periods of neutropenia. Monitoring childhood mortality is crucial for evaluating factors such as healthcare availability and quality, security, nutrition, and protection.

**Methods:** Following the ProFILE workshop at Indus Hospital & Health Network (IHNN), a dedicated taskforce for reduction of infection-related mortality was established in June 2022. Infection control, nursing, critical care and paediatric oncology teams created a rapid response team, led sessions to strengthen early warning signs and initiated a flagging system for multi-drug resistant (MDR) infections. The housekeeping department was trained and monitored for improving environmental cleaning as well as a mandatory fortnightly deep-cleaning of each ward. Monthly hand hygiene refreshers and daily audits of clinical teams were done with the intent of reducing cross contamination. Regular meetings were conducted and a root cause analysis done for each resistant infection.

**Results:** A total of 104 in-patient mortalities were observed at IHNN in 2022 of which 68(65.4%) were infection related causes. Forty (58.8%) were MDR infections, with a high probability of being hospital acquired. Average length of stay in hospital for MDR infections was 15 days, whereas LOS in infections sensitive to first line treatment was 10.67 days (p-value: 0.02833). Over 220 employees were audited for hand hygiene compliance every month. From an increasing trend up to August 2022, the last quarter of the year, post interventions, accounted for a sharp drop with only 8(11.7%) MDR infection related deaths.

**Conclusions:** A dedicated team for quality improvement project is an effective tool. Further studies are required to assess correlation of infections with nutrition and socioeconomic status. Dedicated family education is also needed for underprivileged communities.

EP544/#458 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

### SAFETY AND EFFICACY OF COVID-19 VACCINES IN CHILDREN WITH CANCER

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**Background and Aims:** Children with cancer have a higher rate of severe disease and mortality due to COVID-19 than normal children. Therefore, vaccination of children with cancer became more important. There is some question mark about immunogenicity and safety of vaccines in cancer cases. In this regard, we performed a study to investigate the effectiveness and side effects of the Covid-19 vaccines.

**Methods:** Fifty-eight patients from four centers, who completed at least two vaccinations and were at least 15 days after their last vaccination, were included in the study. Quantitative determination of antibodies to the SARS-COV-2 spike protein levels were measured. Vaccine-related complaints were recorded.

**Results:** There were 33 male and 25 female patients with a mean age of 16.87±2.96 years. The diagnosis were hematological malignancies in 58.6%. Twenty patients were currently under treatment, while 30 completed. Forty-eight patients received chemotherapy alone or in combination with radiotherapy, 13 received immunotherapy and 3 underwent stem cell transplantation. CoronaVac and BioNTech vaccine were administered in 24% and 76% respectively. The mean antibody level was significantly lower in patients who received CoronaVac compared to those who received BioNTech (p<0.05). Although the mean antibody level was within the protective limits in the patients who received cancer treatment, it was found to be significantly (p<0.05) lower than that of patients whose treatment were completed. No correlation was found between antibody level and diagnosis, type of treatment, disease status, time between two vaccines, and time between vaccine and antibody level measurement. The most common side effects were arm pain (37.9%), malaise/fatigue (17.2%) and swelling/redness at the injection site (13.7%).

**Conclusions:** Studies on immunogenicity and safety of COVID-19 vaccines in children with cancer are limited and results are contradictory.



Our study showed that both mRNA and inactivated vaccine elicit an immune response. Side effects were similar to those seen in healthy children.

EP545/#357 | Poster Topic: *AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care*

#### COST-EFFECTIVENESS OF THE IMPLEMENTATION OF THE COLLABORATIVE "HORA DORADA" PROGRAM IN CHILDREN WITH CANCER AND FEBRILE NEUTROPENIA IN A HOSPITAL OF CENTRAL MEXICO

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**Background and Aims:** Febrile neutropenia (FN) treatment exponentially increases the cost of care for children with cancer. In low- and medium-income countries it is vital to design strategies for resource optimization that simultaneously allow to reduce mortality as the implementation of the collaborative program St. Jude Global Mexico opportune administration of antibiotics before the first hour of medical care ("Hora dorada") AIM To know the cost-effectiveness relationship of the collaborative program "Hora Dorada" in children with cancer and FN, attended at the pediatric emergency unit at the "Hospital Materno Infantil del ISSEMyM" in Toluca, Mexico

**Methods:** A cost-effectiveness study was done comparing the approximated costs related to the treatment of children with FN who go to the emergency services unit before and after the implementation of St. Jude Global's regional program "Hora Dorada". The efficacy was defined as the percentage of patients with hospital discharge and no complications that deserve entry to the Intensive Care Unit (ICU), besides the percentage of deaths related to the febrile neutropenia event. An approximation of the global cost, average cost per patient and incremental cost-effectiveness was done in USA dollars.

**Results:** Eighty events per group were evaluated. There were no demographical, diagnosis, gender, or absolute neutrophils count differences

between both groups. 11.76 (5-39) vs 9.04 (3-42) hospitalization days were observed  $p=0.03$ . ICU entries were 12.5% vs 7.5% and death was 7.5% vs 0% before and after the program's implementation. Estimated global costs were \$ 8,720 (3753-25,500) vs 2,532(558-11722) with and incremental cost-effectiveness of \$1551/entry to ICU and \$1,034/death avoided

**Conclusions:** Clinical course and prognosis in children with cancer and febrile neutropenia are related to multiple factors. However, low-cost actions such as the timely administration of antibiotics are cost-effective and can contribute to lower the morbidity, mortality and the approximated costs, allowing resource optimization in a low income country like Mexico

EP546/#37 | Poster Topic: *AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care*

#### SPANISH ADOLESCENT PATIENTS WITH CANCER AND MAIN CAREGIVERS: USING PERCEPTIONS OF CARE TO DRIVE CHANGE IN HEALTHCARE

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**Background and Aims:** To determine whether there are differences in care experience of adolescent cancer patients and their main caregiver, treated in Adolescent Cancer Units (ACUs), compared to those treated in Non-Adolescent Cancer Units (NACUs).

**Methods:** Measurement of Reported Experience in adolescent oncology patients (12-19 years old) and caregivers through ad hoc surveys. The responses of the study group of patients and caregivers treated in Adolescent Units were compared with the group not treated in them.

**Results:** It is noted that the majority of respondents consider that they have not been affected by the COVID-19 pandemic. Significant differences were seen in communication, with better perception by the group of patients treated in ACU (87.1%) and caregivers of ACU (97.3%) compared to patients and caregivers of NACU (53.3% and 68.2% respectively). With regard to information received about the side effects, a better perception was observed among patients treated in the ACU than in the NACU ( $p=0.247$ ). In the transmission of information and the possibility of fertility preservation, a significant difference was observed in favor of ACU in patients and direct caregivers ( $p=0.010$  and  $p=0.018$ ).

**Conclusions:** ACU represents an improvement in the quality perceived by patients and main caregiver on key points in the comprehensive care of the adolescent with cancer such as information, participation in the process and decision making, approach to side effects, psychological

care and help in returning to normal life. However, fertility preservation and strategies for talking about the cancer experience, were identified as areas for future improvement.

EP547/#1431 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

### EARLY INTERVENTIONS IN WARD AFTER 5 YEARS OF SUCCESSFUL IMPLEMENTATION OF A PEDIATRIC EARLY WARNING SYSTEM IN AN ONCOLOGY PEDIATRIC CENTER IN GUATEMALA

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**Background and Aims:** Pediatric Early Warning Systems (PEWS) aid in early identification of deterioration in pediatric oncology patients (POP), the tool classifies high risk as "red" color and guides the clinical team in the early interventions of a deteriorating patient, associated with an algorithm that triggers actions. Spanish adaptation of PEWS, known as EVAT, was implemented in Unidad Nacional de Oncología Pediátrica (UNOP), a POP dedicated facility with limited ICU beds, the aim of this study is describing the results of early interventions in ward after integrating international guidelines for the management of septic shock in patients identified with score  $\geq 5$  points (reds) through EVAT.

**Methods:** A descriptive retrospective study, using EVAT  $\geq 5$  points data base of UNOP for 18 months (January 2021-July 2022). Age, oncology diagnostic, EVAT most common component involved, time for intervention, PICU transfers, need of vasopressors, mechanical ventilation in ward, PICU length of stay (LOS) and mortality were evaluated.

**Results:** A total of 250 "red" events were identified, 16% were transferred to PICU, 5% needed vasopressors in ward before PICU transfer, the most common component involved was cardiovascular, with 88%. One patient, 0.4% required mechanical ventilation on ward. Mean PICU LOS was 7 days, the mean age was 8 years. The most common oncology diagnosis was ALL (47.2%); the mean EVAT/PEWS score was 6 points. Mean time from identification to intervention was 10 minutes and from identification to PICU transfer was 5 hours. Overall mortality was 2.4.1%, all transferred to PICU.

**Conclusions:** A low percentage of EVAT score  $\geq 5$  needs PICU interventions on ward and PICU transfer, POP tend to be more likely to show cardiovascular alterations during deterioration, a POP dedicated facility can reach a short time from identification of risk to intervention after integrating guidelines for management of shock in EVAT staff trainings even in a limited resources setting.

EP548/#1700 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

### QUALITY INDICATORS AND OUTCOMES OF FEBRILE EPISODES IN CHILDHOOD CANCER PATIENTS TREATED AT SIX CENTERS IN CENTRAL AMERICA AND THE CARIBBEAN

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**Background and Aims:** Infection, often signaled by fever, is a common complication which contributes to morbidity, treatment delay, resource use, and mortality in childhood cancer patients. We developed a registry to collect predictors, standard quality measures, and outcomes pertaining to fever management. The pilot cohort included one dedicated pediatric oncology center and five oncology services within general pediatric hospitals in Central America and the Caribbean.

**Methods:** Centers implemented the Fever Registry to provide data on care quality and outcomes onsite. We conducted a retrospective analysis of the initial episodes entered.

**Results:** Between September 9, 2021 and March 6, 2023, six sites entered data on 289 febrile episodes, representing 225 individual patients. Median age at presentation of first fever episode was 7 years (range 0-20 years), 148 patients (66%) had acute lymphoblastic leukemia. Median time to antibiotic therapy from fever development was 135 minutes (range -60 to 5130 minutes). Ninety-three (32%) of episodes occurred in inpatients; 52% of outpatients received antibiotics in 60 minutes or less, and 44% of blood cultures were documented as occurring after antibiotic administration. A clinically documented infection occurred in 37% (n=107) of included episodes. Bacteremia (21%) was the single most common clinically documented infection, with 58 organisms isolated from blood. Death occurred in 7 episodes (2%), and 4 deaths were attributed to multiorgan failure or septic shock

**Conclusions:** Our multicenter study exposes opportunities to improve care quality. Centers can use individual data to identify areas of concern like delays reaching the hospital or obtaining blood cultures. This will inform prioritization of quality improvement interventions. While many febrile episodes had no source identified, this may have been affected by the lack and timing of diagnostic studies. Furthermore, the incidence of bacteremia even with pretreated cultures underscores

the importance of obtaining blood cultures as part of the diagnostic evaluation.

EP549/#933 | Poster Topic: AS05 SIOP Scientific Program/AS05.p  
Supportive Care and Palliative Care

### CREATING MEANINGFUL MEMORIES AFTER CHILDHOOD CANCER DIAGNOSES IN A LOW-RESOURCE SETTING: A PICTURE PROJECT

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**Background and Aims:** Childhood cancer mortality in sub-Saharan Africa is as high as 90%. When children die, families often have limited physical memories of their children. Most recommendations addressing end-of-life support in childhood cancer yield from high-income countries. This project aimed to expand memory-making practices for children and their families in a low-resource setting.

**Methods:** In January 2020, the Texas Children's Global HOPE Program in Malawi introduced a picture project. Each family of a child with an oncological or hematologic diagnosis was offered two pictures (one of the child and another with family members) and a frame. Caregiver consents were obtained and photographs captured outside of medical settings as much as possible. Pictures were printed locally. Frames were made and decorated by caregivers with the assistance of a play therapy team utilizing basic supplies. A mixed-methods quality improvement survey was conducted to evaluate participants and explore the program's impact.

**Results:** Over 300 photos and frames have been distributed since 2020. In a survey of 20 guardians, 60% were mothers and 20% grandparents. All guardians participated in making frames and their children were alive at the time of survey. Evaluated on a Likert scale, guardians believed the project was a meaningful intervention (median 5, IQR 4.75-5), provided them with social support (5, 4-5), and emotional support (5, 5-5). Guardians commented on the value of learning a new skill and connecting with other families. They expressed plans to hang the frames in their homes and share with additional family members.

**Conclusions:** This initiative helped to provide psychosocial and emotional support for families during an illness trajectory with high mortality. Future opportunities exist in capturing additional moments and

exploring potential for economic empowerment utilizing skills gained. This project models a novel memory-making intervention that can be scaled to other diagnoses and low-resource settings.

EP550/#558 | Poster Topic: AS05 SIOP Scientific Program/AS05.p  
Supportive Care and Palliative Care

### CHEMOTHERAPY PRESCRIPTION ERRORS IN A PAEDIATRIC OUTPATIENT SETTING IN A TEACHING HOSPITAL, GHANA

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**Background and Aims:** Medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient, or consumer. There are two types of prescription errors: errors of omission and commission. Prescription errors impact the safety and efficacy of chemotherapy and are considered to have a higher impact on paediatric patients. Information in paediatric is still lacking particularly in primary care settings in lower- and middle-income countries like Ghana. The objective of the study was to estimate the frequency and type of prescription errors in paediatric outpatients receiving cancer chemotherapy and to prevent such errors during the prescription auditing stage.

**Methods:** The study was cross sectional conducted at the Paediatric Oncology Unit (POU) at the Komfo Anokye Teaching Hospital (KATH), Ghana from June to August 2022. All prescriptions documented within the 3-month period were manually reviewed by Pharmacist for potential errors. Data from demographics of patients, prescription details, frequency and types of errors were assessed. Ethical approval was sought before the commencement of the study.

**Results:** In the study, 414 prescriptions were reviewed, males 200 (48.31%) and females 214 (51.69%). Overall, 60 (14.49%) prescription errors were identified. Inaccuracies in body surface area (BSA) calculation 36 (8.69%), omission of medication 10 (2.42%), miscalculated dosage 9 (2.17%), unadjusted dose for weight 3 (0.72%) and inappropriate dosing frequency and duration of chemotherapy 2 (0.48%).

**Conclusions:** Inaccuracy in BSA calculation, the omission of medication, miscalculated dosage for patients, unadjusted dose for weight and inappropriate dosing frequency and duration of chemotherapy, were some of the prescription errors identified. We recommend further interventional studies to limit these prescription errors for improved patient outcome.

EP551/#487 | Poster Topic: AS05 SIOP Scientific Program/AS05.p  
Supportive Care and Palliative Care

## PROGNOSTIC COMMUNICATION BETWEEN CLINICIANS AND PARENTS IN PEDIATRIC ONCOLOGY: AN INTEGRATIVE REVIEW

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**Background and Aims:** Prognostic communication between clinicians and parents in pediatric oncology is complex. However, no review has exclusively examined research on prognostic communication between clinicians and parents in pediatric oncology. We sought to systematically synthesize the evidence on prognostic communication in pediatric oncology and provide recommendations for future research.

**Methods:** We conducted an integrative review searching six databases for studies on prognostic communication between clinicians and parents in pediatric oncology as of August 2022. This search yielded 5,538 results. We excluded 5,249 papers after screening titles and abstracts, and another 90 papers after reviewing the full text. We applied descriptive and narrative approaches to analyze and report the results from 19 studies.

**Results:** Fourteen quantitative and five qualitative studies were included in this review. All studies were conducted in Western high-income countries. In total, 804 parents of 770 children with cancer and 192 physicians were included. Across studies, parents were predominantly female, Non-Hispanic White, and had high school or higher levels of education. Most parents reported that prognostic communication was initiated in the first year after their child's diagnosis of cancer. High-quality prognostic communication was positively associated with trust and hope and negatively associated with parental distress and decisional regret. In qualitative studies, parents suggested that prognostic communication should be open, ongoing, and delivered with sensitivity. Most studies were of moderate quality. The main gaps include a lack of explicit prognostic communication definitions, theories to guide the understanding of prognostic communication, validated measurements, longitudinal studies, and diverse settings and participants.

**Conclusions:** Clinicians should initiate high-quality prognostic communication early on in clinical practice. Future research is needed to develop consensus around prognostic communication definitions and measurements. Future studies should be conducted across settings with diverse populations and in low- and middle-income countries to better understand prognostic communication.

EP552/#1109 | Poster Topic: AS05 SIOP Scientific Program/AS05.p  
Supportive Care and Palliative Care

## CLINICAL IMPACT OF THE "GOLDEN HOUR" IN CANCER PATIENTS WITH FEBRILE NEUTROPENIA IN A PEDIATRIC HOSPITAL IN SOUTHEASTERN MEXICO IN ASSOCIATION WITH ST. JUDE

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**Background and Aims:** A main complication associated with cancer is Febrile Neutropenia (FN) secondary to chemotherapy, increasing complications such as sepsis and being associated with a high rate of morbidity and mortality (every hour of delay decreases 7.6% in survival). Since November 2021, the *Hospital Regional de Alta Especialidad del Niño "Dr. Rodolfo Nieto Padrón" (HRAE "Dr. RNP")* is part of "Mexico in Alliance with St. Jude" (MAS). The goal is to improve the care of the Febrile Hemato-Oncology Patients, from the detection and implementation of care protocols and thus reduce critical interventions. The goal of the "Golden Hour" (GH) is that 70% of pediatric hemato-oncology patients who come to the Emergency Department for fever receive the first dose of antibiotic in less than 60 minutes.

**Methods:** At the HRAE "Dr. RNP" we carried out an observational, prospective, and cross-sectional study of 225 cancer patients who were admitted with FN from November 2021 to February 2023, comparing the time from registration to triage to antibiotic administration using the GH detection mechanisms before and after change interventions.

**Results:** For GH the time of antibiotic administration was measured from the arrival to the triage, before and after the implementation of the change measures; with a baseline of 252 min that decreased to 30 min (improvement of 222 min, average of 50 min) with 100% adherence to treatment and improvement in days of hospital stay from 8.48 to 7.47 days and a decrease in admissions to intensive care.

**Conclusions:** In patients with childhood cancer from developing countries, timely and adequate treatment of febrile neutropenia is a

fundamental aspect; Programs such as MAS help to implement these goals with improvement in the overall survival of patients, the current challenge being sustainability, adherence to internal regulations and continuous education.

EP553/#1478 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### A RANDOMISED TRIAL OF EFFECTIVENESS OF A COMMERCIAL RUTF WITH INDIGENOUS MILLET-BASED SUPPLEMENTARY FEEDING VS. COMMERCIAL SUPPLEMENT IN PROMOTING WEIGHT GAIN IN PEDIATRIC CANCER PATIENTS

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**Background and Aims:** One of the main challenges in childhood cancer in LMICs is malnutrition. Nutritional interventions such as ready-to-use food (RUTF) and commercial supplements are commonly used to improve weight gain, but their effectiveness and acceptance in this population are not well-known. Economic feasibility and cultural acceptance of these agents also vary. This study compared a high-calorie, high-protein diet with RUTF along with millet-based RUSF (Ready-to-use Supplementary Food) with commercial food supplements in promoting weight gain. The study measured the percentage weight gain in both groups and assessed the difference in patient acceptance.

**Methods:** The study analysed 12 pediatric oncology patients (8 males, 4 females) with ALL, AML, and Burkitt's lymphoma. Group 1 (50% of patients) received a high-calorie, high-protein diet with RUTF and millets RUSF and group 2 received commercial supplements in addition to the normal diet received in the hospital/ home. Weekly weight checks and acceptance evaluations were conducted. Statistical analysis compared weight gain and acceptance between groups.

**Results:** All patients were on an oral diet. The average follow-up time in (group 2) was 9.5 and in group 1 was 4 months. At baseline, one child had severe, 5 had moderate and 2 had mild malnutrition. Children aged between 6-13 years. In group 1, the mean percentage of weight gain was 6.8%, while in patients on commercial supplements, the mean weight reduced by -2.87kg and a percentage gain of 0.4% was observed only by 9 months. Patient acceptance was significantly higher in the natural diet with RUTF/RUSF group than in the other group.

**Conclusions:** Addition of millet RUSF to high-calorie, high-protein diets in an effective strategy to improve nutritional status in pediatric oncology patients. It is well-accepted culturally and can ensure weight gain while on an oral diet without the need for nasogastric/parenteral nutrition.

EP554/#1511 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### LONG-TERM NUTRITIONAL CONCERNS IN CHILDHOOD CANCER SURVIVORS

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**Background and Aims:** The long-term health outcomes of childhood cancer survivors are often affected due to nutritional concerns. Dietary habits are a major contributor to metabolic diseases leading to adverse cardiac outcomes. In the present study, we evaluated the nutritional status, dietary habits, and addiction of childhood cancer survivors at our centre.

**Methods:** A prospective study was conducted in our department between September 2021 to March 2022. Children who have completed 5 years from their diagnosis of cancer and are in remission were included. Nutritional assessment of these children along with a survey of dietary practices and addictions were assessed. Dietary diversity was assessed from a 24-hour dietary recall. The food intake data of the subjects were collected by individual single 24-h food recall by a trained dietician using a standard protocol.

**Results:** We evaluated 45 survivors who were consecutively followed up in our survivor clinic. M: F ratio 2.5:1. The median age was 11.5 years (range 6.6-25.2 years). The median follows up was 84.55 months (64-112 months range). The primary diagnosis was ALL in 34 (76%), AML in 2 (4%), Hodgkin lymphoma in 4 (10%), NHL in 1 (2%), 2 LCH, 1 neuroblastoma, and 1 Wilms tumour. >50% belonged to the middle and lower social strata. On anthropometry, a normal BMI (18.5-24.5) was observed in 19/45 survivors (42.2%). 9/45 (20%) were overweight and one was in the obese range. 35% were undernourished. 8 children were above 2SD for weight for age. 2 children had stunting. The average dietary diversity score was 7.8 on working days and 7.55 on holidays.

**Conclusions:** In our series of childhood cancer survivors, both over and underweight were recognized. A lack of dietary diversity was observed in the majority despite being on an unrestricted diet. Focus on dietary

intervention in survivors can help reduce metabolic syndrome in the future.

EP555/#1000 | Poster Topic: *AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care*

### PROSPECTIVE EVALUATION OF THE USE OF COLISTIN AND TIGECYCLINE IN PEDIATRIC CANCER PATIENTS IN A TERTIARY CANCER CENTER IN AN LMIC SETTING

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**Background and Aims:** Multi-drug resistant (MDR) gram-negative bacteria are a significant cause of morbidity and mortality in cancer patients in low- and middle-income countries (LMICs). The last line of defense against such infections is colistin and tigecycline, which are often used indiscriminately. This study aimed to evaluate the use of these antibiotics in pediatric cancer patients at a tertiary cancer center in an LMIC setting.

**Methods:** Prospective enrollment of pediatric cancer patients aged 1-19 years receiving colistin or tigecycline between December 1, 2021, and November 30, 2022. Escalation strategy involved starting with first-line antibiotics (cefoperazone sulbactam and teicoplanin) and later switching to second-line (meropenem) and then third-line (colistin and tigecycline). The de-escalation strategy involved starting third-line antibiotics upfront. An episode of colistin or tigecycline was defined as continuous use without a break in the last dose for more than 24 hours.

**Results:** The study included 74 patients with a median age of 9 years (range: 1-19 years). During the study period, there were 797 episodes of antibiotic use among which there were 101 (12.6%) episodes of use of colistin or tigecycline. The most common diagnosis was acute lymphoblastic leukemia (45 patients), followed by acute myeloid leukemia (29 patients). An escalation strategy was used in 93% of episodes, while a de-escalation strategy was used in 7%. Hospital guidelines for the use of colistin and tigecycline were followed in 71% of episodes. The median duration of colistin or tigecycline use was 9.5 days (range: 1-20 days). The most common indication for starting colistin or tigecycline was hypotension followed by continuous fever.

**Conclusions:** The study highlights the common use of the escalation strategy for starting colistin/tigecycline, which emphasizes the need for implementing antibiotic stewardship. The adherence to hospital guidelines was suboptimal, indicating the importance of strict monitoring and evaluation of antibiotic use in pediatric cancer patients in LMICs.

EP556/#1187 | Poster Topic: *AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care*

### ADHERENCE TO THE RECOMMENDATIONS OF THE FEBRILE NEUTROPENIA PROTOCOL IN PEDIATRIC PATIENTS WITH ACUTE LEUKEMIA IN A CANCER CENTER IN LATIN AMERICA

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**Background and Aims:** Patients with acute leukemia are susceptible to infections during chemotherapy, mainly febrile neutropenia (FN) episodes. Our study aims to identify the rate and the reason of inappropriate empirical antimicrobial therapy (IEAT) during episodes of FN, and risk factors associated with death in patients with FN.

**Methods:** A retrospective cohort of acute leukemia pediatric patients (< 18 yo) with FN under chemotherapy between 2010 and 2020, data were obtained from electronic medical records, after approval by the Institutional Ethics Committee.

**Results:** There were 329 FN episodes in 84 patients. The IEAT rate was 130 (40%), justified in three evaluation moments of FN guideline. The main reason for IEAT was in the 2<sup>nd</sup> moment in three different situations: First, when the cultures back negative, the coverage for gram-positive cocci (GPC) was not removed in 39 (78%) of FN episodes and in 83 (62%) of those patients who recovered from neutropenia. Second, when the cultures were positive, only in 10 (11%) of FN episodes, the antibiotic was not adjusted. Bloodstream infection (BSI) was observed in 73 (22%). A higher proportion of GNB 43 (49%) with *E. coli* 18 (21%), *Klebsiella* spp 20 (23%) and *Pseudomonas aeruginosa* 5 (6%) compared with GPC 20 (23%) with *Staphylococcus* spp with 14 (16%). In the 3<sup>rd</sup> moment, whose antifungal was not associated with antimicrobial therapy 39 (78%). The main risk factors associated with mortality were acute myeloid leukemia, > 13 yo and BSI.

**Conclusions:** Although the IEAT was not associated with a higher risk of mortality, the overuse of antibiotic therapy could be followed by multidrug-resistant bacteria, excessive economic burden, prolonged hospitalization, and dysbiosis of the intestinal microbiota with a potential impact on the underlying disease.

EP557/#1037 | Poster Topic: *AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care*

### PILOTING A PROBLEM-BASED LEARNING (PBL) APPROACH TO BUILD GLOBAL CAPACITY IN GUIDELINE DEVELOPMENT FOR CHILDHOOD CANCER: A ST. JUDE GLOBAL AND SIOP AFRICA COLLABORATION

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**Background and Aims:** Clinical guidelines standardize practice and optimize resource use. However, the time and methodologic expertise needed to produce evidence-based guidelines is often lacking across global settings. To build capacity in Sub-Saharan Africa (SSA), we piloted a training program for clinicians incorporating a PBL approach to developing clinical practice guidelines (CPG) for febrile neutropenia.

**Methods:** The pilot involved South African (SA) and SSA clinicians without prior training in CPG development. A systematic review was performed centrally for all prioritized questions. Each panelist was tasked with selecting studies by applying specific inclusion/exclusion criteria for individual questions. The central methodology team answered questions via email and meetings as needed. The inter-rater agreement was summarized and evaluated according to the question domain (treatment, prognosis, diagnosis) using the Kappa ( $\kappa$ ) statistic with 95% confidence intervals (CI).

**Results:** Altogether, 15 participants from SSA and 16 participants from SA participated in the activity. Twenty-seven questions involving 6183 citations (61 to 717 citations per question) were independently reviewed by participants in pairs. The overall inter-rater agreement was moderate ( $\kappa=0.45$ ; 95% CI: 0.42, 0.480). By question type, inter-rater agreement was moderate for diagnostic ( $\kappa=0.50$ ) and fair for prognosis ( $\kappa=0.29$ ) and treatment ( $\kappa=0.35$ ) questions. The inter-rater agreement for individual questions ranged from poor ( $\kappa=0.13$ ) to good ( $\kappa=0.76$ ).

**Conclusions:** We demonstrate that a PBL approach can be used to teach study selection with a varying degree of reproducibility. The results from this pilot suggest that future panels should include targeted training on research study designs to improve the selection process. As a training program component, PBL could be a valuable tool to support the decentralization of guideline development capacity.

EP558/#1793 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### A MIXED-METHODS STUDY TO SCALE-UP IMPLEMENTATION OF PEDIATRIC EARLY WARNING SYSTEMS (PEWS) GLOBALLY: THE PEWS ADAPTATION TO SUPPORT HOSPITALS IN AFRICA (PASHA) PROGRAM

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**Background and Aims:** Pediatric Early Warning Systems (PEWS) aid with early identification of clinical deterioration and improve childhood cancer outcomes in resource-limited centers where mortality rates are highest; however, implementing evidence-based practices (EBP) like PEWS remains a challenge globally. This study describes the adaptation of a multicenter quality improvement (QI) collaborative for PEWS implementation, originally validated in pediatric oncology centers in Latin America, for use worldwide.

**Methods:** Focus group discussions, structured interviews, and quantitative surveys were used to categorize adaptations and explore their impact on PEWS implementation. Thematic analysis utilizing the Framework for Reporting Adaptations and Modifications to Evidence-Based Implementation Strategies (FRAME-IS) will evaluate the process of adapting the parent QI collaborative. Validated measures will be used to evaluate the acceptability, appropriateness, and feasibility of regional PEWS implementation.

**Results:** The PEWS Adaptation to Support Hospitals in the Alliance (PASHA) program was piloted in 5 pediatric hematology-oncology centers in Africa and Asia. Five staff (3 physicians, 2 administrators) involved in adapting and using the PEWS IS participated in a focus group discussion. Most adaptations were planned proactively based on historic and regional expertise to 1) streamline delivery of PASHA, 2) condense content, 3) reduce resource intensity, and 4) adopt a self-paced, virtual learning platform. Reactive, or unplanned, modifications

were made later to address specific barriers related to 1) staffing and human resources at the level of the trainer and global implementer, 2) external factors influencing regional hiring, and 3) variable need for individualized support to progress through PASHA. Most centers have successfully resolved challenges during the pilot; however, two centers elected to postpone participation.

**Conclusions:** Our findings may inform the global scale-up and implementation of EBP to reduce disparities in childhood cancer outcomes. Regional adaptation of IS requires proactive and reactive modifications to facilitate successful implementation in the local context.

EP559/#1105 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### PERCEPTION OF THE QUALITY OF INTERDISCIPLINARY COMMUNICATION IN THE CARE OF CRITICAL PEDIATRIC PATIENTS IN PEDIATRIC ONCOLOGIC CENTERS IN LATIN AMERICA

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**Background and Aims:** CritCom is a new validated tool to analyze the quality of interdisciplinary communication. PEWS have proven to be an effective strategy for identifying and intervening in patients with deterioration; however, its success depends on effective communication. This study aims to analyze perceptions of communication quality in pediatric cancer centers before PEWS implementation.

**Methods:** We recruited clinical staff who care for patients at risk of deterioration from pediatric cancer centers in Latin America participating in Proyecto EVAT, a quality improvement collaborative to implement PEWS. CritCom survey was sent as an anonymous electronic survey in Spanish or Portuguese with questions rated on a Likert scale of 1 (low quality) to 5 (high quality) in six domains (actionable, clarity, tone, empowerment, collaboration and teamwork, leadership). Results were calculated by averaging items within each domain, and the relationship with demographic variables was analyzed with the Kruskal-Wallis test.

**Results:** We received 262 surveys from participants from 12 pediatric oncologic centers. Averaging all participants, CritCom results were

4.067 (range 1 to 5), with the lowest scoring domain being tone (3.685). Among professions, physicians had lower scores in clarity than nurses (3.999 vs. 4.15,  $p = 0.06392$ ). Related to the practice area, ICU staff reported the highest overall score (4.13), and staff from the emergency department had the lowest score (3.733). Results by Practice Area (Oncology, ICU, General Ward) also showed a significant difference in clarity (4.04/4.242/4.067;  $p = 0.06649$ ) and tone (3.541/3.82/3.767;  $p = 0.05083$ ). Regarding gender, no statistical difference was founded.

**Conclusions:** CritCom is a tool to assess the quality of interdisciplinary communication, components of which are viewed differently by clinicians of different professions, disciplines, and genders. Critcom results can be used to identify areas to improve team communication. This work serves as a first step to assess how PEWS impact communication, identifying a baseline prior to PEWS implementation.

EP560/#1019 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### MICRONUTRIENTS AND CHEMOTHERAPY SIDE EFFECTS EVALUATION AT TIME OF A PEDIATRIC CANCER DIAGNOSIS AND DURING CHEMOTHERAPY

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**Background and Aims:** Children undergoing chemotherapy experience side effects that could be exacerbated due to micronutrient depletion. We conducted a prospective feasibility/pilot study to evaluate six micronutrients and body mass at diagnosis and after 6 months of chemotherapy. We recorded chemotherapy side effects during the study period.

**Methods:** Participants were evaluated within 4 weeks of diagnosis and after six months from diagnosis. Vitamins A, D, E and trace elements copper (Cu), selenium (Se) and zinc (Zn) were assayed. Weight, height, body mass index (BMI) and corresponding Z-scores were recorded. Parents were interviewed to ascertain if they were administering any supplements. A REDCAP data base was used for all data recorded.

**Results:** Twenty-nine patients (16 male, 13 female) with a median (range) age of 8.2 (1.7-17.6) years were enrolled. There were 14 haematological cancers and 15 solid tumours. No patients had a Z score for height, weight or BMI of  $<2SD$  or  $>2SD$ , thus no significant malnutrition was observed. Vitamins A, D, and E were abnormal in 10 (34%), 13 (45%) and 13 (45%) patients at diagnosis, in 8 (29%), 11 (38%) and 11 (38%) after 6 months of chemotherapy. Cu, Se and Zn were abnormal in 12 (41%), 14 (48%) and 13 (45%) patients at diagnosis and in 6 (21%), 8 (28%) and 15 (52%) patients after 6 months. Fourteen patients were receiving supplements prior to diagnosis and 16 during chemotherapy. There were 65 occurrences of side effects, including infection, fever, mucositis, thrombosis and ileus. There were 21 occurrences with fever. Fever and micronutrient depletion, Zn in 6, Se in 8 and Vitamin



E in 6. Two patients died early, did not complete evaluations and were excluded from analysis.

**Conclusions:** Preliminary results suggest that micro-nutrient abnormalities are common at diagnosis and throughout chemotherapy. Side effects of chemotherapy maybe exacerbated by micronutrient depletion.

EP561/#691 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### INCIDENCE AND OUTCOMES OF METHOTREXATE INDUCED NEUROTOXICITY IN PEDIATRIC ONCOLOGY PATIENTS: REGIONAL CANCER CENTRE (RCC) EXPERIENCE

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**Background and Aims:** Methotrexate, an indispensable part of contemporary chemotherapy protocols for management of Pediatric cancers, is associated with various toxicities. Methotrexate induced neurotoxicity is one such toxicity, mechanism of which is poorly understood. This study aims to assess the incidence and outcomes of Methotrexate induced neurotoxicity among Pediatric cancer patients treated at our centre.

**Methods:** Medical records of all children ( $\leq 14$  years) treated at department of Pediatric Oncology, Regional cancer centre, Thiruvananthapuram between January-2018 to December-2022 were retrospectively audited for Methotrexate induced neurotoxicity. Data on clinico-demographic parameters, Methotrexate exposure, grade, duration and course of Methotrexate neurotoxicity were recorded and factors associated with high grade neurotoxicity were analysed.

**Results:** Among 750 patients who got treated with Methotrexate containing protocols (HDMTX  $\pm$  intrathecal Methotrexate), 29(3.8%) had Methotrexate induced neurotoxicity with median age-9.1 years (range: 8 months-14 years) and male predominance (M:F-1.6:1). Methotrexate (MTX) neurotoxicity occurred only in hemato-lymphoid malignant patients of whom 58% were B-ALL. Of the ALL patients developing Methotrexate neurotoxicity, 86% were high risk, 17% had baseline CNS involvement and 31% had tumor lysis during induction. Deranged LFT was noted in 55% of patients prior to onset of MTX neurotoxicity. Median time to develop MTX neurotoxicity after exposure was 9 days (range: 3 to 100 days) with seizure being the most common manifestation (58%) followed by transient stroke like symptoms (34%). Neurotoxicity greater than or equal to CTCAE grade 3 was noted in 79%(23/29). Median duration of the MTX neurotoxicity episode

was 1.5 days with incomplete recovery in 2(7%) patients and 1(3%) developed recurrence. Exposure to high dose Methotrexate (5g/m<sup>2</sup> as 24 hour infusion) with intrathecal compared to intrathecal Methotrexate alone was significantly associated with high grade Methotrexate neurotoxicity (p=0.04). Factors such as age, sex, leukemic lineage, risk, CNS status, organ functions, MTX clearance had no bearing on grade of MTX neurotoxicity.

**Conclusions:** Methotrexate neurotoxicity occurred in ~ 4% of our patients and it was predominantly transient. Subsequent administration of Methotrexate in our patients developing MTX neurotoxicity was feasible.

EP562/#1635 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### CLINICAL AND MICROBIOLOGIC CHARACTERISTICS AND MANAGEMENT OF FEBRILE NEUTROPENIA IN PAEDIATRIC CANCER PATIENTS AT THE NATIONAL CHILDREN'S MEDICAL CENTER OF UZBEKISTAN

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**Background and Aims:** Febrile neutropenia (FN) is the most common hematological toxicity associated with cytotoxic chemotherapy. International guidelines on the diagnosis and treatment of FN are available, but they need to be assessed in the context of regional specifics. There is no standardised protocol for the treatment of FN in pediatric cancer patients in Uzbekistan. Evaluate the clinical and microbiologic characteristics and the management of FN among pediatric cancer patients admitted to the National Children's Medical Centre.

**Methods:** The retrospective and prospective study collected data from the charts of cancer patients admitted from January 1, 2022, and February 28, 2023. Inclusion criteria were: cancer patients under 18 years of age diagnosed with FN; patients with fever and an absolute neutrophil count (ANC) less than 500/mm<sup>3</sup> after chemotherapy. Bacterial cultures of blood, urine, feces, throat, etc. were performed based on clinical symptoms to determine the localization of infection.

**Results:** The total of 50 patients were included in the study, the mean age was 4.7 years. The most common diagnoses were ALL - 12 patients, followed by NHL (non-Hodgkin lymphoma), RMS (rhabdomyosarcoma), brain tumor - 6 patients each, including HD (Hodgkin disease), NB (neuroblastoma), and other diagnoses. Demographic characteristics, clinical data, and FN treatment data were collected using a patient case report form. Of the 50 patients with FN, 47 (94%) received empiric antibiotic therapy (EAT), in which cefepime accounted for 92.3%, followed by amikacin. A culture sensitivity test was performed on 19 (38%) patients.

**Conclusions:** This study showed that the therapeutic approach was adequate, but the frequency of culture test and sensitivity test was low.

Also it should be taken into account that the study region with high antibiotic resistance. In this regard, awareness of the use of culture and sensitivity tests should be raised, which will optimize the use of EAT, reduce the number of hospitalizations and minimize the recurrence of FN.

EP563/#799 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### APPROACHES TO DECISION-MAKING FOR ADVANCED OR INCURABLE PEDIATRIC CANCER AT DIAGNOSIS IN LOW- AND MIDDLE-INCOME COUNTRIES (LMICs)

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**Background and Aims:** Physicians in LMICs face challenging cancer-related decision-making, including whether to recommend curative

versus non-curative therapies at diagnosis to children presenting with advanced cancer. In this study, we sought to understand approaches to treatment decision-making at diagnosis for children presenting with advanced or incurable cancer in LMICs.

**Methods:** Semi-structured interviews were conducted with physicians who routinely care for children diagnosed with cancer across six World Health Organization (WHO) defined regions. Interviews were conducted in English using an online platform, audio recorded, and transcribed. A team of five coders developed a hybrid inductive/deductive codebook and applied codes across transcripts. Thematic content analysis focused on decision-making approaches.

**Results:** Thirty physicians engaged in interviews. Most physicians explained that decision-making begins with consideration of disease-related factors, with initial treatment recommendations shaped by consultation with specialists when available. Subsequently, physician recommendations are substantially influenced by contextual factors including limited hospital resources, family financial hardship, and high or unaffordable treatment costs. After discussion with families, decision-making pathways included families: 1) accepting non-curative, life-prolonging treatment; 2) declining the proposed treatment to return home or seek support from alternative sources; or 3) requesting intensive curative therapy, which physicians inconsistently honored. Physicians reported that challenges in decision-making were exacerbated due to lack of access to guidelines that considered salient contextual variables when recommending treatment for these children.

**Conclusions:** Physicians in LMICs across WHO regions face similar decision-making challenges for children with advanced or incurable cancer despite practicing in unique settings. Future development of treatment guidelines adaptable to different contexts should consider these similarities and integrate contextual variables that modify decision-making in the context of advanced or incurable disease. Future work will explore the perspectives and recommendations of patients and families to inform design of interventions to better support treatment decision-making, including provision of upfront non-curative treatment strategies and early integration of palliative care.

EP564/#690 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### COMPARISON OF DIETARY INTAKE WITH RECOMMENDED DIETARY INTAKE IN CHILDREN WITH CANCER USING MODIFIED DIETARY ASSESSMENT TOOLS

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**Background and Aims:** Appropriate dietary assessment and provision of adequate caloric and protein intake are essential in children

with cancer, but challenging due to the multifactorial alterations in appetite/ oral intake and gaps in standardization. We compared the actual dietary intake with Recommended Dietary Allowance (RDA) in children with cancer at our center using modified dietary assessment tools.

**Methods:** This prospective study was conducted in children 2 - 10 years being treated for cancer in our paediatric oncology unit. In phase 1, modified dietary assessment tools (24-hour recall and food frequency questionnaire; FFQ) were developed and validated; these were used in phase 2 to record the actual dietary intake and compare with nutritional requirements as per Indian RDA. The FFQ included food groups specifically available to children in our hospital including nuts, oilseeds and nutritious snacks. Nutritional assessment and interventions were as per standard SIOP/WHO recommendations. The reliability score of the tools was calculated using Cronbach's Alpha test. The difference in the anthropometric indices, daily energy/protein intake, age group and % RDA for energy/protein were analysed using one-way ANOVA.

**Results:** 150 patients were enrolled, 35 in phase 1 and 115 in phase 2. The reliability score was 0.75. All patients were >1 month from diagnosis and had been assessed and managed by paediatric nutritionists, and 90 % were compliant with nutritional advice. More (n = 66, 57.3 %) children aged 2-6 years consumed energy > 80% RDA compared to ages 7-10 years (n = 49, 42.6%, p<0.001). All patients consumed more than 100% of the protein as per the recommended dietary allowance (RDA) irrespective of age.

**Conclusions:** We developed and validated a tool for assessment of dietary intake appropriate for hospital settings in India; this tool can be modified in similar settings world-over. With proper dietary counselling, the nutritional needs of children on cancer treatment can meet RDA.

EP565/#1303 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### CARDIORESPIRATORY FITNESS, MUSCLE STRENGTH, AND PHYSICAL PERFORMANCE IN CHILDREN AND ADOLESCENTS NEWLY DIAGNOSED CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background and Aims:** Anti-cancer treatment impairs cardiorespiratory fitness, muscle strength, and physical performance in children with cancer throughout the treatment trajectory. However, the extent of these impairments is sparsely investigated in the early stages of treatment. Hence, we aimed to review the evidence on cardiorespiratory fitness, muscle strength, and physical performance of children newly diagnosed with cancer.

**Methods:** Five electronic databases, MEDLINE, Embase, CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL), and Web of Science, were searched on 19.12.2022. Studies were eligible for inclusion if they reported objective measures within the three domains; cardiorespiratory fitness, muscle strength, or physical performance of children diagnosed with cancer assessed within the first 31 days after diagnosis. Random-effects meta-analyses were used to synthesize the results compared with a healthy reference when possible.

**Results:** Thirteen studies, embodying 594 participants and 3,674 healthy controls, were included for analysis. Eighteen different outcomes within the three domains were identified and extracted. Sixteen outcomes showed severe impairments compared with healthy controls. The meta-analysis showed that newly diagnosed children with cancer had significantly lower exercise tolerance (standard mean difference -2.55[95%CI=-2.82 to -2.27], $I^2=0\%$ ), handgrip strength (mean difference -6.42kg[95%CI:-12.16 to -0.69], $I^2=96\%$ ), and walking distance (mean difference: -226.71 meters [95%CI:-255.26 to -198.16], $I^2=42\%$ ) compared with healthy controls. No adverse events were reported related to testing.

**Conclusions:** Children with newly diagnosed cancers, cardiorespiratory fitness, muscle strength, and physical performance are impaired within the first 31 days after a cancer diagnosis. However, the evidence is based on a small number of studies with large clinical heterogeneity; hence, a very low level of certainty in the evidence. Nevertheless, rehabilitation should be implemented to ameliorate further deterioration in cardiorespiratory fitness, muscle strength, and physical performance.

EP566/#1567 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### ACCESSIBILITY OF PAEDIATRIC PALLIATIVE CARE SERVICES IN A TERTIARY HOSPITAL IN A RESOURCE-POOR COUNTRY

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**Background and Aims:** There is a great need for paediatric palliative care (PPC) services globally, but access to services is lacking in many parts of the world, particularly in resource-poor nations. From the estimated 98% of the 2.5 million children that die each year with serious health related suffering nearly 50% are in the African region. However,

PPC services are rare in LMICs and where services exist; they are typically available in few institutions and are not integrated into health care systems. This study sought to evaluate the accessibility of children and their families to palliative care services and factors associated with its non-utilization.

**Methods:** The quantitative study involved data from the Paediatric Oncology of the Komfo Anokye Teaching Hospital (KATH) between January 2021 and December 2022. The data from the sample of 294 patients included the demographic data, accessibility to palliative care (PC) service and what service was provided and the factors associated with the non-utilisation. Data was analyzed using STATA 14.

**Results:** From the total sample of 294 patients taken from the Paediatric Oncology unit records of KATH between January 2021 and December 2022, 169 required PC but 72 were referred for the service but did not receive the full and standard PPC services. The patches of PPC provided to the patients were counselling and basic symptom management. The factors that hinder the delivery of PPC service are lack of education and expertise on PPC, lack of policy on PPC, parental financial difficulties, lack of medications and loss to follow up when cure is not feasible.

**Conclusions:** The accessibility of PPC services is poor, there is a gap in the number of children who need PC services and those referred, and the needs of children and their families are not met due to resource inadequacy and absence of policies and guidelines on PPC.

EP567/#401 | Poster Topic: *AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care*

#### EARLY CENTRAL LINE ASSOCIATED BLOOD STREAM INFECTION (CLABSI) IN PAEDIATRIC ONCOLOGY PATIENTS: AN AUSTRALIAN SINGLE CENTRE RETROSPECTIVE COHORT STUDY

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**Background and Aims:** Surgically inserted central venous access devices (CVADs) are inserted early in therapy to provide reliable venous access to facilitate treatment for paediatric oncology patients. CVADs are totally implantable venous access ports (TIVAPs) or tunneled external catheters (TECs). Insertion of a CVAD carries a risk of central line associated blood stream infections (CLABSI). The aims of this study were to determine the incidence of CLABSI within 90 days of insertion, to identify associated risk factors and to make recommendations regarding institutional practice to reduce CLABSI.

**Methods:** A retrospective cohort study was conducted in an Australian tertiary paediatric hospital between December 2013 and December 2018. Patients aged <18 years with a malignant diagnosis who had CVAD inserted were included. Data was collected from electronic medical records for the first 90 days after CVAD insertion. The

study analysed clinical, sociodemographic and CVAD insertion related variables using univariate and multivariate regression modelling.

**Results:** A total of 150 CVADs were analysed. 68% of CVADs were TIVAPs and 32% were TECs. There were 124 unique patients, 54% had haematological malignancies and 46% had solid malignancies. There were 70 discrete episodes of CLABSI over 12, 896 catheter days. The incidence of CLABSI was 5.4/1000 catheter days. 47.1% of CLABSI events occurred within the first 30 days. Older age (OR 0.31) and solid malignancy (OR 0.2) decreased the odds of developing CLABSI. TECs carried a stronger association with CLABSI compared to TIVAPs (OR 4.39). In haematological malignancies, insertion >14 days from diagnosis had a reduced association with CLABSI (OR 0.14).

**Conclusions:** The incidence of CLABSI was high. Age, diagnosis, type of CVAD and timing of insertion were associated with developing early CLABSI. Consideration should be given to the timing of CVAD insertion and use of TECs limited to those with absolute clinical need.

EP568/#930 | Poster Topic: *AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care*

#### A PROSPECTIVE QUALITY IMPROVEMENT INITIATIVE TO STANDARDIZE PREMEDICATION FOR BLOOD PRODUCT TRANSFUSIONS

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**Background and Aims:** Despite unclear benefit, many patients receive premedication (acetaminophen, antihistamines, and/or hydrocortisone) to prevent transfusion reactions, resulting in practice variability, unnecessary treatments, and additional costs. We developed and implemented an evidence-based algorithm for premedication prior to red blood cell (RBC) and platelet transfusions for oncology patients at MSK Kids.

**Methods:** Our algorithm recommended premedication only in patients with a history of transfusion reaction. Guidance was provided on use of premedication based on severity of previous transfusion reaction (s). Patients with a history of complex transfusion reactions were excluded.

**Results:** Between January-April 2022, 127 patients (858 total transfusions; 52.2% platelets, 47.8% RBCs) met inclusion criteria. Median age at transfusion was 9.1 years (range 0.4 – 18.7). Each patient received a median of 3 transfusions (range 1-52). Algorithm for premedication was followed in 73% (626/858) of transfusions. Following algorithm introduction, premedication was administered in 28.6% of total transfusions (245/858), compared to 72.0% (434/603) prior. For patients

with a history of transfusion reaction, 71.4% (205/287) of total transfusions were premedicated. For patients without a history of previous transfusion reactions, 6.7% (38/565) of total transfusions were premedicated. This reduction in premedication among patients with no transfusion reaction history from 57.5% (222/386) to 6.7% (38/565) is markedly lower following guideline implementation. Transfusion reactions occurred in 1.5% (13/858) of transfusions compared to 3.2% prior to algorithm implementation. Reactions included: rash/pruritus (n=9), fever (n=6), and/or respiratory symptoms (n=1). There was no significant difference in the incidence of transfusion reactions between those that were premedicated (0.8%) versus those that were not (1.8%;  $p=0.45$  by Chi-squared test). No severe sequelae or intensive care unit admissions occurred.

**Conclusions:** Standardization of an evidence-based algorithm and provider education resulted in decreased premedication for blood product transfusions without an increase in frequency or severity of transfusion reactions. Based on this analysis, we implemented our guidelines institution-wide to standardize practice.

EP569/#361 | **Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care**

#### TREATMENT ABANDONMENT: THE MOST COMMON AND A LARGELY PREVENTABLE CAUSE OF TREATMENT FAILURE IN SUB-SAHARAN AFRICA – A REPORT FROM CANCARE AFRICA

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**Background and Aims:** Treatment abandonment is the most common cause of childhood cancer treatment failure in sub-Saharan Africa. A pilot study in Malawi showed a significant decrease in treatment abandonment among newly diagnosed children with common and curable childhood cancer from 19% to 7% ( $P<0.001$ ) with full coverage of out-of-pocket costs for transportation. A previous CANCaRe Africa

study found the need to borrow money to reach the hospital as the only significant predictor of treatment abandonment. Objective was to collect baseline data to plan a family cash support intervention to prevent treatment abandonment in a sustainable fashion.

**Methods:** We conducted a multi-centre, prospective, observational cohort study in five hospitals in Malawi, Ethiopia, Ghana and Cameroon. We included patients younger than 16 years and newly diagnosed with acute lymphoblastic leukaemia (ALL), Hodgkin disease, Wilms tumour, retinoblastoma and Burkitt lymphoma. We described practices and outcomes in prevention of treatment abandonment.

**Results:** Between January 1<sup>st</sup> and September 1<sup>st</sup> 2022 we included 285 patients after the exclusion of seven patients with a misdiagnosis. The median age was 5.8 (range 0.4–15.6 years), 60% were male. The most common diagnosis was Burkitt lymphoma (84/285, 29%). Of these 285 patients, while 12% (34/285) are still on treatment, 19% (55/285) abandoned treatment. Median distance from home to the hospital was 110 (range 1 to 1432 km). Seventy three percent (208/285) of families borrowed money to reach the hospital for diagnosis and start of treatment. Ninety eight percent (278/285) of families were counselled about the diagnosis and treatment and 95% (270/285) about the importance of completing treatment.

**Conclusions:** Poverty and families' inability to pay for out-of-pocket costs such as transport costs are an overriding cause of treatment abandonment in sub-Saharan Africa. Future work will include continued collaborative efforts, joint advocacy and an implementation research informed cash family support intervention.

EP570/#1634 | **Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care**

#### THE CHALLENGES OF EARLY DEATHS IN CHILDREN DIAGNOSED WITH ACUTE LEUKEMIA IN MOZAMBIQUE

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**Background and Aims: Background and aims** Despite the advances in diagnosis and treatment of acute leukemia (AL), early deaths are

still a major problem in countries with limited resources. The aim of this study was to characterize the cases of pediatric death, and those occurring early after diagnosis of AL, in a reference Hospital in Mozambique.

**Methods:** Retrospective clinical and demographic data, including the period to death, were collected from clinical files from children diagnosed with acute AL at the Hemato-Oncology Service at Hospital Central de Maputo, from January 2020 to December 2022. Immunophenotypic data was collected at Instituto Nacional de Saúde. Early death was considered as those occurring before or during the induction phase of chemotherapy. Chi-square test was used for frequencies comparison.

**Results:** A percentage of 40.00% (16/40) of death was observed among children diagnosed with B-cell acute lymphoblastic leukemias (B-ALL), 35.29% (6/17) for T-cell acute lymphoblastic leukemias and 55.56% (15/27) for acute myeloblastic leukemia (AML). No difference was found on rate of death between groups ( $p=0.3254$ ). Twenty-four early deaths were observed. Of these, 24.32% (9/37) before and 40.54% (15/37) during the treatment induction phase. Among these early deaths, 41.66% (10/24) were AML cases. Overall, 78.38% (29/37) deaths occurred in children aged between 1-10 years and 83.78% (31/37) had white blood cells count lower than 1, at time of diagnosis. Moreover, 75.67% (28/37) of children were classified as high risk. Moderate anemia and severe thrombocytopenia at diagnosis were identified in 68.57% (24/35) and 21.62% (8/37) of cases, respectively.

**Conclusions:** We found high early death rate among children diagnosed with AL, particularly those with AML. The study reinforces need to strengthen the early diagnosis and optimization of supportive care to reduce the mortality rates in children diagnosed with AL in Mozambique. Additional studies are needed to understand the causes of early deaths.

EP571/#188 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### CAN SERUM LACTATE ON ADMISSION TO INTENSIVE CARE PREDICT LENGTH OF STAY? A RETROSPECTIVE ANALYSIS OF PEDIATRIC ONCOLOGY PATIENTS

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**Background and Aims:** Pediatric oncology patients suffer significant morbidity and mortality, and nearly 50% require pediatric intensive care unit (PICU) admission. The significance of raised serum lactate remains unknown in this cohort. Patients who require PICU admission have worse outcomes, and may undergo additional treatments in efforts to normalise lactate. We assessed the association between serum lactate in pediatric oncology patients and the length of stay (LOS).

**Methods:** We conducted a retrospective observational study of patients admitted to the oncology service at a tertiary children's hospital from 2015-2020. Admissions were categorized into those requiring PICU admission and those who did not. The primary outcome was PICU LOS. Multiple regression modelling assessed the association between lactate measured at PICU admission and PICU LOS, controlling for patient demographic and clinical covariates. The secondary outcome was hospital LOS.

**Results:** Of 22,773 admissions, 654 (431 children) were admitted to PICU. Of these PICU admissions, 206 (31.5%) had serum lactate  $\geq 2$  mmol/L on admission, 233 (35.6%) had normal lactate levels and the remaining 215 (32.9%) did not have lactate measured on admission. The median PICU length of stay was 31.6 hours (Interquartile Range 21.5,70.4). Of the patients admitted to PICU, 294 (68.2%) were diagnosed with solid tumour, 84 (19.5%) hematologic malignancy and 53 (12.3%) received a bone marrow transplant. In unadjusted models, increased lactate was significantly associated with longer PICU LOS ( $\beta 0.06, 95\%$  Confidence Interval [CI] 0.01, 0.11). After adjusting for demographic and clinical covariates, the effect of lactate was no longer significant. Higher lactate on admission to PICU was associated with longer hospital LOS in both unadjusted and adjusted models.

**Conclusions:** After adjusting for clinical and demographic covariates, hyperlactatemia at PICU admission was not associated with PICU LOS in pediatric oncology patients, but had significant association with hospital LOS. Improving our understanding of raised lactate in this population may prevent unnecessary and potentially harmful interventions.

EP572/#61 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### EVIDENCE-BASED PRACTICE FOR OCCUPATIONAL THERAPISTS IN PEDIATRIC ONCOLOGY: A SCOPING REVIEW

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**Background and Aims:** Being affected by cancer during childhood or adolescence disrupts the activities of daily living and participation in expected life roles. To be able to help children or adolescents reach their full potential, occupational therapists need to be aware of the newest available evidence supporting their role and interventions. Thus, the purpose of this scoping review is to map, organize, and analyze the articles published about occupational therapy practice in pediatric oncology for making clinical practice recommendations.

**Methods:** We searched CENTRAL, MEDLINE, Embase, CINAHL, PEDro, conference proceedings, and the reference lists of relevant studies and reviews. We also contacted oncology rehabilitation researchers working in pediatric oncology to identify additional studies. Following the Arksey and O'Malley (2006) framework for scoping reviews, the first author screened titles and abstracts, and all four

authors reviewed sets of the included articles. Conflicts were discussed until consensus was reached. Study quality was rated by the Grading of Recommendation Assessment, Development and Evaluation (GRADE) criteria.

**Results:** Articles included research studies and practice analyses. The occupational therapy interventions were diverse, ranging from play-based interventions for hospitalized children to self-expressive group activities for survivors. Furthermore, the majority of papers were rated as of low quality and with little evidence of outcomes from treatment.

**Conclusions:** A wide range of OT roles and interventions have been identified. This review identified a lack of empirical research available to date for occupational therapists to support their practice and inform them on the most effective assessments and interventions. There is an urgent need for research and development of evidence-based intervention within our profession.

EP573/#1119 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### DEFINING AND PRIORITIZING SUPPORTIVE CARE TOPICS FOR THE ADAPTED RESOURCE AND IMPLEMENTATION APPLICATION (ARIA GUIDE) CARE BOOK: A GLOBAL MULTIDISCIPLINARY CONSENSUS-BUILDING EXERCISE

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**Background and Aims:** Optimal outcomes during childhood cancer treatment necessitate effective management of therapy-related toxicities. A lack of consensus on essential supportive care priorities impedes development and dissemination of best practices. This exercise aimed to identify and prioritize supportive care topics for development of clinical practice recommendations in the ARIA Guide Care Book.

**Methods:** Two rounds of brainstorming and prioritization exercises were conducted from September – December 2022 using Qualtrics. Participants were nominated to ensure geographic and resource representation using purposive sampling. An initial core list of topics was generated by ARIA content experts. In round one, participants reviewed core topics and could recommend additional topics. The ARIA

content experts reviewed the additional topics for inclusion. In round 2, participants first prioritized topics using a 7-point Likert scale, then ranked factors influencing their prioritization of topics. The results were summarized using descriptive statistics.

**Results:** Fifty-seven individuals (57/114; 50% response) representing 32 countries (22 low- or middle-income countries, representing 68% of respondents [39/57]) completed the survey. Respondents included paediatric oncologists (n= 33), radiation oncologists (n= 9), general surgeons (n=3), neurosurgeons (n=3), nurses (n=3), pharmacists (n=5), and a patient advocate from a non-profit foundation (n=1). The initial list included 46 topics; 81 additional items were suggested; after removing duplicates and out-of-scope topics, the final list contains 62 topics. Five topics (febrile neutropenia, sepsis, blood-stream infections, pain, and mediastinal mass) were ranked the highest priority. Nine factors were identified that influenced prioritization; the top three were mortality, morbidity, and frequency.

**Conclusions:** Using a multidisciplinary and globally representative process, we defined priority topics and factors influencing prioritization of supportive care for children with cancer. Next, we will use this to generate clinical practice recommendations for priority topics. This list supports WHO CUREALL efforts to define supportive care needs for policymakers and health systems administrators.

EP574/#1044 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### ESTABLISHMENT OF THE FIRST PEDIATRIC PALLIATIVE CARE CLINIC IN ARMENIA

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**Background and Aims:** City of Smile Foundation supports children and young adults, through the age of 25, with cancer and blood disorders by covering all their treatment expenses.

Until 2021, there was not any facility for pediatric oncology patients with palliative care needs in Armenia.

City of Smile Charitable Foundation decided to fill in that gap and initiated the construction of the first ever pediatric cancer palliative care clinic in Armenia.

**Methods:** To begin with, a qualitative survey regarding the necessity and need of pediatric cancer palliative clinic service was conducted among the families of pediatric cancer patients who unfortunately lost their battle to cancer. The main question asked was: "Would you rather prefer your child spend his last days in a specialized palliative care center, or at home". As a result of that survey, 90% of the survey

participants emphasized the need of specialized care place for their children, given multiple logistical, pain management, patient care and other difficulties both for patients and their family members. By the initiative and funding of City of Smile Foundation and with the advisory support of US-based St. Jude Children's Research Hospital, the first pediatric palliative care clinic of Armenia was opened on September 28, 2021, at the Hematology Center after Prof. R. Yeolyan.

**Results:** After the opening of the Pediatric Palliative Care Clinic, not a single child with palliative care needs has been left without specialized care. The mission of the Pediatric Palliative Care Clinic is to provide physical, sensory and spiritual care to kids whose diseases do not respond to treatment, in order to improve the quality of life of patients and their families as much as possible.

**Conclusions:** Thanks to the City of Smile Foundation, a historical event took place in the field of pediatric palliative cancer care in Armenia.

EP575/#1160 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### NAMED PATIENT PROGRAM USE OF PEDMARK® TO REDUCE THE RISK OF CISPLATIN-INDUCED OTOTOXICITY IN PEDIATRIC PATIENTS WITH VARIED SOLID TUMORS

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**Background and Aims:** Cisplatin induced-ototoxicity (CIO) with permanent hearing loss is observed in 60-90% of pediatric patients with any solid tumor. PEDMARK® (sodium thiosulfate, Fennec formulation) reduced the proportion of patients with hearing loss by half as observed in Phase-3 trials (SIOPEL 6 & COG ACCL0431). PEDMARK® is approved for use in the US. The aim was to evaluate

PEDMARK® provided to pediatric patients via a multi-national Named Patient Program (NPP).

**Methods:** Physicians requested PEDMARK® for patients with solid tumors, treatment plans including a cisplatin-containing regimen, and cisplatin infusion time  $\leq 6$  hours. PEDMARK® was administered intravenously 6-hours after each cisplatin infusion. Demography, tumor-type, and adverse events (AEs) were recorded (APR2018-FEB2023). Hearing and tumor outcomes were provided retrospectively.

**Results:** The NPP has been open 4.8-years. Fifty hospitals in 14 countries requested PEDMARK®, totaling 133 requests, of which 18 patients had varied solid tumors other than hepatoblastoma. Of the 18 patients, the median age and weight was 10-years (range: 3-19) and 28-kg. Frequent tumors were medulloblastoma (n=6), osteosarcoma (n=4) nasopharyngeal carcinoma (n=3) and glioma (n=2); other tumors (n=1) included atypical teratoid/rhabdoid tumor, retinoblastoma, and primary CNS neuroblastoma. Of patients with available data (n=13), most had newly diagnosed disease (n=10) and received a median of 4-cycles of cisplatin and PEDMARK® (range: 1-6). Patients with pre- & post-treatment hearing exams (n=12), n=7 (58%) maintained a Brock Grade-0, of the remaining with hearing loss, n=3, had cranial-radiation. Post-treatment outcomes (n=13) included complete responses (CRs), stable and progressive disease in 10, 1, and 2 patients. All CRs were sustained at a median follow-up of 14.4-months. Grade 1-2 nausea/vomiting was reported (n=10). No Grade  $\geq 3$  related-AEs were observed.

**Conclusions:** PEDMARK® was well-tolerated when supplied via a NPP to reduce the risk of CIO in pediatric patients with varied solid tumors. Real-world post-treatment hearing and tumor outcomes were consistent with Phase-3 trial results.

EP576/#717 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### MUSICAL INTERVENTION DURING THERAPEUTIC LUMBAR PUNCTURE IN CHILDREN WITH LEUKEMIA: A RANDOMIZED CROSS-OVER STUDY

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**Background and Aims:** **Background:** Therapeutic lumbar puncture (LP) is a stressful procedure experienced by children with leukemia. Inadequate pain and anxiety relief during the procedure may have long-term consequences. Non-pharmacological pain therapies may benefit during the procedure. **Objective:** To evaluate the effect of musical intervention during therapeutic LP in children with leukemia

**Methods:** A randomized cross-over trial study was conducted in 2021-2023. All patients underwent two sessions of therapeutic LP during the enrolled period. One session of therapeutic lumbar puncture, musical intervention using personal headphones with patient-preferred music



was intervened. Pain assessment using verbal numerical rating score and FLACC score, vital signs, satisfaction, and distress were assessed and compared between two therapeutic lumbar sessions with and without musical interventions.

**Results:** Of Twenty-three patients (11 male, 12 female), the median age of 9-10 years (range 3-18 years) were enrolled. The patient's pain score during and after therapeutic LP with musical intervention is less than in the session without musical intervention, with no statistical significance ( $p$  0.935, 95%CI -1.05 - 1.14). The overall satisfactory score during the procedure was also higher in the session with musical intervention, with an average score of 4.23 and 3.91, with no statistical significance ( $p$  0.104, 95%CI -0.81 - 0.08). Interestingly, 14 of 23 patients (60%) would like to perform the next therapeutic LP with musical intervention.

**Conclusions:** Musical intervention affects pain, vital signs, and satisfaction and may be an optional non-pharmacological pain therapy in children who need repeated therapeutic pain procedures.

EP577/#648 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### TREATMENT RELATED MORTALITY IN ACUTE LYMPHOBLASTIC LEUKEMIA: REALITY IN A LOW MIDDLE INCOME COUNTRY

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**Background and Aims:** High treatment-related mortality (TRM) is one of the limitations in managing children with malignancies in LMICs, soliciting the need for efficient and low-toxicity protocols. This analysis was performed to evaluate TRM in ALL at our referral tertiary care hospital.

**Methods:** Analysis of deaths from 2018 to 2021 (4 years) was done from case records. Therapy was as per the Indian Childhood Collaborative Leukemia Group (ICiCLE) protocol using prophase steroids for 7 days followed by chemotherapy as per risk allocation (Standard-SR, Intermediate-IR, and High-HR). Patients stay near the referral center up to the maintenance phase, subsequently attending the hospital 1-3 monthly from home, with regular virtual monitoring of counts.

**Results:** Five hundred sixty-seven patients were treated between 2018 and 2022. There were 35 induction deaths (6.1%). Four patients did not achieve remission. Thirty-eight patients expired after achieving complete remission (7.1%) giving a cumulative TRM of 12.8%, with sepsis accounting for 85% of deaths. *Induction deaths (35):* Twenty-six (75%) were secondary to infection [76% bacterial and 19% fungal]. A bleed accounted for 3 (8.5%) deaths and tumour lysis syndrome for 2%. *Post-induction deaths (38):* Fourteen (36%) were in intensive phases (consolidation and intensification; IR -2; HR-4) all related to sepsis (75% bacterial, 20% fungal). Six deaths occurred in the interim maintenance phase (74% sepsis, 4-SR; 2-HR) and 18/38(47%) expired in

the maintenance phase of therapy. Only one of the 18 patients did not have an infective focus (tracheostomy bleed). Six patients with an infective focus died en route to the hospital (a distance of 100-250km from centre)

**Conclusions:** Superior infection control and prevention practice is the way forward in combating sepsis, a modifiable problem, in LMICs to improve overall survival. The need to ensure the 'golden hour' in surviving sepsis & develop shared care in peripheral hospitals to provide immediate care cannot be overemphasized.

EP578/#1260 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### THERAPY ABANDONMENT IN SOLID TUMOURS: A PERSPECTIVE FROM A TERTIARY CARE CENTRE IN INDIA

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**Background and Aims:** Abandonment is one of the prime causes of treatment failure, seen to affect up to 60% of the cancer-affected children in LMICs. Multifactorial reasons are cited, essentially the demographics, per capita income, and health care system. In this analysis we rigorously tracked patients [throughout the duration of therapy] with solid tumours commenced on therapy over a period of 18 months (Aug 21-Dec 2022) to ensure completion of therapy, record abandonment & evaluate reasons.

**Methods:** A spreadsheet was made for each solid tumour and divided amongst the registrars. The registrars kept a 2 weekly track of patients throughout the course of therapy and telephoned patients when they were observed to miss a clinic appointment. The tumours included Wilms' tumour[WT], Neuroblastoma[NB], Hepatoblastoma, Osteosarcoma[OS], Rhabdomyosarcoma, Ewing's sarcoma, Germ cell tumour, Retinoblastoma[RB] and Hodgkin's Lymphoma. Financial & lodging assistance was offered to all. Upfront abandonment was not analysed.

**Results:** Two hundred-one patients (3 years [3m-12y]) commenced treatment with nineteen (9.4%) abandoning therapy. Surgical issues were a major cause of abandonment in 15/19 [78%] patients -6 (40%) defaulted after surgery [WT, GCT& NB-2 each], citing chemotherapy as unnecessary after surgery; nine (1-OS, 6- RB & 2-NB) refused surgery, wanting treatment only with chemotherapy. Social demographics could not be compared owing to small numbers in each group of tumours. Two cited family issues and 2 patients with metastasis defaulted as the

prognosis was bleak. Notably, patients refused phone calls after being contacted a few times.

**Conclusions:** These observations suggest fear of surgery as a contributory factor towards abandonment, finances possibly being the tip of the iceberg. The possibility of disfiguring surgery resulted in 7/19 patients abandoning therapy with 6/19 considering surgery as the final treatment. Personal family issues and a poor prognosis were additional reasons. These findings highlight the need for continuous education & the necessity for social services, often limited in LMICs.

EP579/#468 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### THE APPLICABILITY OF THE CENTRAL LINE-ASSOCIATED BLOODSTREAM INFECTION (CLABSI) CRITERIA FOR THE EVALUATION OF BACTERAEMIA EPISODES IN PAEDIATRIC ONCOLOGY PATIENTS

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**Background and Aims:** The aim of this study was to investigate the applicability of the central line-associated bloodstream infection (CLABSI) criteria of the Center of Disease Control and Prevention (CDC) in paediatric oncology patients.

**Methods:** Bacteraemia episodes from 2020-2022 in a cohort of paediatric oncology patients with a central venous catheter were included prospectively. All episodes were classified by three medical experts following the existing CLABSI criteria as a CLABSI or non-CLABSI (i.e. contamination, other infection source, or mucosal barrier injury-laboratory confirmed bloodstream infection (MBI-LCBI)). Subsequently they were asked if and why they (dis)agreed with this diagnosis following the criteria, when looking at the clinical data of the patient. All non-unanimous outcomes were discussed until all experts agreed, final judgement was based on the majority if an unanimous outcome could not be reached. The primary outcome of this study was the percentage of episodes where the experts clinically disagreed with the diagnosis given following the CLABSI criteria.

**Results:** In total, 84 bacteraemia episodes in 71 patients were evaluated. Following the CLABSI-criteria, 34 (40%) episodes were classified as CLABSIs and 50 (60%) as non-CLABSIs. In 11 (13%) cases the experts clinically disagreed with the diagnosis given by the CLABSI

criteria. All cases of disagreement concerned CLABSIs following the criteria; i.e. 11 (32%) out of 34 CLABSIs. Disagreement by the experts with the CLABSI criteria mostly occurred when the experts found translocation and thus an MBI-LCBI a more plausible cause of the bacteraemia than a CLABSI due to the presence of a gram negative bacteraemia (*Pseudomonas aeruginosa* n=3) and mucositis.

**Conclusions:** The CLABSI criteria are applicable for paediatric oncology patients. However, adding *Pseudomonas aeruginosa* as an MBI pathogen and incorporating the presence of mucositis in the MBI-LCBI criteria, might increase the applicability of the criteria for this patient group.

EP580/#496 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### CENTRAL VENOUS CATHETER-RELATED BLOODSTREAM INFECTIONS CAUSED BY ENTEROBACTERALES IN PAEDIATRIC ONCOLOGY PATIENTS; CATHETER SALVAGE OR REMOVAL

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**Background and Aims:** The aim of this study was to determine whether salvage treatment with antibiotics is safe and effective after diagnosis of a bloodstream infection caused by *Enterobacterales* in paediatric oncology patients with a central venous catheter (CVC).

**Methods:** A retrospective study including oncology and stem cell recipient patients from 0-20 years old with a CVC and a positive blood culture with *Enterobacterales* at the Princess Máxima Centre, Utrecht, the Netherlands, was performed. Analyses were performed for all bloodstream infections (BSI) included and for episodes meeting the central line-associated bloodstream infection (CLABSI) criteria. The primary outcome was cumulative event-free survival (events: removal, intensive care unit admission, reinfection or death) after salvage treatment for *Enterobacterales* CLABSIs. Patients were followed-up for a maximum of 60 days after the BSI. Furthermore, risk factors for CLABSI related events were assessed.

**Results:** A total of 95 CVC-related *Enterobacterales* episodes in 82 patients were included, direct CVC removal was performed in 12 (13%) episodes and catheter salvage was attempted in 83 (87%). Of these 83 salvage episodes, 45 (54%) met the CLABSI criteria. Cumulative event-free survival after salvage treatment for BSIs (n=83) and CLABSIs (n=45) were 43% and 28%, respectively. Episode related CVC removal was performed for BSIs and CLABSIs in 47% and 60% of cases, respectively. Re-infections after BSIs and CLABSIs occurred in 6% and 4% of

cases, respectively. Intensive care unit admission was required for BSIs and CLABSIs in 16% and 16% of cases, respectively. Death resulting from BSIs and CLABSIs was observed in 5% and 2% of cases, respectively. No risk factors appeared to be associated with CLABSI related events.

**Conclusions:** Salvage treatment for CLABSI caused by *Enterobacteriales* in paediatric oncology patients results in low cumulative event-free survival. Immediate CVC removal is therefore advised for this patient group.

EP581/#180 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### PHYSICAL FRAILITY DETERIORATES AFTER A 5-DAY DEXAMETHASONE COURSE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA, RESULTS OF A NATIONAL PROSPECTIVE STUDY

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**Background and Aims:** Physical vulnerability in pediatric patients is associated with adverse outcomes, such as higher infection rates, increased hospitalizations and impaired survival. Dexamethasone is important in the treatment for acute lymphoblastic leukemia (ALL) but induces muscle atrophy with consequences for physical strength and abilities. We aimed to study the effect of a 5-day dexamethasone course on sarcopenia and physical frailty in children with ALL, and to explore prognostic factors.

**Methods:** Patients with ALL aged 3-18 years were included during maintenance therapy. Patients had a sarcopenia/frailty assessment on the first day of a 5-day dexamethasone course (T1) as well as the day after this course (T2). Sarcopenia was defined as low muscle strength in combination with low muscle mass. Prefrailty and frailty were defined as having two or  $\geq$ three of the following components respectively: low muscle mass, low muscle strength, fatigue, slow walking speed and low physical activity. Paired tests were used to assess differences between T1 and T2. Logistic regression models were estimated to explore patient- and therapy-related prognostic factors for frailty.

**Results:** We included 105 patients. Median age was 5.3 years (range: 3-18.8). At T1, sarcopenia, prefrailty and frailty were observed in respectively 2.8%, 23.5% and 4.2% of patients. At T2, the number of patients with sarcopenia and prefrailty were similar, whereas frailty had increased to 17.7% ( $p=0.002$ ). Low muscle mass had increased with 14.5%, fatigue with 44.6% and low physical activity with 18%

( $p<0.01$ ). Weight (OR=0.54, 95%CI:0.33-0.89), maintenance treatment week (OR=0.94, 95%CI:0.9-0.98), muscle mass (OR=0.49, 95% CI:0.28-0.83), handgrip strength (OR=0.41, 95% CI:0.22-0.77), walking speed (OR=2, 95%CI:1.2-3.39) and physical activity (OR=0.98 95%CI:0.96-0.99) at T1, were associated with frailty at T2.

**Conclusions:** Physical frailty increased strikingly after a 5-day dexamethasone course in children with ALL. Children with poor physical state at start of the dexamethasone course were more likely to be frail after the course.

EP582/#673 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

#### PROFILE AND OUTCOME OF PROVEN INVASIVE FUNGAL DISEASES (IFDS) AMONG PEDIATRIC HEMATOLYMPHOID CANCER PATIENTS: EXPERIENCE FROM A TERTIARY CANCER CENTRE IN SOUTH INDIA

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**Background and Aims:** Invasive fungal diseases (IFDs) occur mainly in pediatric hemato-lymphoid patients secondary to the immunosuppressive effects of chemotherapy, prolonged use of antibiotics and indwelling catheters. Nevertheless, proven fungal infections are rare and we aimed to assess the clinical presentation, risk factors and outcome of the proven fungal infections in our centre.

**Methods:** Retrospective audit of electronic medical records of pediatric hematolymphoid patients treated between January-2018 to December-2022 at pediatric oncology department, Regional Cancer Centre, Thiruvananthapuram was conducted.

**Results:** Of the 964 hemato-lymphoid malignant patients treated during the study period, 65(6.7%) had proven IFDs, with median age of 3years (range:9months to 13years) and Male:Female:0.97:1. Proven IFDs occurred predominantly in B-Acute Lymphoblastic Leukemia (79%) followed by Acute Myeloid Leukemia (9%), T-Acute Lymphoblastic Leukemia and Burkitt lymphoma (5% each). During IFD episodes, three fourth of patients (50/65) had received steroids and close to two-third (37/65) had Central lines insitu; 11% of patients had documented hyperglycemia and 5% were on total parenteral nutrition. Main focus of these IFDs include blood (65%), skin and soft tissue (19%) and sputum (6%). Candida species was the most common fungal isolate (66%) followed by Aspergillus flavus (20%), Fusarium (4.6%), Histoplasma (1.5%), Trichoporon asahii (1.5%), Rhizopus (1.5%) and Microsporium canis (1.5%). All the candidal isolates were sensitive to azoles. IFDs resulted in delay in scheduled chemotherapy in 37% patients (median

delay-6.5days). Seventy percentage (45/65) cleared their fungal focus within a median of 4days (range:5 to 17days), and 5patients (8%) had persistent infection. The median duration of hospital stay during proven IFDs was 18days, where 11(17%) had hemodynamic instability requiring inotropes, 9(13%) required ICU support/mechanical ventilation. Proven IFDs resulted in death in 15%(10/65) of the patients. Central lines were significantly associated with blood stream fungal isolate (Odds ratio:4.183(95%CI:1.422-12.304; p= 0.009).

**Conclusions:** Proven IFDs was associated with significant morbidity including prolonged hospital stay, chemotherapy delay, intensive care admissions and 10% mortality among pediatric hematolymphoid patients treated at our centre.

EP583/#443 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

### EFFECTIVENESS IN THE IMPLEMENTATION OF “GOLDEN HOUR” PROJECT IN THE CHILDREN'S HOSPITAL OF TAMAULIPAS, MEXICO

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**Background and Aims:** Background and objectives: The “Golden Hour” is an initiative to improve the quality of care that consists of the administration of antibiotics to pediatric patients with solid tumors or hematological neoplasms with febrile neutropenia (FN) during the first hour after arrival at the hospital in order to decrease its morbidity and mortality. We evaluated the effectiveness of “Golden Hour” in a pediatric hospital in Mexico.

**Methods:** Longitudinal study that includes 57 events of febrile neutropenia that attended the emergency room. “Golden hour” protocol was followed, which includes: taking body temperature, complete blood count, and blood cultures. Broad-spectrum antibiotics were administered within the first hour of arrival, according to the institutional guide. The following clinical effectiveness parameters were measured: Percentages of sepsis, infectious focus at admission, sepsis with infectious focus, critical interventions, transfer to intensive care unit (ICU) and mortality rate.

**Results:** 57 events were evaluated. All with blood cultures on admission. 85.9% antibiotic was administered during the first hour. Clinical effectiveness measures: % sepsis 5.2% (N=3). Infectious focus at admission 29% (N=17), of them 5.2% (N=1) presented sepsis during the first 48 hours. Critical interventions: 3.5% (N=2), transfer to ICU: 1.75% (N=1) mortality rate 1.4% (N=1)

**Conclusions:** This improvement project exceeded the initial goal that was the administration of antibiotics during the first hour to 70% of the patients, reaching a percentage of 85.9%. Secondary to this, the indicators of clinical effectiveness are lower than those reported in the literature, highlighting a very low mortality rate. The implemen-

tation of this project in pediatric units for childhood cancer care is recommended.

EP584/#1045 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

### STRUCTURED PEDIATRIC CARE AIDS THE AI (ARTIFICIAL INTELLIGENCE) IN PRIOR-AUTHORIZATIONS FOR FINANCIAL ASSISTANCE – NAVYA-AI AND INDIAN CANCER SOCIETY – CANCER CURE FUND STUDY

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**Background and Aims:** NavyaAI in collaboration with Indian Cancer Society – Cancer Cure Fund (ICS-CCF), have piloted, validated, and implemented Artificial Intelligence (AI) prior-authorization for sanctioning of financial assistance to cancer patients, on a National level. From 2011 to 2022, 9800 underprivileged cancer patients received USD 23 Million through the ICS-CCF project. We report the findings of cohort analysis characterizing pediatric experience as compared to adults.

**Methods:** NavyaAI is a clinically validated AI model that matches clinical data of beneficiary applicants (Input) with available clinical evidence and expert recommendations/guidelines, adapted to the ICS-CCF approval criteria (Output). The Due Diligence Team (DDT) formed the first tier of concordance evaluation and General Advisory Council (GAC) was the second tier of authorizing body. If the output treatment options matched the planned treatment, the application was authorized and sent directly to GAC, otherwise rejected or referred to DDT. Pediatric and Adult cohorts were compared for approvals, rejections, referrals and potential Expert-time-saves.

**Results:** From February 2021 to March 2023, 4739 patient applications were processed through NavyaAI for ICS-CCF. Of these, 919(19.39%) were pediatric and 382(80.61%) were adults. NavyaAI approved 800/919(87.05%) of pediatric and 2931/3820(76.73%) of adult applications. The concordance with final approval by GAC was 99.75% and 99.49% respectively. NavyaAI rejected 3/939(0.33%) of pediatric and 47/3820(1.23%) of adult applications. The concordance with GAC for rejections was 100% and 91.49% respectively. A 116/919(12.62%) of pediatric applications and 842/3820(22.04%) of adult applications, processed by NavyaAI, required referral to Expert-based DDT for review before final decision by GAC. Expert-time-save was equal for pediatric and adult cohorts based on averages.

**Conclusions:** Streamlined guidelines-based pediatric cancer care helped AI in independently making higher final prior-authorization decisions as compared to adult patients with cancer. Our study demonstrates an inventive offtrack benefit of structured pediatric healthcare systems.

EP585/#1572 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

## END-OF-LIFE PSYCHOSOCIAL SUPPORT FOR SIBLINGS OF CHILDREN WITH CANCER

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**Background and Aims:** Siblings of children with cancer experience psychosocial challenges, are at risk of having unmet needs, and may benefit from interventions. The aim of this study was to explore health care practitioners' (HCPs') perspectives on supporting siblings of children with poor prognosis cancers, in part to delve into care provided near end-of-life.

**Methods:** We used interpretive description to conduct and analyze 14 semi-structured interviews with HCPs at a Canadian pediatric oncology centre

**Results:** We identified four themes that influenced HCPs' ability to provide psychosocial support to siblings: (1) Sibling as an Individual, (2) Parents' Roles in Protecting their Children, (3) Realities of Practice for HCPs, and (4) Systemic Factors Influencing Sibling Support. Participants worried that sibling perspectives are not consistently considered near end-of-life. For example, siblings may not be included in difficult conversations or end-of-treatment celebrations. Sibling goals related to meaning making, such as going "to the park with their sibling for an afternoon before they pass", were noted to be explored less often compared to patient and parent goals. While sibling support is routinely offered, parents may choose to defer support for several reasons, including focusing on the patient and maintaining a sense of normalcy for siblings. Parents may limit siblings' contact with HCPs, fearing disclosure of prognostic information. Participants addressed this issue by building rapport with families and respecting parents' decision-making, in hopes that information would be shared with siblings later. In terms of system-level factors, resources and time constraints were noted as barriers to psychosocial support.

**Conclusions:** Our study highlights challenges to sibling support prior to bereavement and opportunities to improve care. Key practices should include standard procedures to connect siblings with psychosocial support, asking about sibling goals for meaning making at

end-of-life, and inviting siblings to participate in significant events in hospital.

EP586/#1468 | Poster Topic: AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care

## A QUALITATIVE ANALYSIS OF CHILDHOOD CANCER PATIENTS' EXPERIENCES OF A STRUCTURED EXERCISE PROGRAM

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**Background and Aims:** Childhood cancer patients are exposed to increased morbidity due to physical inactivity, fatigue, and reduced health-related quality of life. Using qualitative methods, we examine patients' experiences of personalized and standardized exercise interventions and their effects on well-being, coping and self-image.

**Methods:** The current research represents first insights of a single center experience within the FORTEe multicenter trial. We conduct participant observations during training units, qualitative interviews with patients aged 6-21 years and, as required, with their parents, and keep field notes on informal visits. The data is analyzed using a hermeneutic phenomenological framework.

**Results:** All patients participating in the interventions reported predominantly positive effects on their overall wellbeing, endurance and fitness, awareness of their own body, and ability to concentrate. Participants emphasized as positive the individualization of their exercise therapy, the possibility to co-determine the training units, and being asked about their own assessment of their performance and experience. With reference to coping, patients pointed out that occasional achievements raised hope and confidence and that experiencing one's physical capabilities can counterbalance negative experiences. Lastly, the exercise program affects the patients' self-image: exercising enabled them to perceive themselves as *not only* ill and they reported positive experiences of trying out new activities.

**Conclusions:** These preliminary results indicate that personalized exercise therapy can be a significant element of support for childhood cancer patients during their treatment. It can serve as a space where they can exercise agency and experience self-efficacy, and it can mitigate the experienced "disruption" that often accompanies their diagnosis. Patients' positive appraisal of the study implementation hints at the necessity to involve them in the design of exercise therapy and to tailor it to their needs. Acknowledgements *This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 945153.*

EP587/#79 | Poster Topic: *AS05 SIOP Scientific Program/AS05.p Supportive Care and Palliative Care*

### ARE EXISTING MORTALITY PREDICTION MODELS SUITABLE FOR PEDIATRIC HEMATOLOGY/ONCOLOGY PATIENTS ADMITTED TO THE PEDIATRIC INTENSIVE CARE UNIT DUE TO SEPSIS?

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**Background and Aims:** Children with hemato-oncological diseases and after stem cell transplantation (SCT) are at high risk for life-threatening infections, and constitute a substantial part of pediatric intensive care unit (PICU) admissions due to sepsis. The current pediatric prognostic scoring tools to evaluate illness severity and mortality risk are designed for the general pediatric population, and may not be adequate for this vulnerable subpopulation. Our Aim was to evaluate the suitability of two major prognostic scoring tools: the Pediatric Logistic Organ Dysfunction-2 (PELOD-2) and the Pediatric Risk of Mortality III (PRISM III) in children with hemato-oncological diseases. In addition, we set out to create a new risk-assessing model to account for the unique characteristics of this patient population.

**Methods:** We conducted a retrospective cohort study, at the largest referral pediatric hemato-oncology center in Israel. We collected and analyzed demographics, clinical and laboratory data, and PICU outcomes from all admissions to the PICU due to sepsis of children with hemato-oncological diseases or after SCT, between 2008-2021 (n=233).

**Results:** The survival rate was 83%. The diagnostic capabilities of PELOD-2 and PRISM III, as determined by the area under the receiver operating characteristic curve (AUC), were 82% and 74%, respectively. Models including the existing scoring tools and 9 new clinical parameters (age, SCT, viral or fungal infection, central venous line removal, vasoactive inotropic score, bilirubin level, C-reactive protein level, and prolonged neutropenia) significantly improved the above AUCs to 90% ( $p=0.01$ ) and 87% ( $p<0.001$ ), respectively.

**Conclusions:** The diagnostic capabilities of the PELOD-2 and PRISM III scores are reduced in children with hemato-oncological diseases, admitted to the PICU due to sepsis. Our results highlight the unmet need to develop a risk-assessing tool adjusted to this special popula-

tion. Such new scoring should represent their unique characteristics and be validated in a large multi-center prospective study.

EP588/#1590 | Poster Topic: *AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)*

### ENGAGING WITH CHILDREN AND YOUNG PEOPLE TO DETERMINE RESEARCH PRIORITIES FOR CHILDREN'S CANCER IN THE UNITED KINGDOM

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**Background and Aims:** Previous priority setting exercises have sought to involve children and young people, but in the final reporting it is evident that few children, especially young children, had engaged through the process. A primary aim in the UK Children's Cancer Priority Setting Partnership was to find out from children what future research should focus on.

**Methods:** We followed well-established James Lind Alliance processes, collecting and shortlisting questions via online surveys with adult survivors of childhood cancer, carers, and professionals, and holding a final workshop. Alongside this, a parallel process to collect and prioritise questions from children was undertaken. We created animations for parents/carers to explain the project to children, gathered questions via online surveys, and held a workshop with children to identify their priorities.

**Results:** Sixty-one children/young people with cancer and 10 siblings, aged 3-21 years, submitted 252 potential questions via the surveys. Submissions were refined into 24 summary questions. These questions were discussed at a workshop with eight children/young people; they also added more questions on topics of importance to them which were not already covered. Workshop participants prioritised the Top 5 questions; top priority was, 'How can we make being in hospital a better experience for children and young people? (like, having better food,

internet, toys, and open visiting so other family members can be more involved in the child's care). The Top 5 questions addressed cancer prevention, treatments closer to home, early diagnosis, and emotional support. These questions were taken to the final workshop at which the overall Top 10 priorities were decided, all five children's priorities were reflected in the Top 10.

**Conclusions:** We successfully engaged with children and young people in setting priorities for childhood cancer research. The Top 10 priorities reflect the voices of children and young people and should inform the funding of future research.

EP589/#1485 | Poster Topic: AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)

### SOCIAL RISK SCREENING OF FAMILIES AS A STANDARD OF CARE IN CHILDREN WITH CANCER

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**Background and Aims:** The diagnosis of the child with cancer has a great impact on the family environment. Patient, parents, and siblings face the challenge of a long treatment and unknown processes that weaken the social structure and cause added stress to the patient and their caregivers. Social risk screening identifies these situations and allows health personnel to intervene to prevent them. The aim is to describe the importance of assessing the social risk of families and its impact on the standard of care of children with cancer.

**Methods:** Observational study with cross-sectional intervention in families of patients registered in the Pediatric Hemato - Oncology Department (HOPE) of the Hospital de Clínicas - FCM - UNA, for a period between 2.009 to 2.022. Social risk indicators developed and validated by HOPE were used for the evaluation.

**Results:** 1360 families were evaluated. 72% (992/1360) have a high social risk defined by origin from rural areas, parents with basic schooling and no fixed income. 40% of families come from rural areas. 53% (729/1360) live in precarious conditions with limited access to basic services, 75% live in overcrowding and 73% (996/1360) have no fixed income. In education there is 4.4% illiteracy and only 9.6% have higher education. HOPE has designed tools to intervene on these indicators: 1) School for Parents Program with educational talks; 2) Psychosocial Area for support and 3) economic support for mobility, laboratory studies and shelter management, recognizing these as the pillars of the standard of care for cancer patients.

**Conclusions:** The identification of the social risk of families allows the development of a care plan aimed at the patient and caregivers, so that early intervention avoids abandonment, non-compliance, and failure of treatment. This initiative has been developed within the My

Child Matters Program of the Sanofi Spoir Foundation and the ReNACI Foundation.

EP590/#1079 | Poster Topic: AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)

### PROVIDER PERSPECTIVES ON THE IMPACT OF MYTHS ABOUT DISEASE ORIGIN AMONG PATIENTS WITH OSTEOSARCOMA AND RETINOBLASTOMA IN GUATEMALA, JORDAN, AND ZIMBABWE

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**Background and Aims:** Stigmatizing myths about disease origin and blame have adverse impacts on children with cancer, delaying their ability to seek early diagnosis and treatment. This study aims to explore provider perspectives on the role of myth in cancer decision-making among children diagnosed with osteosarcoma or retinoblastoma in Guatemala, Jordan, and Zimbabwe.

**Methods:** The study included semi-structured interviews with 19 healthcare providers at three tertiary care facilities. Interviews were audio recorded in English, Spanish, Arabic, and Shona. They were transcribed and translated into English for analysis. Transcripts were individually coded and reconciled with a third-party adjudicator. Our codebook defined "myth" as any misconceptions or community beliefs about cancer and "origin" as any reference to cancer causation.

**Results:** Providers suggested that the myths about the source of cancer may cause patients to delay treatment by seeking alternative-care providers. All providers mentioned the need to educate patients on cancer origin. In Jordan, providers described assuring caregivers

that cancer is not punishment from God. In Guatemala and Zimbabwe, they emphasized the myth that cancer was a result of vengeful witchcraft. Providers across the sites agreed that public awareness interventions might mitigate the adverse effects of communal misconceptions and encourage families to accept medical care sooner. Many providers worried that visiting a medicinal healer complicated the care of patients and led to them presenting with late-stage disease, affecting rates of amputation/enucleation, progression, and mortality.

**Conclusions:** The findings demonstrate the impact providers in Jordan, Zimbabwe, and Guatemala perceive myths to have on cancer care decision-making and outcomes. Future interventional work should focus on providing public awareness and educational opportunities to mitigate stigmatizing misconceptions. Continued research on the impact of myths on treatment delays could help further inform interventions.

EP591/#1235 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

#### PARENTS' EXPERIENCES WITH GERMLINE GENE PANEL SEQUENCING IN PEDIATRIC CANCER: A QUANTITATIVE EXPLORATION

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**Background and Aims:** Large-scale germline sequencing is gradually becoming a routine practice in pediatric oncology. However, little attention has been paid to the experiences of families undergoing this procedure. This study examines the motivations, worries, and knowledge of parents participating in sequencing.

**Methods:** We recruited parents whose children participated in a nationwide gene panel study (involving 142 genes) and administered a questionnaire to them while they were awaiting the sequencing results. We developed a questionnaire, based on literature and clinical knowledge, to measure motivations and worries on a 5-point Likert scale. Knowledge was assessed using an adapted version of the PIPseqKQ, which comprised 22 statements (true/not true/unsure) in three domains. Descriptive statistics were used.

**Results:** Out of 338 eligible families, 213 agreed to participate. 176 mothers and 128 fathers of 188 patients completed the questionnaire. The most frequently reported motivations to participate in sequencing were: helping doctors/scientist (96%), helping future patients (94%),

obtaining information about their child's cancer (69%), possible preventative measures for future disease (62%), and obtaining knowledge about risks for siblings (60%). The most reported worries were: concerns that their child's life would be burdened because of the study (25%), concerns about receiving stressful results (15%) and concerns about life-insurance for their family (13%). 70% of the parents agreed on having sufficient knowledge about genetics to make a well-informed decision to participate in the sequencing study, the rest was either unsure (24%) or disagreed (6%). Regarding the knowledge questionnaire, parents scored on average 64% correct on general genetic concepts, 75% correct on genetic concepts of general health & cancer and 44% correct on genomic sequencing concepts.

**Conclusions:** Motivations for participating in sequencing are both altruistic and individual, while worries are minor, and knowledge differs. Parents will benefit from more tailored counseling tools and strategies in the future.

EP592/#1005 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

#### RECONSTRUCTION OF IDENTITY IN OUT-OF-TREATMENT PATIENTS AND YOUNG SURVIVORS FROM GUATEMALA WHO HAVE UNDERGONE AN AMPUTATION DUE TO OSTEOSARCOMA DURING ADOLESCENCE

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**Background and Aims:** Identity construction is one of the main developmental processes of adolescence addressing the question, "Who am I?" The changes an adolescent experiences after amputation for osteosarcoma impact multiple spheres of their lives: biological, psychological, social, and spiritual. This study focused on how identity is affected and constructed when an adolescent from Guatemala has undergone an amputation due to osteosarcoma.

**Methods:** Following Charmaz and Corbin & Strauss' grounded theory, semi-structured interviews were conducted with 10 adolescents and/or young out of treatment patients between the ages of 15 and 29 who had been amputated for osteosarcoma during adolescence at the Unidad Nacional de Oncología Pediátrica (UNOP) in Guatemala. Data saturation was achieved by the comparative systemic analysis of each interview and a focus group conducted with some interviewed participants.

**Results:** The experience of living with an amputation entails a process of readjustment, accompanied by a new body image, transformation of plans and functional adaptation to the amputation. The role of the support network is important in this process. Young participants were identified as having coping strategies that support their development and the existential components that give meaning to their experience. The Identity Reconstruction Theory, which emerged from the analysis, is based on a rupture in identity that surrounds the amputation process



and is described by three principles: identity, personal script, and grief, and are presented as a process within a timeline.

**Conclusions:** Identity reconstruction is formed through multiple losses (psychological, social, spiritual and cultural) that add to amputation. Long-term psychological care, psychoeducation for the family and community, along with interventions in socio-political spaces can ease the process towards a more functional identity for patients who have just had an amputation and for those who have had it for a longer period.

EP593/#1317 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

#### INTELLECTUAL QUOTIENT AND EXECUTIVE FUNCTIONING OF THE SURVIVORS OF CHILDHOOD MALIGNANT TUMOURS: IMPACT OF SOLID MALIGNANT TUMOURS AND THEIR MANAGEMENT

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**Background and Aims:** The aim of the present study was to screen the survivors of childhood solid malignant tumours for intellectual disabilities and to assess their executive functioning.

**Methods:** Survivors were screened for Intellectual Disabilities with help of the Binet-Kamat Test of Intelligence. The executive functioning (cognitive interference and sustained & divided attention) was assessed using Stroop Colour Word Test (SCWT) and Children Colour Trail Test (CCTT).

**Results:** One hundred forty-five survivors with a mean age of 10 years were included. There were 57 males (72.15%) and 22 females (27.85%). These survivors had a diagnosis of 60 Wilms Tumour (WT) (41.38%), 25 Neuroblastoma (NB) (17.24%), 18 Hepatoblastoma (HB) (12.41%), 29 Malignant Germ Cell Tumour (MGCT) (20.0%) and 13 others (8.97%). The evaluation was done at a median age of 136 months after treatment completion. Intelligence Quotient (IQ) assessment was done for 142 patients. 108 (76.06%) survivors had an average or above-average IQ. 34 (23.94%) patients had some level of intellectual disability (21 (14.79%) below-average IQ, 8 (5.63%) borderline intellectual disability, 2 (1.41%) mild intellectual disability and 3 (2.11%) moderate intellectual disability). Executive Function was assessed using the SCWT. 11 (10.09%) patients had difficulty inhibiting cognitive interference. Sustained & divided attention was assessed in 105 using the CCTT and CTT. 14 (13.33%) patients had sustained and divided attention below the 16<sup>th</sup> percentile. Birth order, age at evaluation, father's & mother's

education, mother's occupation and platinum-based chemotherapy (CT) have a significant effect on the IQ of the child. Further, age at evaluation, mother's education, number of siblings of the survivors, socioeconomic status, and time since diagnosis & treatment completion, CT had a significant impact on the inhibiting cognitive interference ability.

**Conclusions:** About 1/4th of survivors have some level of intellectual disability and 10-15% of them have executive functioning impairment thus, they must be closely monitored for co-morbid cognitive sequelae.

EP594/#1011 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

#### PRIMARY CAREGIVER OF SURVIVORS OF CHILDHOOD WITH SOLID MALIGNANT: LONG-TERM EFFECTS ON THEIR PSYCHOLOGICAL HEALTH

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**Background and Aims:** The adverse effects of solid malignant tumours just do not affect the psychological health of the survivors but also vastly impact the psychological health of their primary caregivers. The aim of the present study was to assess the psychological health of the parents of survivors of childhood solid malignant tumours.

**Methods:** Parents of survivors of solid malignant tumours were assessed for depression, anxiety and stress with the help of Depression, Anxiety and Stress Scale - 21 (DASS-21). Parents were further assessed for parental stress with the help of the Parenting Stress Index (PSI-4).

**Results:** Parents of 145 survivors of childhood solid malignant tumours were included. The parents were assessed after 11 years (median) of treatment completion. 130 parents were assessed for stress, depression and anxiety using DASS-21. Normal levels of stress, depression and anxiety were observed in 115 (76.92%) parents. Lower levels of stress were observed in 17 (13.08%) parents and 16 (12.31%) and 28 (21.54%) parents displayed lower levels of anxiety and depression respectively. Higher levels of anxiety were observed in 13 (10.0%) parents while only 4 (3.08%) parents showed higher levels of depression. 137 parents were assessed for parental stress using PSI-4. 112 (81.75%) parents had normal levels of parental stress. Overall parental stress was reported by 25 (18.25%) parents. 19 (13.87%) parents perceived they have a difficult child, 18 (13.14%) parents perceived a threatened interaction with their affected and 30 (21.90%) parents

perceived to have tumour-related distress. Tumour type, related factors and its management had no significant impact on the psychological health of the parents. Socio-economic status and the father's education level had a significant effect on the parent's level of anxiety and parents' interaction with the affected child.

**Conclusions:** Since the psychological health of the caregivers of tumour survivors is vastly affected, they must be closely monitored for psychological consequences.

EP595/#294 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

#### EXTENDED VITALS IN PATIENTS UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANT: IMPACT ON PATIENT-REPORTED SLEEP DISTURBANCES

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**Background and Aims:** Patients undergoing hematopoietic stem cell transplant (HSCT) face many barriers to sleep during transplant hospitalization. Frequent vitals checks, necessary during conditioning and immediately post-transplant, may be less necessary as time from transplant increases. The current analyses from a larger trial testing the feasibility of extended vitals (EV) in HSCT, examine the impact of extending time between vitals checks from 4 to 6 hours on patient-reported sleep disturbances.

**Methods:** 40 patients between the ages of 8-21 years (M age=13.9, SD=3.4; 52% male) undergoing HSCT for hematologic or oncologic conditions (30% autologous, 70% allogenic) completed the 8-item PROMIS Sleep Disturbances short-form. The current analyses focus on sleep prior to the intervention (Day 0-+5) and after 5 days of EV (Days +6-+10), comparing patients randomized to intervention (EV Group n=22) or to a delayed intervention group (Comparison Group n=18). Patients were reassessed daily for medical eligibility to receive EV. In the EV group, patients were medically eligible on 44% of days and received EV 38% of these days, 54% of patients received 2+ days of EV. Fever was the most common reason patients were ineligible.

**Results:** Patients in both groups reported more sleep disturbance in the period after transplant compared to normative values (mean of 50; M=55.3, SD=8.1,  $t(39)=4.1$ ,  $p<.001$ ). The EV Group reported significant, meaningful reductions in sleep disturbances relative to the Comparison Group (EV group change M=2.7, Comparison group change M=0.9; Difference between groups=3.4; PROMIS Minimal Important Change=3).

**Conclusions:** Sleep disturbances are elevated in the peri-transplant period. Offering patients EV may improve patient-reported sleep disturbances. Shortly after transplant, many patients still required monitoring and were ineligible for EV, resulting in modest improvements in sleep. As time from transplant increases, more patients may be eligible for EV, thus considering EV for pediatric patients when safe may reduce one barrier to sleep during transplant.

EP596/#1696 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

#### SLEEP OVER CAMP: A SAFE AND SUCCESSFUL MENTAL HEALTH INTERVENTION DURING COVID

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**Background and Aims:** Background: Data suggests 48-89% of childhood cancer patients (CCP) and long term survivors (LTS) now meet criteria for depressive or anxiety disorders. These numbers have risen dramatically since the COVID pandemic. One of the most impactful programs we instituted in 1984 for improving overall mental wellness for our patients and their sibs ages 7-15 years is our weeklong summer camp – Camp Periwinkle. No in-person camps were held in 2020 and 2021 due to the pandemic. In 2022 we successfully held our first in-person camp since the pandemic!

**Methods:** Design /Methods: In order to attend camp as a camper or staff we required proof of double vaccination, negative PCR within 72 hours of camp, negative rapid COVID test on arrival to camp and to be symptom free. No outside visitors were allowed and campers and staff remained on property the entire week.

**Results:** Due to the vaccination requirement, only 96 campers attended in 2022 compared with our usual camper number of 190. Only one camper developed brief symptoms of COVID, was required to leave camp but returned the following day symptom free with a negative PCR. In the three weeks following camp, no camper, family member or staff developed COVID.

**Conclusions:** These specific COVID restrictions proved highly successful allowing us to have a safe, COVID free camp. Camper and parent comments describe its impact on overall well-being. Representative quotes include: *Camper:* "It is the only time I was able to do activities with others in over a year and I began to feel like my old self again-independent and happy"; *Parent:* "It was so rewarding to receive such a strong young man after attending camp – almost as if his leukemia had

faded away. Camp Periwinkle without question was a huge blessing to our son and our family.”

EP597/#939 | Poster Topic: AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)

### IMPACT OF COVID-19 CONTAINMENT MEASURES ON CHILDREN WITH CANCER IN INDONESIA

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**Background and Aims:** COVID-19 containment measures to limit COVID-19 spreading profoundly impact children around the globe, especially in low- and middle-income countries such as Indonesia. The aim of this case series study is to uncover the impact that COVID-19 containment measures have on Indonesian children with cancer and their families.

**Methods:** A case series study was conducted in July 2021. Investigators identified three children diagnosed with cancer at an Indonesian referral hospital and studied their medical records. Caretakers were interviewed inside the hospital by an independent interviewer using a semi-structured questionnaire.

**Results:** This study presents three children with cancer and their families. Access to proper healthcare was hindered during the COVID-19 pandemic due to mobility restrictions, medical staff shortage, limited chemotherapy and blood products availability, postponed medical procedures, and delayed or modified treatment administration. Financial hardships resulted because caretakers lost their jobs due to the lockdowns and that medication costs were no longer fully covered by health-insurance. Children and their relatives suffered from mental health issues. Anxiety, depression, stress and loneliness were caused by the fear of receiving suboptimal cancer treatment, serious concerns about financial difficulties, and restricted social interactions. All families believed that COVID-19 containment measures worsened their children's survival chances.

**Conclusions:** COVID-19 containment measures adversely impact children with cancer and their families in Indonesia, and most likely in other low- and middle-income countries as well. Disruptions in timely and adequate childhood cancer treatment administration may importantly deteriorate survival chances. Governments and policymakers should take these indirect effects into account to protect vulnerable children and their families.

EP598/#1195 | Poster Topic: AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)

### CURRENT AND FUTURE INTERVENTIONS ADDRESSING DETERMINANTS OF QUALITY COMMUNICATION TO IMPROVE FAMILY-CLINICIAN COMMUNICATION IN PAKISTAN

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**Background and Aims:** Fostering high-quality communication between clinicians, families, and patients is an essential part of patient-centered care. The purpose of this study was to evaluate potential interventions to improve family-clinician communication in the care of children with cancer in Pakistan.

**Methods:** Semi-structured interviews were conducted with 20 clinicians and 18 caregivers at two hospitals in Pakistan: Indus Hospital in Karachi and Children's Hospital Lahore. A codebook was developed with a priori codes and novel codes. Thematic analysis explored potential interventions aimed at determinants of high-quality family-clinician communication.

**Results:** Clinicians and parents discussed active efforts and future interventions to improve family-clinician communication. Current efforts by clinicians, acknowledged by parents as useful, included storytelling and showing pictures of survivors of childhood cancer to communicate and support family hope. To address the issue of language differences between medical staff and patient families, clinicians described the need for dedicated interpretive services and suggested developing educational materials (e.g., pamphlets, videos) in multiple languages or using pictures and graphics to educate families. Another potential intervention discussed by clinicians was support groups for patients and families to come together. Parents described the helpfulness of housing provided by the hospital and suggested increasing the number of rooms available to help more families with children undergoing treatment. Lastly, clinicians emphasized the need for more time with patients and suggested increasing staff, particularly psychosocial support, to allow for this. As parents described team communication, they emphasized the importance of bedside manner and the nature of this communication.

**Conclusions:** This study emphasizes the need for multi-level interventions to improve the quality of communication when provid-

ing care for children with cancer in Pakistan. Future interventions focusing on methods of communication, language barriers, hospital staffing, and family support should be implemented to improve family-clinician communication and should be adapted to the local cultural context.

EP599/#784 | Poster Topic: AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)

#### DIFFERENCES IN THE PERCEPTION OF HEALTH AMONG THE MEDICAL CARE PERSONNEL AT UNIDAD NACIONAL DE ONCOLOGÍA PEDIÁTRICA IN GUATEMALA

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**Background and Aims:** The Unidad Nacional de Oncología Pediátrica (UNOP) is the only specialized center for pediatric cancer in Guatemala, diagnosing more than 500 new cases per year. There is no published data on the physical and mental health of pediatric oncology personnel in Guatemala. This study investigated the perception of health and causes of concern for medical care professionals at UNOP.

**Methods:** The Brief PHQ (Patient Health Questionnaire), Spanish version, was administered to medical care professionals working at UNOP. Based on findings, qualitative interviews that sought to understand aspects that cause concern in participants, were conducted. The interviews were transcribed for thematic analysis.

**Results:** A total of 49 questionnaires (15 nurses, 12 doctors, 8 psychosocial professionals, 7 dietitians, 3 from other medical care professions, 4 unknown) were analyzed. Correlations between older age and fewer signs of depression, as well as a between being a woman and showing greater concern, were identified. Five participants showed symptoms of depression, and eight participants symptoms of high anxiety and panic attacks. One participant met both criteria. Six percent reported taking medication for anxiety, depression or stress. Twelve percent indicate "a lot" of discomfort with their health. An open question explores stress-causing situations; four recurring themes of concern were identified: financial, family, health, and work-related situations. Five qualitative interviews were conducted (1 doctor, 2 nurses, 1 social worker, 1 dietitian, and 1 psychologist). The causes of difficulties are both internal and external to UNOP.

**Conclusions:** The perception of physical and mental health among medical care personnel was studied. In contrast to reported literature, concerns focus not only on labor aspects, but also relate to economic, family, and health factors. Health care professionals play multiple roles.

In addition to their labor demands, there is also constant concern about other aspects of their lives.

EP600/#944 | Poster Topic: AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)

#### "ADDRESSING SUFFERING IN GUATEMALA: BIOPSYCHOSOCIAL MODEL THROUGHOUT THE COURSE OF THE DISEASE FROM A TRANSDISCIPLINARY PERSPECTIVE."

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**Background and Aims:** Multidisciplinary teams including Pediatric Palliative Care, Psychology, Social Work and Child Life specialists have been utilized to ease suffering, however they are often applied only in times of crisis. We hypothesized that the systematization of a pre-established biopsychosocial approach along the course of the disease could ease suffering from the time of diagnosis and change outcomes for children with cancer.

**Methods:** This began in 2007 at Unidad Nacional de Oncología Pediátrica (UNOP) in Guatemala. Specific interventions focused on five moments: 1) Diagnosis; 2) Moments of high risks of death; 3) Palliative Care; 4) Families on risk of abandon treatment; 5) Transition to Survival. At each time point, the multidisciplinary team held case discussions focused around a biopsychosocial model to identified patients at high risk for suffering. Rate of abandonment were examined before and after implementation of this integrated model.

**Results:** Different moments of treatment required increase attention from different disciplines. Psychology, Social Work and Child Life were heavily involved during diagnosis while Palliative Care was increasingly present for patient with poor prognoses from the time of diagnoses and at all the admissions to intensive care with high risk of death as well as transitions to palliation. For patients at risk of abandonment, Psychology and Social Work interventions played an important role and Child Life specialists helped to survivorship. Each discipline preserved and go beyond through its own philosophical approach toward easing suffering. At the time this model was implemented in 2007, abandonment rates were 6.6%. In 2022 abandonment had fallen to 0.6%.

**Conclusions:** This transdisciplinary approach, with focused interventions during critical moments has the potential to improve quality of care and reduce treatment abandonment. Adaptation and adoption of this model should be the subject of future research.

EP601/#1055 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

### MENTAL HEALTH ISSUES IN ADOLESCENTS AND YOUNG ADULTS (AYA) WITH CANCER REFERRED TO PSYCHO-ONCOLOGY SERVICE IN TERTIARY CARE CANCER CENTRE SET IN A LMIC

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**Background and Aims:** Recent literature has found an increased risk of depression in adolescent and young adult cancer patients and survivors, affecting their quality of life and functioning. We aimed to evaluate mental health issues in AYA with cancer referred to a psycho-oncology service in a LMIC setting.

**Methods:** We did a retrospective analysis of referrals of AYAs between 15 to 39 years old with cancer referred and assessed in a psycho-oncology service from January 2021 to December 2022. Patients were on disease directed treatment or supportive care. Data was extracted from case notes and electronic medical records. Mental health disorders were diagnosed by clinical interview using International Classification of Diseases (ICD10).

**Results:** A total of 546 AYAs were referred of whom (306, 56%) were male and (283, 52%) were inpatients. The most frequent cancer diagnoses were hematolymphoid (160, 29%), bone and soft tissue (129, 24%) and brain tumor (64, 12%). Mental health disorders were diagnosed in (272, 50%) patients. Adjustment disorder was found in (116, 21%), anxiety disorder (42, 8%) and depressive disorders in (41, 7%) of the patients. Organic mental disorder diagnosed in (37, 7%), Psychosis (20, 4%) and substance use disorder (16, 3%). Patients who did not meet any criteria for psychiatric diagnosis were (274, 50%). Premorbid psychiatric condition was found in (69, 13%) patients. Immediate psycho-pharmacotherapy intervention needed in (98, 18%) AYA cancer patients.

**Conclusions:** About half of the AYAs with cancer referred to Psycho-oncology service had major mental health issues around one in five of them needed psychopharmacotherapy. Timely detection of mental health disorders is important for improving mental health care in AYA cancer patients in low-resource settings.

EP602/#698 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

### FUNCTIONS OF PATIENT- AND FAMILY-CENTERED PEDIATRIC CANCER COMMUNICATION IN PAKISTAN

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**Background and Aims:** Communication is an essential aspect of high-quality patient- and family-centered care. A model for pediatric cancer communication developed from the perspectives of parents of children with cancer in the United States has defined eight communication functions, however it is unknown how this model may or may not apply in diverse cultural settings. The purpose of this study was to explore the relevance of these eight communication functions in Pakistan.

**Methods:** Semi-structured interviews were conducted with 20 clinicians and 18 caregivers of children with cancer at Indus Hospital in Karachi and Children's Hospital of Lahore. Interviews were conducted in Urdu or English and transcribed and translated as necessary prior to analysis. Two independent coders used a combination of a priori codes related to the communication model as well as novel codes derived inductively from transcript review.

**Results:** Clinicians and parents in Pakistan discussed the importance of all eight communication functions previously identified by parents from the United States including: *information exchange, decision-making, managing uncertainty, enabling family self-management, responding to emotions, supporting hope, providing validation, and building relationships*. However, the operationalization of these functions in Pakistan differed from that in the United States, influenced by cultural context. For example, religion and traditional beliefs were an important component of *managing uncertainty* and clinicians' *response to emotions* aided families transitioning from denial to acceptance. Essential to all eight functions was *trust* between the family and the medical team.

**Conclusions:** These findings support the use of this functional communication model in diverse pediatric oncology settings and emphasize the importance of trust to all eight communication functions. Culturally sensitive operationalization of these functions could be used to develop communication interventions aimed at supporting the needs of parents of children with cancer in diverse settings.

EP603/#710 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

### THE IMPACT OF STIGMA ON CANCER DECISION-MAKING AMONG PATIENTS WITH OSTEOSARCOMA AND RETINOBLASTOMA IN GUATEMALA, JORDAN, AND ZIMBABWE

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**Background and Aims:** Stigma is a known barrier to healthcare acceptance among patients with a myriad of chronic health conditions but has been understudied in pediatric oncology. We sought to explore the ways in which stigma impacts decision-making and cancer care acceptance and identify potential strategies to mitigate stigma in three culturally and economically diverse tertiary cancer hospitals in Guatemala, Jordan, and Zimbabwe for patients with osteosarcoma and retinoblastoma.

**Methods:** The Health Stigma and Discrimination Framework, a previously published model to facilitate global stigma research, was used to design a semi-structured interview guide which was adapted for use in each cultural context. Thematic analysis focused on stigma drivers and mitigators, as well as outcomes of experienced stigma. Participants included parents, adolescent patients (12-18 years old), and healthcare providers. Interviews were conducted in English, Spanish, Arabic, or Shona, translated as necessary, and transcribed for analysis by two coders using a priori and novel codes.

**Results:** A total of 56 interviews (28 parents, 19 healthcare providers, 9 patients) were conducted across the three sites. Factors driving stigma included concerns about aesthetics and functionality, fear of social and economic ramifications, myths or misconceptions, blame, and peril, or the threat caused by a cancer diagnosis. Potential stigma mitigators included post-surgical options such as prosthetics, support from the community, family, medical team, and survivors, increased cancer knowledge, and returning to a sense of normalcy. Participants described broad implications regarding the impact of stigma on treatment adherence and abandonment, as well as psychosocial outcomes including resilience and regret.

**Conclusions:** Stigma plays an important role in cancer care decision-making for patients with osteosarcoma and retinoblastoma in diverse global settings. Interventions aimed at stigma mitigation, including public awareness campaigns, advocacy surrounding prosthetic devices, and patient and family centered education can impact outcomes and should be the focus of future research.

EP604/#1102 | Poster Topic: AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)

### RADAR: A RISK SCORE ASSESSMENT FOR PREDICTING TREATMENT ABANDONMENT IN CHILDHOOD CANCER IN COLOMBIA

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**Background and Aims:** Cancer treatment abandonment (TxA) is a major factor for relapse. Assignment of TxA risk at diagnosis allows for early interventions to prevent TxA. We developed **RADAR**, a TxA risk score. Here we describe RADAR's performance.

**Methods:** To construct RADAR, we selected potential predictors from a systematic literature review. To train and test the models, we used data from children (<15 years) with a new diagnosis of childhood cancer from ten Colombian cities enrolled prospectively in our Childhood Cancer Surveillance System (VIGICANCER), during 2009-2020. We used multivariate Cox's regression stratified by city and diagnosis period, competing risks models, and logistic regression. We choose the final predictors by the backward stepwise method and by using Lasso regression with cross-validation. Lastly, bootstrapping was used to evaluate the robustness of the predictors.

**Results:** The cohort included 5,442 patients and 335 TxA events. Cumulative incidence of TxA at 24 months was 9% (95%CI: 8, 10). The score included the following predictors: insurance type, rural residence, and residence in a province without a pediatric oncology unit. We classified risk in 3 categories: low (<3%), intermediate (3 to 6%), and high (>6%). Twelve-months probability of TxA for the minimum score (1) was 2% and for the maximum score (7) was 12%. The area under the receiver operating characteristics curve (ROC) at 3 months was 0.74 and at 24 months 0.69.

**Conclusions:** RADAR showed a 70% probability of distinguishing between TxA cases and non-TxA cases, with only a minor decline in performance of its prediction capacity over time. RADAR uses only three predictors at diagnosis for TxA risk, contributing to simplicity and feasibility, which are key attributes for successful implementation in clinical settings. RADAR is currently applicable in Colombia. Next steps involve further validation and adaptation to other Latin-American countries.

EP605/#1462 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

### ACCEPTABILITY OF RECORDING DIAGNOSIS CONVERSATIONS FOR COMMUNICATION RESEARCH PURPOSES IN PEDIATRIC ONCOLOGY

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**Background and Aims:** In order to improve the quality of communication research in paediatric oncology, the combination of recorded data, surveys and interviews is recommended. However, gatekeeping and ethical issues of recording conversations for research purposes challenge this research method. The aim of this study is to explore patient, parent and healthcare provider (HCP) acceptability of recording diagnosis conversations for research purposes.

**Methods:** A semi-structured survey was distributed among patients suffering from acute leukaemia, their parents and HCPs who participated in a mixed-method study on communication during the diagnosis trajectory in paediatric oncology in the Netherlands which included audio recording. The survey consisted of both open and Likert-type questions regarding the acceptability of recording diagnosis conversations. Descriptive analyses were performed with SPSS.

**Results:** A total of 2 patients (aged 12 and 19), 22 parents (45% male) and 10 HCPs participated in the study. Both patients and most parents (n=20, 91%) indicated not to be bothered by the question to record the diagnosis conversation. One father expressed to be overwhelmed by the question. The majority of HCPs indicated they were not bothered by asking parents for permission to record the conversation (n=7, 70%). Three HCPs indicated they felt as if parents were overwhelmed by the question and one HCP felt as if parents would not dare to decline the recording. Both patients, most parents (n=20, 91%) and all HCPs implied the conversation was not disturbed by the recording, one father indicated he felt constricted to show his emotions because of the recording.

**Conclusions:** This study showed that most patients, parents and HCPs were not bothered by the informed consent procedure of audio recording diagnosis conversations nor by the recording itself. Recording of diagnosis conversations seems to be an acceptable method for communication studies, not disturbing the conversation.

EP606/#209 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

### THE COURSE OF HEALTH-RELATED QUALITY OF LIFE AFTER THE DIAGNOSIS OF CHILDHOOD CANCER: A NATIONAL COHORT STUDY

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**Background and Aims:** Comprehensive insight in the longitudinal development of health-related quality of life (HRQOL) after childhood cancer diagnosis could improve quality of care. Thus, we aimed to study the course and biopsychosocial determinants of HRQOL in a unique national cohort of children with cancer.

**Methods:** HRQOL of 2154 children with cancer was longitudinally reported (median: 3 reports) between diagnosis and 5 years after, using the pediatric quality of life inventory generic core scales (PedSQL). HRQOL was modelled over time since diagnosis using mixed model analysis for children 2-7 years (caregiver proxy-reports) and  $\geq 8$  years (self-reports). Differences in the course between hematological, solid and central nervous system malignancies were studied. Additional associations of demographics, disease characteristics (age at diagnosis, relapse, diagnosis after the national centralization of childhood cancer care and treatment components) and parental distress (Distress thermometer) were studied.

**Results:** Overall, HRQOL improved with time since diagnosis, mostly in the first years. The course of HRQOL differed between diagnosis groups. In children aged 2-7 years, children with a solid tumor had most favorable HRQOL. In children aged  $\geq 8$  years, those with a hematological malignancy had lower HRQOL around diagnosis, but stronger improvement over time than the other diagnosis groups. In both age-groups, the course of HRQOL of children with a CNS tumor showed little or no improvement. Small to moderate associations ( $\beta$ : .18 to .67,  $p < 0.05$ ) with disease characteristics were found. Centralized care related to better HRQOL ( $\beta$ : .25 to .44,  $p < 0.05$ ). Parental distress was most consistently associated to worse HRQOL ( $\beta$ : -.13 to -.48,  $p < 0.01$ ).

**Conclusions:** The presented course of HRQOL can be used for early recognition of children with insufficient recovery of HRQOL after a cancer diagnosis. Future research should focus on ways to support children, especially those with a CNS tumor, for example by decreasing distress in their parents.

EP607/#390 | Poster Topic: AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)

#### EXPLORING THE PSYCHOLOGICAL IMPACTS OF A CHILDHOOD CANCER DIAGNOSIS ON GRANDPARENTS: NEGATIVE OUTCOMES, POSITIVE OUTCOMES, AND COPING STRATEGIES - A QUALITATIVE STUDY

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**Background and Aims:** Childhood cancer is usually a traumatic experience for patients and their families. However, little is known about the effect on grandparents. Studies have shown that they experience more distress, anxiety, depression, anger, and sleep issues than grandparents of healthy children. Nevertheless, most grandparents develop coping mechanisms to deal with their negative feelings, and some even report positive outcomes. We aimed to describe the negative and positive psychological outcomes and coping strategies of grandparents of childhood cancer patients on treatment in Switzerland.

**Methods:** We collected data using semi-structured interviews and applied thematic content analysis.

**Results:** We conducted 18 interviews with 20 grandparents (11 females) between January 2022 and February 2023. Participants were on average 67 years old (range:57-82). The mean time since diagnosis was 13 months (range:6-23), and grandchildren were on average 8 years old (range:1-19). We found that grandparents were in shock, especially in the early period after diagnosis, and experienced strong feelings of fear and helplessness. The worst for most grandparents was to see their grandchild suffer. In terms of the future, they

were particularly afraid that the child might experience a relapse or be infertile. Many grandparents stated that their fears were always present, sometimes leading to mental tension and sleep problems. Grandparents used coping strategies that are problem-focused (e.g., information seeking, providing support) and emotion-focused (e.g., distraction, holding on to glimmers of hope, meeting friends). Some even reported positive outcomes, such as getting emotionally closer to family members and appreciating things that had previously been taken for granted.

**Conclusions:** Grandparents suffer greatly when their grandchild is diagnosed with cancer. However, many use a variety of coping strategies, and some even discover silver linings. Several grandparents would have appreciated a professionally supervised peer support group. **Funding:** Swiss National Science Foundation (Grant no.10001C\_182129/1)

EP608/#773 | Poster Topic: AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)

#### PATIENT-REPORTED OUTCOMES, HEALTH BEHAVIORS, AND TRANSITION READINESS AMONG ADOLESCENT SURVIVORS WITH OVERWEIGHT AND OBESITY

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**Background and Aims: Objectives/Purpose:** Survivors of childhood cancer are at increased risk for morbidity and mortality, particularly those with overweight or obesity. Understanding patient-reported outcomes, health behaviors, and transition readiness from pediatric to adult care among this unique population may better inform needs and intervention targets to promote a healthy, long-term survivorship.

**Methods:** In this cross-sectional study, 48 adolescents (Age: M = 14.75; SD = 1.81; Race/Ethnicity: white = 73%; non-Hispanic = 81%; solid tumor = 34%, CNS tumor = 32%; leukemia/lymphoma = 34%), 3-12 months off treatment completed the Transition Readiness Questionnaire (TRI), the PROMIS Pediatric Profile-49, and Youth Risk Behavior Surveillance Survey. Age, sex assigned at birth, treatment intensity, and overweight/obesity status (>85%) were obtained through medical chart review. Regression analyses were used to explore associations between BMI percentile with patient-reported outcomes and transition readiness, after adjusting for known covariates.

**Results:** Nearly 42% (N=20) had overweight/obesity. After adjusting for sex assigned at birth, ethnicity, treatment intensity, and age,



having overweight/obesity increased risk of depression ( $\beta=.34$ ,  $p=.02$ ), prescription misuse ( $\beta=.28$ ,  $p=.05$ ), and marijuana use ( $\beta=.29$ ,  $p=.05$ ) as compared to survivors without overweight/obesity. Survivor overweight/obesity status was associated with worse perceived healthcare provider relationship/communication ( $\beta=-.41$ ,  $p=.006$ ), but was not associated with other transition readiness domains.

**Conclusions:** Discussion: Survivors with overweight and obesity were more likely to report depression and engage in certain risky health behaviors compared to survivors without overweight/obesity, compounding risks for future health. Additionally, survivors with overweight/obesity were less likely to perceive positive relationships and have open communication with their healthcare team, which may interfere with their willingness to participate in transition to adult survivorship care. These findings suggest that survivors with overweight/obesity may experience increased stigma and unmet emotional needs. Interventions aimed at addressing health behaviors should also include specific goals for improving relational understanding and communication within the healthcare dyad.

EP609/#788 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
*Psychosocial (PPO)*

#### IMPACT OF PSYCHOSOCIAL SUPPORT ON PARENT PERCEPTIONS OF YOUTH SOCIAL REINTEGRATION FOLLOWING CANCER-DIRECTED THERAPY IN PEDIATRIC PATIENTS

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**Background and Aims:** Childhood cancer survivors are at risk for social functioning difficulties. The transition off therapy is marked by social reintegration after an often-prolonged absence, suggesting a critical time for psychosocial support to prepare youth for social experiences following cancer-directed therapy. This project sought to better understand the frequency of receipt of psychosocial support for youth completing cancer-directed therapy and parent-reported impact of this support on social reintegration.

**Methods:** Fifty-five parents of youth (age at treatment completion:  $M = 7.89$ ,  $SD = 5.41$ ) who completed cancer-directed therapy participated in an online survey to understand psychosocial supports families were offered, the timing of these supports, and the impact of these supports on how well their children reintegrated socially.

**Results:** Thirty-five percent ( $n = 20$ ) of families were offered support related to their child's social reintegration following cancer-directed therapy. Families reported receiving support most often from psychologists (55%), child life specialists (50%), and social workers (40%) and typically from more than one psychosocial discipline (60%). Many families reported receiving this support near the end or after completion

of treatment (60% and 65%, respectively). Almost all families endorsed finding this support to be helpful (95%). A chi-square test of independence was performed [ $X^2 (2, N = 46) = 6.18, p < .05$ ] and revealed those not receiving support were more likely to report their child's social reintegration did not go well or were neutral about how it went in comparison to those who received support.

**Conclusions:** Results suggest that offering psychosocial support related to social reintegration for youth following cancer-directed therapy may serve to decrease the likelihood of parent-reported negative social experiences for their child at the transition off therapy. Future research is needed to examine child and adolescent perspectives on the impact of psychosocial support on their social reintegration following treatment.

EP610/#498 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
*Psychosocial (PPO)*

#### PSYCHOSOCIAL FUNCTIONING OF ADULT SIBLINGS OF DUTCH VERY LONG-TERM SURVIVORS OF CHILDHOOD CANCER: DCCSS-LATER 2 PSYCHO-ONCOLOGY STUDY

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**Background and Aims:** Siblings of children with cancer are impacted by their brother or sister's disease. Knowledge on siblings' wellbeing on the very long term is lacking, while such insight may inform the support of families in childhood cancer care. The aim of the current paper is to describe psychosocial outcomes among adult siblings of very long-term childhood cancer survivors (CCS), to compare these outcomes to reference populations and to identify factors associated with siblings' psychosocial outcomes.

**Methods:** Siblings of survivors (diagnosed <18 years old, between 1963-2001, >5 years since diagnosis) of the Dutch Childhood Cancer Survivor Study DCCSS-LATER cohort were invited to complete questionnaires on HRQoL (TNO-AZL Questionnaire for Adult's HRQoL),

anxiety/depression (Hospital Anxiety and Depression Scale), post-traumatic stress (Self-Rating Scale for Post-traumatic Stress Disorder), self-esteem (Rosenberg Self-Esteem Scale) and benefit and burden (Benefit and Burden Scale for Children). Outcomes were compared to a reference group if available, using Mann-Whitney U and chi-Square tests. Associations of siblings' sociodemographic and CCS' cancer-related characteristics with the outcomes were assessed with mixed model analysis.

**Results:** 505 siblings (response rate 34%, 64% female, mean age 37.5, mean time since diagnosis 29.5) of 412 CCS participated. Siblings had comparable HRQoL, anxiety and self-esteem to references with no or small differences ( $r=.08-.15$ ,  $p<.05$ ) and less depression. Proportions of symptomatic PTSD were very small (.4-.6%). Effect sizes of associations of siblings' sociodemographic and CCS cancer-related characteristics were mostly small to medium ( $\beta=.19-.67$ ,  $p<.05$ ) and no clear trend was found in the studied associated factors for worse outcomes.

**Conclusions:** On the very long-term, siblings do not have impaired psychosocial functioning compared to references. Cancer-related factors seem not to impact siblings' psychosocial functioning. Early support and education remain essential to prevent long-term consequences.

EP611/#850 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
*Psychosocial (PPO)*

#### IMPACT OF A PSYCHOSOCIAL SUPPORT PROGRAM FOR CAREGIVERS AND CHILDREN WITH CANCER

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**Background and Aims:** Treatment abandonment is prevalent among children with cancer receiving care in centers in low- and middle-income countries (LMIC). Several factors, including financial, socio-cultural, and psychological stresses, may impact compliance to the often-long treatment schedules. In order to meet the needs of children with cancer, parents and families frequently change their functionality and responsibilities. Pediatric oncology advancements have shown the importance of providing children and their families with psychosocial support. This project aimed to implement a psychosocial support program for children and caretakers at Mulago Hospital Oncology Service and evaluate its impact on promoting treatment compliance and care retention.

**Methods:** A team comprising of: a clinical psychologist, social worker, nurse, nutritionist, and counsellor was formed in November 2020. It provided extra counselling services, bereavement support, mobilized resources for transporting patients, clothing, supportive treatment, and nutritional supplements for the children with cancer in the service. Resources for the program were sourced from donations, back-

yard sales, and local fundraising campaigns, such as the \$3 monthly contribution campaign from well-wishers.

**Results:** 198 patients were attended to from January to September 2021. Most of the support was directed towards transportation to the hospital (49%), and welfare support during admissions at the hospital (40%). Burial and other supplementary drug support were 3% and 8%, respectively. During this period, the rates of missed appointments for treatment and patient retention were 11% and 86%, compared to 14% and 79% in 2020, respectively.

**Conclusions:** We show the feasibility of a locally sustainable psychosocial support program in Uganda. The psychosocial support reduced the burden of care on caregivers and increased the retention of children in care. Comprehensive psychosocial programs for children and their families are urgently needed to contribute to efforts aimed at improving the survival outcomes of childhood cancers in LMIC.

EP612/#1063 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
*Psychosocial (PPO)*

#### PSYCHOSOCIAL CONCERNS AND SERVICES IN PEDIATRIC ONCOLOGY IN LOW AND LOWER-MIDDLE-INCOME SETTINGS

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**Background and Aims:** While pediatric cancer survival rates have improved in high-income countries, they remain much lower in low- and middle-income countries (LMICs). While recent focuses have been on remediating the survivorship gap in resource-limited settings, less is known about the psychosocial needs and availability of psychosocial services in LMICs. Unsurprisingly, low- and lower-middle-income countries (L/LMICs) have additional challenges due to fewer resources, compared to upper-middle-income countries (UMICs), including less access to essential cancer medicines. Our study aims to explore psychosocial concerns and resources specific to L/LMICs.

**Methods:** A questionnaire was distributed by the SIOP Global Health Network Psychosocial Working Group in early 2020. Thirty-six respondents from L/LMICs and thirty respondents from UMICs completed the questionnaire, with a wide variety of professional disciplines represented. A total of thirty-one countries were represented; sixteen were L/LMICs.

**Results:** The overall median frequency of psychosocial problems encountered by survey respondents was 66.5%. Respondents' perceptions of anxiety in patients and depression in caregivers revealed statistically significant higher rates in L/LMICs vs. UMICs, with p-values of 0.04 and 0.01, respectively. The availability of social workers ( $p=0.025$ ), psychologists ( $p=0.003$ ) and non-professional volunteers ( $p=0.007$ ) in L/LMIC was significantly lower compared to UMICs. There were no significant differences between L/LMICs and UMICs

for the availability of child life specialists ( $p=0.592$ ), psychiatrists ( $p=0.285$ ), and chaplains ( $p=0.385$ ).

**Conclusions:** Our study highlights pediatric oncology providers' perceptions of psychosocial concerns. Based on responses, proposals for minimum standards of care are made, as well as the importance of training for existing providers and funding additional psychosocially-focused professionals. Results demonstrate that while LMICs likely can benefit from additional resources, L/LMIC appear to be most vulnerable; improvements of pediatric oncology resources in the most resource-limited settings are vital for enhancing the psychosocial well-being of patients and their caregivers, as well as health care providers' working conditions.

EP613/#1436 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

### PHYSICAL ACTIVITY BARRIERS AND FACILITATORS AMONG ADOLESCENTS AND YOUNG ADULTS WITH CANCER: A MIXED METHODS STUDY

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**Background and Aims:** Physical activity (PA) during cancer treatment can benefit physical functioning, mental health and quality of life. Adolescents and young adults (AYA), a developmental group with steep PA declines, are likely to engage in limited PA during cancer treatment. Via mixed methods, this study examined AYA experiences and correlates of PA to identify potential targets for intervention to increase PA.

**Methods:** Twenty AYA [Mage=18.3 (SD=2.9), 55% female, 50% non-Hispanic, White] on treatment completed the PROMIS PA scale, the Multi-Process Action Control Questionnaire to assess PA correlates, and the PA Barriers after Cancer scale to assess cancer-specific barriers. Qualitative interviews were conducted, transcribed and coded to explore themes surrounding barriers and facilitators and PA needs.

**Results:** Most (80%) AYA reported that cancer made them less active. Self-reported PA was positively associated with PA attitudes ( $r=.60$ ,  $p=.005$ ), habit ( $r=.62$ ,  $p=.004$ ) and identity ( $r=.56$ ,  $p=.010$ ), but not significantly associated with intentions ( $r=.37$ ,  $p=.108$ ), motivation ( $r=.32$ ,  $p=.170$ ), perceived capabilities ( $r=.19$ ,  $p=.412$ ), opportunities ( $r=.33$ ,  $p=.152$ ) or behavioral regulation strategies ( $r=.38$ ,  $p=.094$ ). Barriers were negatively associated with PA ( $r=-.52$ ,  $p=.018$ ). Qualitative

interviews revealed attitudes towards PA were generally positive, with AYA acknowledging perceived physical and mental health benefits, particularly helping keep their mind off cancer. Salient barriers included treatment-related fatigue and lack of motivation to move when not feeling well. Many AYA reported lack of specific guidance about how much and what types of PA were safe and recommended.

**Conclusions:** AYA experience many treatment-related barriers to PA that may compound non-cancer-related PA barriers in emerging adulthood. Educating AYA on the safety and benefits of PA during treatment, and incorporating recommendations tailored for their current medical status and abilities, may help to improve PA attitudes and subsequent PA levels. More research is needed to understand how to best tailor individualized PA recommendations for AYA with cancer.

EP614/#1406 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

### INTOLERANCE OF UNCERTAINTY IN ADULT SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY

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**Background and Aims:** Intolerance of uncertainty (IU) is a dispositional tendency to perceive uncertainty as unacceptable or threatening. Despite the uncertain nature of childhood cancer survivorship, no studies have examined IU and its associated risk factors in this population.

**Methods:** A representative sample of 228 adult survivors enrolled in the Childhood Cancer Survivor Study (50.4% female; median[range] age 40[22-64] years; 32.8 years since diagnosis) completed self-report measures of IU (Intolerance of Uncertainty Scale-Short Form; IUS-12), clinically significant depression (Patient Health Questionnaire 8-Item;  $\geq 10$ ), clinically significant anxiety (Generalized Anxiety Disorder 7-Item;  $\geq 10$ ), chronic pain (2 items assessing pain lasting  $\geq 3$  months), and perceived poor health status (1-item yes/no). Total scores on the IUS-12 range from 12 to 60, with higher scores indicating greater IU. Grade 2-4 chronic health conditions were used, based on CTCAE v4.03. Linear regression models adjusted for sex, race, age at diagnosis, and current

age estimated mean effects (B) with 95% confidence intervals (CI) for associations of key risk factors with IU.

**Results:** The mean level of IU among survivors was 26.2 (95%CI[24.9-27.5]). Higher IU was associated with female sex (B [95% CI]; 2.7 [0.1-5.3]), unemployment (5.2[1.8-8.6]), chronic pain (5.8[3.3-8.4]), clinically significant depression (8.5[5.8-11.2]) and anxiety (13.4[10.9-15.9]), cardiovascular conditions (5.1[2.3-8.0]), neurological conditions (4.8[1.1-8.4]), and poor health status (8.8[5.4-12.2]), but not diagnostic group or cancer treatment factors.

**Conclusions:** Overall, levels of IU were comparable to those observed in non-clinical samples. The current findings also suggest associations between IU and distress observed in the general population occur among childhood cancer survivors also, while highlighting factors potentially specific to the experience of elevated IU among survivors, including chronic pain, poor health status, and chronic conditions. Further research is needed to elucidate the direction of the association between IU and depression and anxiety, which will help inform psychosocial screening and intervention in survivors.

EP615/#1704 | Poster Topic: AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)

#### UNDERSTANDING EMOTIONAL PROCESSING AND PERCEIVED KNOWLEDGE DURING TIME OF DIAGNOSIS AND IMPACT OF A PSYCHOLOGICAL THERAPY TOOL „MY LOGBOOK - I KNOW MY WAY AROUND“

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**Background and Aims:** The diagnostic phase of childhood cancer is considered as particularly crucial. It includes multifaceted challenges and is associated with anxieties and insecurity. This makes it all the more important to provide psychosocial services at an early stage to ensure compliance during therapy, prevent PTSD, anxiety disorders or even enable a resilient developmental outcome. The Quality Improvement Project “My Logbook” presents a method to develop a consensus-based and patient-oriented tool to systematically translate standards of psychosocial care into clinical practice.

**Methods:** Tools on building trust, coping mechanisms in crisis situation, preparation and debriefing information on diagnosis were collected and resulted in two booklets: “All I need to know” and “My path to diagnosis”. Two face-to-face sessions cover psychoeducational, activity &

practice and reflective aspects. The pilot run at German-speaking sites involves a process-oriented screening at four time points to evaluate perceived emotional state and level of knowledge; analysis involved Poisson regression, a generalized linear mixed model and Wilcoxon rank-sum/signed-rank test.

**Results:** Patients at standard risk (N=50, 6-14 years) according to the Pediatric Psychosocial Preventative Health Model showed a significant decrease in neutral (-0.170,  $p = .045$ /slope = -0.247,  $p = .054$ ) and negative (-0.374,  $p < .001$ /slope = -0.469,  $p < .001$ ) emotions, while positive emotions remained stable (slope = 0.026,  $p < .001$ /slope = -0.1213,  $p = .165$ ). However, a general positive attitude related to the situation confronted with the hospital setting was detected. Elevated negative emotions self-evident while confronted with the diagnosis showed a short-time relief after only one session. In general, perceived knowledge of patients improved significantly ( $V = 41.5$ ,  $p = .002$ ,  $r = 0.27$ / $V = 4$ ,  $p = .035$ ,  $r = 0.28$ ).

**Conclusions:** The process-oriented evaluation supports a differentiated understanding of patients' needs during diagnostic phase. Moreover, it proves effectiveness of early patient-oriented and age-appropriate psychological interventions to foster confidence.

EP616/#1284 | Poster Topic: AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)

#### SWAHILI TRANSLATION AND CULTURAL ADAPTATION OF A PEDIATRIC CANCER STIGMA SCALE (CASS) FOR USE IN THE NON-PATIENT POPULATION IN TANZANIA

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**Background and Aims:** The Cataldo Cancer Stigma Scale (CASS) was developed to measure patient experienced stigma, and further modified for use in non-patient communities. The aim of this study was to adapt a Swahili language version of the CASS for use in the Tanzanian non-patient community, to identify the current level of stigma towards children with cancer and create a measure to monitor changes in perceptions following future community-based interventions.

**Methods:** An expert group of medical providers, community advisors, and social scientists reviewed the 26 original statements in the CASS survey to determine relevancy in the Tanzanian context and Swahili language. Translated survey was evaluated with cognitive interviewing, with sequential rounds of five non-patient community members in the Mwanza region of Tanzania until >80% comprehension was reached for each question. Pilot survey was then distributed to 220 community

members in Mwanza region randomly sampled from 3 rural and 3 urban communities for further validation.

**Results:** Three rounds of cognitive interviews were completed, with minor grammar and word selection changes to clarify the item's meaning. The distributed pilot survey included 26 core and 10 alternate questions covering 5 core areas of stigma: avoidance, awkwardness, financial, policy, and severity. Structural validity and reliability of the items were evaluated with final 19 questions selected for sub score analysis (Cronbach's alpha >0.7). Of the stigma categories, severity had the highest community endorsement (62.6%) and policy scored the lowest (13.2%). Only the severity sub score differed between urban and rural communities (43% vs 57%), and avoidance sub score differed between female and male respondents (41% vs 59%).

**Conclusions:** This validated, Swahili-adapted pediatric CASS for use in the non-patient community will allow for a meaningful evaluation of intervention response that can be used in cancer stigma research throughout East Africa.

EP617/#1280 | Poster Topic: AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)

#### TRUST - TAKE RESPONSIBILITY UPON SUSTAINABLE TREATMENT OF CANCER

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**Background and Aims:** The rising cost of treating childhood cancer presents financial hurdles for patients, their families, and health care providers. Therefore, new approaches of care that are both cost-saving and sustainable are becoming increasingly important.

**Methods:** In this prospective longitudinal, single-arm utility study, we used our newly developed ePROtect-APP to provide virtual care (VC) for maintenance treatment of childhood acute lymphoblastic leukemia in different regions of Austria and Italy. Outcomes were measured by the number of VC compared with outpatient visits, quality of care, reduction in travel distances and CO2 savings for patients before and after the launch of VC on January 15, 2023.

**Results:** Before implementation, patients with leukemia (n=95) had an average of 66.4 (IQR, 54.4-85.2) outpatient visits. However, there was a strong asymmetry in distance between patients living near to the hospital or in remote areas (median distance per patient: 1,600 versus 8,400 kilometers,  $p < 0.05$ ). Simulation of VC showed that the greatest benefits in terms of time, distance, and CO2 savings occurred with a 75% reduction in outpatient visits. Therefore, ¾ of outpatient visits were replaced by VC, and 16 patients were enrolled within 2 months of implementation. A total of 73 VCs were performed, resulting in median

reductions in travel distance of 162 kilometers (IQR, 139.5-190.5), travel time of 114 minutes (IQR, 102-129), and CO2 emissions of 28.35 kg (IQR, 24.41-33.31) per visit. No changes were observed in quality of care. Overall satisfaction with VC was > 90% among physicians, patients, and institutional health care providers, respectively.

**Conclusions:** The integrated use of patient-reported outcome measures, primary care physician blood analysis and telemedicine maintained excellent quality of care, generated high satisfaction among users, and reduced travel costs and CO2 emissions. Our results may help to expand VC for childhood cancer treatment.

EP618/#1834 | Poster Topic: AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)

#### STEP-YA: DEVELOPING AND TESTING A LOW-INTENSITY CBT INTERVENTION FOR YOUNG ADULT CANCER SURVIVORS WITH INSOMNIA

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**Background and Aims:** Background and Aims: As many as 25% of young adult cancer survivors (YACS) suffer from chronic insomnia even years after treatment. Cognitive Behavioral Therapy for Insomnia (CBT-I) is a highly effective but largely underused treatment due to limited availability and burdensome treatment requirements. To address this, we developed the Sleep Treatment Education Program for Young Adults (STEP-YA), a low-intensity educational intervention delivered virtually. In this study, we test the efficacy of STEP-YA to improve insomnia and mood in YACS, and assess the utility of individualized coaching to improve treatment effects.

**Methods:** Methods: 74 off-treatment YACS aged 20-39 with significant insomnia are eligible. Each participant completes the STEP-YA session in a synchronous, 90-minute online session. Participants are randomized to receive STEP-YA alone, or with two individual telephone coaching sessions. Follow-up measures are collected 4 & 8 weeks post-intervention.

**Results:** Results: 16 YACS are enrolled and 30 more expected in the next six months. When asked about STEP-YA, 12 participants (75%) rated STEP-YA as "excellent," and 4 (25%) as "very good" on a 5-point Likert scale from "excellent" to "poor." Additionally, 14 participants (88%) reported finding STEP-YA content "very useful" and 2 (22%) stated it was "moderately useful." Coaching sessions were also positively rated: 6 of 6 coaching participants (100%) rated sessions as "excellent," or "very good," and 6 (100%) rated the information presented as "very useful" or "moderately useful." Expanded results, including intervention effects on insomnia and mood, participant satisfaction, and effects of coaching on outcomes will also be reported.

**Conclusions:** Chronic insomnia has significant negative effects on YACS' medical, educational, and psychological functioning. STEP-YA holds promise for addressing their needs; study results will determine if the intervention warrants future effectiveness and dissemination studies, and if individualized coaching is necessary for adequate treatment response.

EP619/#77 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

### DETERMINANT FACTORS IMPACT HEALTH-RELATED QUALITY OF LIFE IN CHILDREN WITH CANCER IN THAILAND: PARENTS VS. CHILDREN PERSPECTIVE

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**Background and Aims:** Health-related quality of life (HRQOL) is a vital assessment to demonstrate the achievement in pediatric cancer care parallels with medical treatment. The Pediatric Quality of Life Inventory (PedsQL) 3.0 Cancer Module in Thai Version becomes a standard tool to access the HRQOL among Thai children with cancer and their families. This study aimed to explore the HRQOL and factors related HRQOL among pediatric oncology patients using PedsQL 3.0 Cancer Module.

**Methods:** A single institution, cross-sectional study was conducted on children with cancer and their families. A paired-samples t-test was performed to evaluate the differences between HRQOL scores of the child and parent reports. Linear regression was used to evaluate factors associated with HRQOL and which particular domains of the PedsQL 3.0 Cancer Module were influenced.

**Results:** Eighty-five children with cancer and their families were enrolled. The patients' mean age was 10.82±5.48 years. The most common cancer types included acute lymphoblastic leukemia (n=32, 67%), central nervous system tumors (n=13, 15%), osteosarcoma (n=10, 27%) and neuroblastoma (n=9, 24%), in rank. The mean HRQOL scores in child and parent reports were 74.37±15.7 and 70.42±17.15, respectively ( $p=0.034$ ). Factors associated with HRQOL in parent reports were the number of outpatient visits ( $p=0.019$ ) and hospital admissions ( $p=0.002$ ). The number of hospitalizations was the only independent factor that affected HRQOL ( $p=0.044$ ). The number of outpatient visits and/or hospital admissions was influenced by pain and hurt, nausea, procedural anxiety, and communication domains ( $p<0.05$ ). Only the number of hospitalizations was an independent factor that influenced the procedural anxiety domain in HRQOL ( $p=0.005$ ).

**Conclusions:** HRQOL among Thai children with cancer was desirable from both children and parent perspective. Differences between child and parent HRQOL scores were observed. The number of outpatient visits and hospital admissions affected HRQOL, particularly in the procedural anxiety aspect.

EP620/#388 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

### POST PANDEMIC TRENDS IN EDUCATIONAL STATUS AMONG CHILDREN WITH CANCER IN EL SALVADOR

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**Background and Aims:** A diagnosis of pediatric cancer interferes with a child's education. Educational continuity is established as a psychosocial standard. In El Salvador, school continuity has been historically challenging. The COVID-19 pandemic worsened the quality of education. We aimed to establish an institutional-based registry of educational status after COVID-19 pandemic.

**Methods:** This was a descriptive study. Prospective data from 200 structured interviews with caregivers of 132 patients diagnosed with pediatric cancer, mean age 10.8 (SD=3.7), recorded educational status data regarding enrollment, grade, lag, and institutional practices from August 2021 to February 2023.

**Results:** 111 (55.5%) patients were actively attending school and 89 (44.5%) were not enrolled or were enrolled but not attending. Among records with active status, 57 (52%) were attending virtually: 20 (19%) due to COVID-19 and 36 (63.2%) due to treatment restrictions. 114 (57%) had never lost a school year due to cancer, 59 (29.5%) lost a year or less due to cancer treatment. 17 patients (8.5%) had lost from two to six years of schooling due to the disease. Finally, 2 patients (1%) with long-term history of cancer had lost seven years of attendance. The most common cause of absenteeism among interviews with inactive status was treatment restrictions (n=55, 64%). Other reasons included parental concerns for health risks (n=6, 11%) and 5 (6%) patients not willing to attend school. 46 (23%) patients reported grade skipping. This was more common among cases registered with inactive status (n=35, 76%) than with active status (n=11, 24%).

**Conclusions:** The COVID-19 pandemic provided the opportunity to attend school virtually. Still, an alarming number of children and adolescents remain out of school due primarily to treatment regimen demands, parental concerns, and school practices. This provides for the need to create an in-hospital educational support program aimed to work in coordination with regular schools.

EP621/#155 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

**“ARE WE GOING TO MEET TODAY?”: ADOLESCENTS WITH  
CANCER ARE HIGHLY SATISFIED WITH IN-HOSPITAL  
OPPORTUNITIES TO INTERACT**

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**Background and Aims:** During adolescence, individuals experience an increasing interest in peer interactions. A cancer diagnosis halts typical social development due to constant appointments, long-term hospitalization, and safety measures for infection control. Research suggests that during cancer treatment youth identify social interaction as a priority of care and as a dimension of normalcy. Thus, a psychosocial standard of care has been established to provide the opportunity for social interactions during cancer care and survivorship. We aimed to establish a socialization group for teens with cancer.

**Methods:** Three different approaches were tested (social skills workshop, round table, and informal meeting). An informal meeting approach was selected given the proximity to organic peer-to-peer interactions. The intervention consists of two-hour sessions held twice per week for patients 11 years and older. Participants are involved in activities that promote collaboration and conversation (i.e., egg drop). A sample of patients in active treatment responded to an eight-question satisfaction survey using a 10-point scale assessing global satisfaction, intention to return, satisfaction with facilitators, positive affection during the meeting, and satisfaction with activities. Consent and assent were obtained.

**Results:** 27 patients (18 female), mean age 13 (SD=1.6) answered the survey. Mean score for global satisfaction was 9.3 (SD=1.5). The intention to return mean score was 9.4 (SD=0.9). Satisfaction with facilitators mean score was 9.2 (SD=1.35). The positive affection scored a mean of 8.8 (SD=1.6). Satisfaction with activities scored a mean of 8.7 (SD=1.9).

**Conclusions:** Youth positively value the opportunity to interact at the treatment center and perceive the group as a space to discuss intimate issues, experience tranquility due to disconnection from the disease reality. Activities are low-cost and engage teens in conversations and working in collaboration. The intervention promotes the development of new friendships, social support, and teamwork. Facilitators play a key role in creating a safe and friendly atmosphere.

EP622/#1855 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

**MENTAL DISORDERS AMONG ADOLESCENTS AND YOUNG  
ADULTS WITH CANCER: A CANADIAN POPULATION-BASED  
AND SIBLING MATCHED COHORT STUDY**

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**Background and Aims:** A cancer diagnosis may increase the risk of mental health disorders among adolescents and young adults (AYAs). We aimed to compare cumulative incidence of mental disorders among AYAs with cancer to general population and their siblings.

**Methods:** In this retrospective, population-based, matched cohort study, all individuals, ages 15 to 39, diagnosed with cancer (1989 and 2019), in Manitoba, Canada, were included. The population-based cohort was matched on age, sex, socioeconomic status, and area of residence. Outcomes included the incidence of (i) mood and anxiety disorders (ii) substance use disorders, (iii) suicide attempts or death by suicide, (iv) psychotic disorders, and (v) a composite of any of the preceding four categories. Cox proportional hazards regression models with a competing risk of death were used to estimate adjusted subhazards ratios (aSHR) and 95% confidence intervals (CI).

**Results:** 3,818 AYAs with cancer were matched 1:5 with a population-based cohort. AYAs with cancer were more likely to be diagnosed with incident mental disorders than the matched population-based cohort: aSHR [95% CI] for mood and anxiety disorders at 0-6 months (11.27, [6.69, 18.97]), 6-12 months (2.35, [1.54, 3.58]) and 12-24 months (2.06, [1.55, 2.75]); for substance use disorders at 0-6 months (2.73, [1.90, 3.92]); and for psychotic disorders at 0-6 months (4.69, CI, 2.07, 10.65). After matching 1,717 AYAs with cancer 1:1 with siblings, cancer was

associated with a higher risk of mood and anxiety (11.02, [2.61, 46.51]) and any mental health disorder (3.98, [2.06, 7.71]) during first six months post-cancer diagnosis.

**Conclusions:** AYAs with cancer experienced a greater incidence of mental disorders primarily within the first two years post-cancer diagnosis, with highest incidence immediately post-cancer diagnosis compared to the general population and siblings. These findings highlight the vulnerable mental health of AYAs immediately after a cancer diagnosis and a critical window of opportunity for intervention and prevention.

EP623/#993 | Poster Topic: AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)

#### DELAY IN DIAGNOSIS: A REPORT FROM EL SALVADOR

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**Background and Aims:** Early diagnosis of childhood cancer is essential for timely treatment. Some identified determinants of delays in diagnosis are patient/parental factors such as level of education and socioeconomic status as well as healthcare system factors. This study explores the time it took patients to reach a diagnosis since the onset of symptoms and reasons for delays in diagnosis in childhood cancer patients in El Salvador.

**Methods:** A qualitative semi-structured interview method was conducted with 50 caregivers of newly diagnosed patients at the pediatric oncology program in El Salvador. Interviews were done from July 2022 to February 2023. The disease timeline was based on the parent's recollection of events and dates.

**Results:** From the cohort of interviews, it took caregivers an average of 15 (SD=32) days to consult from the onset of symptoms. Caregivers consulted an average of 3 times before being referred to tertiary care. Once in tertiary care, it took an average of 8 (SD=20) days to reach a diagnosis. Overall, it took patients an average of 81 (SD=123) days from the onset of symptoms to the cancer diagnosis. 48% of caregivers consulted in a private clinic, 36% consulted in a public health clinic, and 14% in public health insurance facilities[AM1]. 54% of caregivers' level education was below 9<sup>th</sup> grade and 46% had part of high school or university studies. It took 66% (n=33) of patients more than 30 days to reach a cancer diagnosis from the onset of symptoms. Of this 66%, 39% came from rural and 60% from urban areas.

**Conclusions:** The greatest delay is due to healthcare providers' failure to refer to tertiary care.[AM1] Families incur out-of-pocket expenses despite having availability of free medical services. They believe private care is more trustworthy although the greatest delay came from

private physicians. Most families consult with more than one care provider.

EP624/#1251 | Poster Topic: AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)

#### PREVALENCE OF BEHAVIOURAL PROBLEMS IN SURVIVORS OF CHILDHOOD SOLID MALIGNANT TUMOURS

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**Background and Aims:** The adverse health outcomes experienced by survivors of paediatric solid tumours can be both physiological, psychological, and behavioural. The aim of the present study was to assess the long-term psychological and behavioural effects faced by the survivors of solid malignant tumours.

**Methods:** Survivors were assessed for behavioural problems with help of the Child Behaviour Checklist (6-18 years).

**Results:** One hundred forty-five survivors with a median age of 11 years (6-18 years) were included. These survivors had a diagnosis of 60 Wilms Tumour (WT) (41.38%), 25 Neuroblastoma (NB) (17.24%), 18 Hepatoblastoma (HB) (12.41%), 29 Malignant Germ Cell Tumour (MGCT) (20.0%), 9 Rhabdomyosarcoma (RMS) (6.21%) and 4 Ewing sarcoma family of tumours (ESFT) (2.76%). There were 95 males (65.52%) and 50 females (34.48%). The sample was further split into three age groups: 6-9 years (n=57, 39.31%); 10-14 years (n=60, 41.38%) and 15-18 years (n=28, 19.31%). The evaluation was done at a median age of 136 months after treatment completion and the median age of time since diagnosis was 88 months. Out of these 145 survivors, 137 survivors were assessed for behavioural problems. One or more behavioural problems were found in 38 (27.77%) patients. Out of these Internalizing problems were found in 15/137 (10.95%) patients (anxiety issues (n=7, 5.11%), depression (n=6, 4.38%)). Attention problems were found in 16 (11.68%) patients. Externalizing problems were found in 24 (17.52%) patients (conduct problems (n=16, 11.68%) and oppositional-defiant behaviour (n=4, 2.98%)). Age at evaluation had a significant effect on the patient having internalizing and externalizing problems. Gender, type of tumour and time since diagnosis & treatment completion had no significant effect on internalizing and externalizing problems.

**Conclusions:** About more than one-fourth of survivors of childhood cancer experience significant long-term behavioural and psychological consequences and must be closely monitored for co-morbid behavioural and psychological consequences.



EP625/#670 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

### DISTRESS THERMOMETER FOR PARENTS OF CHILDREN WITH CANCER

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**Background and Aims:** The unexpected as well as life threatening diagnosis of cancer and the intense treatment that follows will create an array of stressful events for the family. Distress Thermometer for Parents (DT-P) developed and validated by Lotte Haverman et al, consists of a thermometer score from 0 (no distress) to 10 (extreme distress) and a problem list (practical, social, emotional, physical, cognitive, and parenting domains). This study was designed to assess the feasibility of DT-P in assessing distress among parents of children with cancer.

**Methods:** This prospective observation study was conducted at paediatric oncology outpatient clinic of a tertiary cancer centre. DT-P was translated into local language with a forward– backward translation procedure. Malayalam translated DT-P was self-administered to parents of children with cancer, aged <14 years, getting treatment at the centre. Following this, QQ10 questionnaire was filled by the parents, which provided the value and burden score of the DT-P.

**Results:** The questionnaires were administered in 30 parents with median age of the parent and their children were 32 and 4 years respectively. Majority of the participants were mothers, comprising 63.3% (n=19) and 43.3% (n=13) parents were graduates. Completion rate of Malayalam translated DT-P questionnaire was 98.25%. QQ10 tool noted that Value score (72.91) is more than the burden score (31.25). DT-P identified a mean overall distress score of 6.83. With a cut-off score of 4, 90% (n=27) parents were identified to require support for the distress, however only 66.6% (n=20) wished for referral to psychology clinic. Among the problem domains, emotional problems were attributed to stress in majority of the parents. Higher overall distress was seen in parents with girl children, children having lower survival probability and those with higher education status.

**Conclusions:** DT-P can be used as a tool to screen for distress among parents of children cancer.

EP626/#1712 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

### EMOTIONAL INTELLIGENCE, COPING AND LIFE PERCEPTIONS: COMPARISON BETWEEN ADOLESCENTS WITH ONCOHAEMATOLOGICAL DISEASE AND HEALTHY PEERS

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**Background and Aims:** Several studies identified lower adolescents' psychological wellbeing after the Covid19 pandemic and the important protective role of coping and emotional intelligence (Delvecchio et al., 2022; Mastorci et al., 2021). The aims of this study are to assess the coping strategies and emotional intelligence scores in adolescents with oncohematological diseases in post-pandemic period and comparing them with those of matched healthy peers.

**Methods:** Participants were 23 adolescents, 16 males and 7 females, with a mean age of 15.1 (SD=2.1; range: 12-18 years old) recruited at the Pediatric Hematology-Oncology (University of Padua) and a control group of healthy peers matched by age and gender. Sixteen patients had a hematology disease and 7 had a solid one. After the signature of informed consent by parents and by themselves, the adolescents had an interview with the clinical psychologist filling in the Emotional Quotient Inventory, Coping Responses Inventory, and the Ladder of Life scale.

**Results:** Patients' coping strategies scales were placed at an average level compared to the reference population. In general, adolescents used more approach strategies and less the problem solving one. Intrapersonal scale of emotional intelligence obtained a score that was below the average in most patients. The clinical group used more coping strategies than the healthy group, specifically positive reappraisal [t(22)=-3.04 p=.003], seeking guidance and support [t(22)=-2.63 p=.014], problem- solving [t(22)=-2.66 p=.007], search for alternative gratifications [t(22)=-1.73 p=.048] and emotional outburst [t(22)=-1.73 p=.049]. In the perceptions of their life, the patients significantly reported lower results in the current scale [t(22)=3.3 p=.002], but a better future life perception [t(22)=-1.71 p=.05] than controls.

**Conclusions:** It is of paramount importance for adolescent patients to be flexible and diversify responses to face a stressor based on one's resources, past experiences, and situational factors. Acknowledgements: A special thanks to Italian Ministry of Labour and AIL that supported this study

EP627/#585 | Poster Topic: AS05 SIOP Scientific Program/AS05.q  
Psychosocial (PPO)

### INTRODUCING A REDEVELOPED QUESTIONNAIRE PTGQ-CA (POSTTRAUMATIC GROWTH) AND EXPLORING CORRELATIONS WITH RUMINATION IN CHILDREN AND ADOLESCENTS WITH CANCER IN A CROSS-SECTIONAL STUDY

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**Background and Aims:** The study examines posttraumatic growth (PTG) and rumination as a result of struggling with trauma among children and adolescents with cancer. The aim is to (1) describe PTG in German children through the developed questionnaire PTGQ-CA within the different phases of disease, and (2) elucidate first indications thought being relevant to the PTG process in children and adolescents.

**Methods:** The patients were recruited at the clinic of pediatric Hematology and Oncology at Hannover Medical School, Germany. Eligibility criteria include (1) age 11 to 19, (2) diagnosis of cancer without constraints, (3)  $\geq 2$  weeks from diagnosis at T1, (4) German-speaking, (5) no significant cognitive or sensory deficits, (6) three measurement points were established in a half year rhythm. So far, 75 participants were recruited at the first measurement point. A full spectrum of PTSD is rare among those patients, thus the focus was set on a more subclinical level. PTG is measured using a redeveloped version of the posttraumatic growth questionnaire for children and adolescents (PTGQ-CA; 26 items) to assess the five areas of PTG related to the questionnaires (PTGI) by Kilmer et al. (2009) and Maercker & Langner (2001). An examination of the five areas was ensued by a factor analysis. Further, in reference to former research and based on the pivotal process of rumination types, a rumination scale for children and adolescents (RS-CA; 10 items) was composed to assess intrusive and deliberate rumination. The results have been correlated with the five key areas depicted through the PTGQ-CA.

**Results:** Providing results of a factor analysis of the PTGQ-CA of the first measurement point, finding first in detailed indications of the PTG process in conjunction with the two different types of rumination.

**Conclusions:** Our careful analysis process will be completed by the end of July.

EP628/#280 | Poster Topic: AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)

## THE PERCEIVED IMPACT OF CANCER FOR ADOLESCENTS AND YOUNG ADULTS

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**Background and Aims:** A cancer diagnosis during adolescence and young adulthood (ages 15-22, AYA) can have a significant impact on quality of life (QOL). This impact can be emotional – changes in per-

ceived identity – and functional – changes in perceived ability to achieve goals. It is essential to better understand how these perceived impacts are associated with one another and QOL during different phases of cancer treatment (on- vs off-therapy) to provide optimal support to AYAs.

**Methods:** AYA with cancer, aged 15-22, either on-therapy (n=24,  $M_{age}=18.39\pm 2.42$ ,  $M=5.88\pm 2.25$  months post-diagnosis) or off-therapy (n=34,  $M_{age}=19.97\pm 1.67$ ,  $M=2.41\pm 1.08$  years off-therapy) were enrolled. Participants completed measures of the emotional impact of cancer [Centrality of Events (CES)], the functional impact [Young Adult Cancer Impact Scale (YACIS)], and QOL (PedsQL).

**Results:** On- ( $M=3.81\pm 0.61$ ) and off-therapy ( $M=4.08\pm 0.62$ ) AYA perceived a significant emotional impact of cancer (CES:  $t(56)=-1.67$ ,  $p=.10$ ). On-therapy AYA perceived greater functional impact on educational achievement ( $t(56)=2.51$ ,  $p=.01$ ), romantic relationships ( $t(56)=2.05$ ,  $p=.04$ ), and living independently ( $t(56)=3.10$ ,  $p=.003$ ). There were no between-group differences for social interaction ( $t(56)=1.81$ ,  $p=.08$ ) or career goals ( $t(55)=1.24$ ,  $p=.22$ ). Perceived emotional impact was associated with a greater functional impact, but only for off-therapy AYA (CES and educational achievement  $r(34)=-.618$ ,  $p<.001$ ), social interaction  $r(24)=.451$ ,  $p=.007$ , romantic relationships  $r(34)=.458$ ,  $p=.006$ ). Both groups reported fair QOL (On:  $62.24\pm 15.15$ , Off:  $69.72\pm 21.01$ ,  $t(55)=-1.47$ ,  $p=.15$ ). A greater perceived impact of cancer was associated with worse QOL, though more strongly for off-therapy AYA (CES  $r(34)=-.418$ ,  $p=.014$ ; all YACIS  $r$ 's  $>-.512$ , all  $p<.01$ ).

**Conclusions:** AYA perceive emotional and functional impacts of cancer, which are associated with QOL. Off-therapy AYA perceive a stronger association between changes in their identity and their perception of the functional impact of cancer; this is associated with reduced QOL. Understanding how AYA perceive the impact of cancer on their goals and identity development is crucial for creating interventions targeting these concerns.

EP629/#519 | Poster Topic: AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)

## INTERNALIZED STIGMA AMONG PATIENTS WITH OSTEOSARCOMA AND RETINOBLASTOMA TREATED IN GUATEMALA, JORDAN, AND ZIMBABWE

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**Background and Aims:** Internalized stigma adversely impacts childhood cancer survivors, limiting their ability to reintegrate with their communities and maintain social networks. However, the impact of internalized stigma on children undergoing cancer treatment is unknown. This study aims to explore internalized stigma during the treatment of children diagnosed with osteosarcoma or retinoblastoma in Guatemala, Jordan, and Zimbabwe.

**Methods:** Semi-structured interviews were conducted with 19 health-care providers, 9 adolescent patients aged 12-18, and 28 parents at tertiary care centers in Guatemala, Jordan, and Zimbabwe. Interviews were conducted in Spanish, Arabic, Shona, and English, transcribed, and translated into English for analysis. Transcripts were coded by two coders with disagreements resolved by consensus and third-party adjudication. Thematic content analysis explored internalized stigma defined a priori as “a patient’s own adoption of negative societal beliefs or feelings, including changes in self-identification”.

**Results:** All types of participants described internalized stigma. Some patients adopted negative beliefs about cancer and associated internalized stigma with psychosocial fragility. However, other patients denied explicit changes in self-identification following diagnosis and described a lack of internalized stigma which manifested as confidence and self-esteem. Parents and providers similarly described internalized stigma as contributing to patients’ poor mental health, self-isolation, and avoidance behaviors; inversely, they perceived patients who did not adopt societal stigmas as being more accepting of their situation and resilient. Parents and providers also discussed the importance of support from family members, the medical team, and childhood cancer survivors in helping patients remain confident following their diagnosis, although these supports were not specifically endorsed by patients themselves.

**Conclusions:** These findings demonstrate the importance of internalized stigma from the time of diagnosis. Future interventional work should focus on providing multilevel support to patients to mitigate internalized stigma. Continued research on how internalized stigma evolves throughout the treatment process could further inform interventions.

EP630/#1172 | Poster Topic: AS05 SIOP Scientific Program/AS05.q Psychosocial (PPO)

#### CHALLENGES EVALUATING CRITICAL CARE COMMUNICATION IN PEDIATRIC ONCOLOGY ON A GLOBAL SCALE

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**Background and Aims:** CritCom is a bilingual (English and Spanish), valid measure of interdisciplinary, interprofessional communication quality around clinical deterioration for children with cancer (CritCom). CritCom evaluates communication quality across six domains: actionability, clarity, tone, empowerment, collaboration/teamwork, and leadership. However, global use requires pragmatic measures available across languages and cultural contexts. This study describes key linguistic considerations when translating this communication measure into different languages.

**Methods:** CritCom was translated to Arabic and Portuguese by native speakers. Translation validity was determined by an independent translator to back-translate to English and review with the original translations. Cognitive interviewing further assessed the quality of translation and linguistic context. Finally, synthesis across languages was completed to ensure clarity and construct similarity in both languages.

**Results:** In Arabic, four of six domains had translatability concerns. For example, the concept of an action being done in a “timely manner” (actionable domain) did not translate well and was back-translated as “appropriate amount of time.” Additionally, the concept of “empowerment” was lost in translation as it pertained to self-empowerment, and there is not an Arabic verb to capture the concept of self-empowerment. Once back-translated, it read, “an ability to freely communicate.” In the Portuguese translation, four of the six domains similarly presented translatability concerns. For example, “actionable” communication was back-translated as “effective” communication. These challenges were resolved using serial translation/review and cognitive interviewing.

**Conclusions:** Care must be taken when translating a validated English measure to maintain construct validity as English concepts pertaining to teamwork and communication may not have an applicable concept in another language. English homonyms should be carefully assessed along with potential homonyms in the translation language. A rigorous methodology of forward translation followed by back-translation and cognitive interviewing can overcome interpretation barriers to support global research in pediatric oncology.

EP631/#1186 | Poster Topic: AS05 SIOP Scientific Program/AS05.r Epidemiology, Policy and Advocacy

#### DIAGNOSIS OF CHILDHOOD MALIGNANCY AT A TERTIARY CARE PEDIATRIC CENTER VARIABILITY WITH TIME OF THE YEAR

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**Background and Aims:** There is scant literature on variability of time of year of diagnosis of pediatric malignancy. At our institution, there was a consensus that there was an increase in diagnoses in fall and decrease in winter compared to the other seasons. We sought to determine if the time of the year was a significant predictor of incidence of childhood malignancy.

**Methods:** We reviewed the records of all patients newly diagnosed with malignancy at the Children's Hospital of Eastern Ontario (CHEO), a tertiary care pediatric hospital in Ottawa, Ontario, Canada with a large catchment area. We reviewed our data in the provincial database (POGONIS) which contains all patients newly diagnosed with malignancy at CHEO. We extracted type of cancer diagnosis (grouped as leukemia/lymphoma, CNS tumor, non-CNS solid tumor) and time period of diagnosis grouped in 3 month intervals for all patients diagnosed from January 1, 2003 to December 31, 2022. Data was analyzed using SPSS software.

**Results:** There were a total of 1,640 patients diagnosed with cancer during the study time period, 742 with leukemia/lymphoma, 314 with CNS tumors, and 584 with non-CNS solid tumor. Of these, 386 were diagnosed between January and March, 418 from April to June, 393 from July to September and 443 from October to December. Chi-squared analysis of the data revealed that there was no statistical significance between time of the year and diagnosis for the overall data set ( $p=0.213$ ), and when grouped in 5 year intervals ( $p=0.199$ ).

**Conclusions:** While there was a feeling from oncology health care providers that the diagnosis of cancer is increased at certain times of the year, analysis of cases over the last 19 years does not show any preponderance with specific time of the year. The condensed data from POGONIS limited our analysis and more robust conclusions may be possible without grouping in 3 month intervals.

EP632/#1106 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### BEYOND ASSESSMENT: NATIONAL IMPACT OF PEDIATRIC ONCOLOGY FACILITY INTEGRATED LOCAL EVALUATION (PROFILE) IN CAMEROON

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**Background and Aims:** In 2020, the Cameroon Paediatric Oncology Group (CPOG) in collaboration with the Ministry of Health set out to conduct a formal baseline assessment of childhood cancer services nationally. The ProFILE tool was used with facilitation from the St Jude

team. We sought to assess achievements two years after this baseline assessment and priority setting.

**Methods:** The ProFILE assessment was conducted at three paediatric oncology centres and a national stakeholder workshop was organized to identify priorities and develop an action plan. The workshop was led by the Ministry of Health and the WHO country office was in attendance together with other paediatric cancer stakeholders. Priority actions were grouped into capacity building, strengthening data systems and fundraising. A summative report was submitted to all stakeholders including the Minister of Health.

**Results:** Within 25 months, one paediatrician is completing paediatric oncology fellowship; a paediatric oncology nursing summer school has been created at the University of Bamenda; 2 annual palliative care trainings have been organized; CPOG has secured more funding for research and a childhood cancer fund has been created for local fundraising. The Minister of Health requested for inclusion in the Global Initiative for Childhood Cancer (GICC) and funding from the WHO has contributed to: harmonization of treatment and supportive care protocols; harmonization of monitoring and evaluation tools; chemotherapy safety workshops; a national leukaemia workshop; retinoblastoma early detection workshop with ophthalmologists; and commemoration of International Childhood Cancer Day. The GICC-related activities are directly supervised by the Ministry of Health.

**Conclusions:** To date, three quarters (75%) of priorities identified through ProFILE have been addressed and 82% of the GICC-related activities have been addressed. However, there is need for a mechanism to track meeting resolutions and finalize key documents to achieve desired outputs. Moreover, priorities need to be re-defined and this will require a further in-depth assessment.

EP633/#1323 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### SUPPORTING SUSTAINABLE CARE FOR CHILDREN WITH CANCER IN UKRAINE DURING WAR

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**Background and Aims:** Childhood cancer care in Ukraine was disrupted by the Russian invasion and subsequent destruction of civilian infrastructure. As a result, over 1,000 Ukrainian children with cancer were forced to leave, and pediatric oncology capacity was affected by occupation and ongoing conflict. We present a literature review and

modelling to provide evidence-based actionable recommendations to sustain and improve pediatric cancer care in Ukraine.

**Methods:** A literature review was conducted to describe the state of pre-war cancer care in Ukraine, the impact of the war on healthcare, and health system recovery planning. Fifty-four articles and reports were included. Using available data sources such as SAFER Ukraine patient registry, Ukrainian population-based cancer registry, World Health Organization (WHO), United Nations Children's Fund (UNICEF) data, we modeled the estimated number of new pediatric patients requiring cancer treatment in Ukraine in 2023-2025. A summary of recommendations to support sustainable childhood cancer services was produced.

**Results:** Prior to the war, Ukraine managed approximately 1,000 new pediatric cancer diagnoses per year. We project 630 new children (range 451-809) will require cancer care in Ukraine by the end of 2023. By the end of 2024 and 2025, this number is modeled to rise to 664 (range 502-827) and 697 (range 546-848) children, respectively. Informed by the literature review, key recommendations to promote sustainable pediatric oncology care include: Alignment of childhood cancer services with national recovery efforts; Centralization of resources and expertise following international guidelines; Securing access to essential medications; Strengthen national and international collaboration to provide coordinated support and efficient resource allocation.

**Conclusions:** The number of children with cancer in Ukraine is anticipated to steadily increase. Long-term sustainability of pediatric cancer care depends on access to healthcare facilities, safeguarding financing, and stable medication procurement. To achieve this, centralization of resources, referral pathways, and international collaboration are essential.

EP634/#80 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### QUALITY IMPROVEMENT PROJECT AND AUDIT OF BONE MARROW ASPIRATION AND BIOPSY IN PEDIATRIC HEMATOLOGY ONCOLOGY

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**Background and Aims:** Bone marrow aspiration is an invasive procedure that plays an important role in diagnosing and staging many malignancies. Good technical skill is crucial to obtain suitable samples for interpretation as inadequate bone marrow samples compromise patient care and may require expensive and painful repeat procedures. The aim is to provide a practical evaluation of the bone marrow aspirate quality and to identify the factors that compromise it.

**Methods:** This audit is a quality Improvement Project, Plan-Do-Study-Act (PDSA) type done in Princess Nora Oncology Centre at King Abdul-Aziz Medical City, it was in done out-patient and in-patient settings between June 2021 and April 2022. It is a retrospective study, data entering, analysis, and statistical comparison carried out by Excel. The source of information is the Best-Care hospital system. The Intervention was by standardized training for the operators covering the technique, slide preparation, definition of good quality samples, and troubleshooting it was conducted as a mandatory with 100% attendance achieved.

**Results:** The haemodiluted bone marrow (BM) improved in pre-data from 33% to 17%. The sample quality showed improvements with adequate samples increasing from 63% to 83%, suitable samples increasing from 10% to 15%, and inadequate samples decreasing from 24% to 2%. When comparing the data at diagnosis to screening, the diagnosis decreased from 41% to 25%, and screening decreased from 30% to 15%. Analyzing the data from Day 29 compared to the diagnostic data for the leukaemia group, Day 29 decreased from 42% to 11%, while diagnostic data decreased from 50% to 15%. In relation to complete blood count (CBC), the cytopenia group decreased from 44% to 31%, while the non-cytopenia group decreased from 29% to 8%

**Conclusions:** The study demonstrated significant improvements in bone marrow quality across various bone marrow indicators, patient diagnoses, and treatment backgrounds following the intervention in both inpatient and outpatient settings. These findings highlight the importance of compliance with the intervention measure to sustain the current performance levels. To ensure consistency and adhere to acceptable international practices, it is crucial to implement standardized training that is consistent and ongoing.

EP635/#1643 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### ESTABLISHING A REGIONAL DISSEMINATION AND IMPLEMENTATION SCIENCE SCHOLARS' PROGRAM TO IMPROVE CHILDHOOD CANCER CARE ACROSS GLOBAL HOPE SITES IN AFRICA

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**Background and Aims:** Approximately 100,000 children in Sub-Saharan Africa (SSA) develop cancer annually with fewer than 20% of those diagnosed surviving. Pediatric cancer healthcare providers in SSA must be trained in dissemination and implementation science (DIS) to devise innovative strategies to increase the integration of evidence-based pediatric cancer care interventions to improve treatment outcomes. We describe the establishment of a DIS scholars' program to train pediatric cancer multidisciplinary teams at the Global HOPE (GH) sites.

**Methods:** A survey completed by medical directors at GH sites identified priority areas for quality improvement (QI). Course documents including standard operating procedures for QI and clinical practice guideline (CPG) development were created by course faculty. The 6-month course format included the GH Learning Academy online course on QI in Health Care, biweekly virtual 1-hour group discussions and project work. Scholars were required to develop and implement a joint QI project. Participant feedback was obtained at the end of the course.

**Results:** Forty-one applicants from 8 GH sites in 6 countries representing 6 disciplines completed the program. Participants were assigned to four multisite working groups which included, pain, nutrition, Wilms tumor, and community outreach. Each working group completed one PDSA cycle of their project. The pain working group developed a CPG for pain assessment and management, the nutrition and Wilms tumor working groups are developing their respective CPGs and the outreach working group evaluated community childhood cancer education. Overall, the scholars found the experience worthwhile and identified areas for improvement.

**Conclusions:** Clinical practice guideline development requires in-depth evidence synthesis and multiple key stakeholder engagements. The scholars' program is the first step towards establishing a collaborative learning network for childhood cancer in SAA. Lessons learned will improve future implementation of the program and our understanding of the obstacles to evidence based practice in our setting.

EP636/#237 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### SELECTION AND AUTHORIZATION OF ESSENTIAL MEDICINES FOR CHILDHOOD CANCER: A SITUATIONAL ANALYSIS OF CAMEROON

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**Background and Aims:** The 2021 World Health Organization (WHO) Essential Medicines List for Children (EMLc) includes priority

medicines for childhood cancer (CC), especially in resource-limited settings. However, access to medicines for CC remains a significant challenge in sub-Saharan countries like Cameroon. This analysis aimed to measure the proportion of medicines in the WHO EMLc present in Cameroon's National essential medicines list (NEML) and with a marketing authorization (MA) in Cameroon.

**Methods:** Medicines for CC were extracted from the 2021 WHO EMLc and compared to Cameroon's 2017 NEML. An online search of the Directory of Pharmaceutical products and Marketing Authorizations of the Ministry of Health was performed on February 24<sup>th</sup> 2023 to identify medicines on the WHO EMLc with a MA. The proportion of medicines for CC on the EMLc in the NEML and those with a MA were summarized as a surrogate of medicine access.

**Results:** Sixty nine percent (29/42) of antineoplastics and supportive medicines for CC in the WHO EMLc were found in the Cameroon NEML. According to the category, all hormones and antihormones (4/4), 75% (21/28) of cytotoxics, 66.7% (2/3), 33.3% (2/6) of targeted therapy were listed on the NEML. Filgrastim the only immunomodulator on the EMLc was not present in the NEML and had no local MA. Twenty-two (52.4%) of the medicines in the EMLc had a local MA. Three (13.6%) out of the 22 medicines with a MA were not on the NEML. The MA for thirty-six percent (8/22) of the medicines for CC had expired.

**Conclusions:** Medicines for CC are a key determinant of outcomes and a more collective effort is required to ensure access. The inclusion of most priority medicines for CC in the NEML and maintenance of up-to-date MAs will ease importation, cost, and access for patients in need.

EP637/#1816 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### RAPID BASELINE ASSESSMENT OF THE CANCER HEALTH SYSTEM FOR CHILDHOOD CANCER CONTROL IN THE PHILIPPINES: RESULTS AND KEY FINDINGS

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**Background and Aims:** The Philippines, as part of the WHO Global Initiative for Childhood Cancer (WHO GICC) core commitments, underwent a detailed cancer health system capacity assessment and pediatric cancer action planning in 2021. We report the findings.

**Methods:** We performed mixed-methods research using the framework of the WHO Global Health Systems Framework for Childhood Cancer Control. Primary data sources were key informant interviews and surveys. Secondary data were gathered from institutional

research, hospital- and population-based cancer registries, publications, and case studies. Multi-stakeholder consultative meeting was held for validation and action planning.

**Results:** For Service Delivery, survival rates for the six index cancers were only 20-50%. Studies reported a long lag time to diagnosis, advanced disease at presentation, and high treatment abandonment rates. For manpower, there is an inequitable distribution of cancer specialists across the archipelago with the ratio of pediatric oncologists:patients of 1:13 in the National Capital Region vs. to 1:50-100 in the Visayas and Mindanao islands. For information systems, the country's regional population cancer registry reports incidence only; and few centers have hospital cancer registries. For governance, the national cancer control plans include pediatric programs but have yet to be enacted. For financing, the out-of-pocket medical costs are high as the national social health insurance has a 20 % support value only. For medical products and technologies, hospital pharmacies suffer frequent chemotherapy stockouts, despite the national cancer medicine access program. For family support and community engagement, poverty, poor educational attainment of parents, and inaccessibility to cancer hospitals adversely affect families' health-seeking behavior. A panel of 46 stakeholders vetted the findings and prioritized 2 action plans for each dimension.

**Conclusions:** The Philippines is in Step 2 of the Lancet Oncology Country Road Map for Childhood Cancer Care. Several action plans are now ongoing, namely, the creation of a patient navigation curriculum and population-based cancer survival.

EP638/#951 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### A GLANCE AT IMPLEMENTING THE PEDIATRIC ONCOLOGY FACILITY INTEGRATED LOCAL EVALUATION (PROFILE) TOOL AT A TERTIARY CARE HOSPITAL IN IRAQ

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**Background and Aims:** After four decades of wars and economic sanctions causing a collapse of Iraq's infrastructure in general and health service, we needed a comprehensive, systematic, and cost-effective evaluation of non-biological factors that affect survival in pediatric cancer. From August 2022 to May 2023, the Pediatric Hematology Oncology (PHO) team at Children Welfare Teaching Hospital (CWTH), Baghdad, Iraq, joined the ProFILE Beta 3 cohort. ProFILE helps identify opportunities and develop a quality improvement strategy to improve PHO care. We aim to describe our implementation experience and its outcomes.

**Methods:** The 9-month implementation included three phases: preparation, assessment, interpretation, and action. The site coordinator (SC) and physician lead (PL) recruited a 15-member multidisciplinary team. The SC and PL participated in weekly online mentoring sessions. The team completed data collection of 26 forms over seven weeks and conducted six quality improvement (QI) exercises to practice improvement methods. Three members of our team completed the Institute for Healthcare Improvement (IHI) Basic QI Certificate. We received a score-based and descriptive report during the interpretation and action phase. A 2-day prioritization workshop was conducted to get consensus regarding improvement opportunities we will include in our action plan.

**Results:** The form completion rate was 100%. A polar graph was generated with scores of <50% for all modules except for Surgery (51%) and Patients and Outcomes (58%) modules. The lowest was Service Capacity (23%). There were 219 opportunities in the impression sections. Opportunities prioritized the need for a pediatric cancer control plan, vital statistics, nurse retention, improving drug procurement, implementing basic infection control protocols, and strengthening the multidisciplinary care team.

**Conclusions:** ProFILE guided CWTH stakeholders and the PHO team to identify limitations in health service by appreciating the contributing non-biological factors. We are developing our 3-year action plan to work on the identified priorities.

EP639/#1203 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### BARRIERS AND FACILITATORS TO CARE FROM THE PERSPECTIVES OF ADOLESCENTS AND YOUNG ADULTS WITH CANCER IN LATIN AMERICA

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**Background and Aims:** Most adolescents and young adults (AYAs) with cancer live in low- and middle- income countries (LMIC). They face significant psychological and social challenges in addition to their medical needs. This study investigated AYAs with cancer perspective on their cancer experience in parts of Latin America (LA).

**Methods:** Focus group discussions (FGD) were conducted over Zoom in Spanish with AYAs who had completed cancer treatment. FGD were recorded and translated from Spanish to English. Key themes were identified using Atlas.ti. Focus groups are ongoing, and we are presenting initial results.

**Results:** Eleven participants representing three countries representing 3 countries (Peru, Dominican Republic, Guatemala) participated in one of four focus groups, providing 284 minutes of transcript data. The major themes fell into 6 domains: access (e.g. traveling long distance to the hospital, limited availability of psychological services), the AYA experience (e.g. dedicated AYA facilities, lack of autonomy), the illness experience (e.g. experiences during and after treatment including symptoms and follow up care), sources of support (e.g. family, religion), the diagnosis experience (e.g. the event of diagnosis disclosure, not being told about diagnosis), fertility issues and treatment (e.g. desiring more information about fertility and long-term consequences), and areas of education for doctors (e.g. better interpersonal communication, empathy for patients' emotional experiences).

**Conclusions:** This study elucidates factors that impact the care of AYAs with cancer in LA. The participants provided insights into what they believed were important areas of education for physicians and health care team members. These survivors of cancer are important voices to how cancer care for this population can be improved and expanded in these countries, including improvements for educational modules for providers. We are continuing to conduct focus groups with the aim of thematic saturation.

EP640/#723 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

## THE IMPACT OF COVID-19 ON ONCOLOGY CARE FOR ADOLESCENTS AND YOUNG ADULTS IN LATIN AMERICA

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**Background and Aims:** The majority of adolescents and young adults (AYAs) with cancer live in low- and middle- income countries (LMIC), which were disproportionately impacted by the COVID-19 pandemic due to limited healthcare infrastructure and slower roll out of vaccinations. From high-income countries (HIC), we know that AYAs receiving cancer treatment reported increased anxiety and psychological distress during the COVID-19 pandemic and there is data to suggest delays in diagnosis due to enforced lockdowns. However, little is known about the impact in LMIC. We report here on experiences of physicians and non-physician providers of AYAs with cancer in Latin America during the COVID-19 pandemic.

**Methods:** Physicians who treat AYAs with cancer in Latin America and non-physician stakeholders were interviewed about their experiences caring for this patient population. Participants were not asked specifically about the COVID-19 pandemic, but pandemic-related challenges organically arose in the interviews.

**Results:** Sixty-seven participants were interviewed: 37 physicians and 30 non-physician stakeholders (e.g. nurses, psychologists). Pandemic related challenges were discussed 43 times by 26 participants (40%). Both groups discussed challenges worsened by the COVID-19 pandemic, including: limited space in the hospital, restrictions on travel,



reduced funding and fundraising for AYA cancer services, limited staff, limited services, and changes to treatment. However, improvements in telemedicine and providing distance learning for inpatient AYAs were noted.

**Conclusions:** The COVID-19 pandemic substantially impacted the experience of AYAs receiving cancer care in Latin America. Gaps in access to care and many basic oncology services, which were already limited in some parts, were further exacerbated, similar to HIC. However, the positive innovations that came out of the COVID-19 pandemic can be carried forward to improve care for AYA patients with cancer. Further research is needed to contextualize the impacts of these changes on AYA patients' treatment outcomes and psychological and emotional wellbeing.

EP641/#666 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
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#### THE GAP IN PAEDIATRIC AND PAEDIATRIC ONCOLOGY PHARMACY TRAINING OPPORTUNITIES IN AFRICA

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**Background and Aims:** Paediatric training is essential for paediatric oncology (PO) training as paediatric pharmacokinetics and pharmacodynamics differ from adults. Qualified paediatric and PO pharmacists with specific training in PO are part of multidisciplinary teams in well-resourced settings. In line with the WHO Global Initiative for Childhood Cancer (GICC) initiatives, we explored training opportunities in paediatric and PO pharmacy in Africa. AIM: To explore numbers of certified African paediatric and PO pharmacists and available pharmacy training programmes.

**Methods:** Online searches were performed to identify paediatric and PO pharmacists and training programmes in Africa. Pharmacists involved in oncology pharmacy in Africa and regional pharmacy forums were contacted through public online platforms to assess paediatric pharmacy needs. The African Oncology Pharmacy Group was contacted to identify trained oncology pharmacists or those with an interest in paediatric oncology pharmacy. A WhatsApp poll explored views relating to pharmacy training in Africa.

**Results:** The African Oncology Pharmacy Group comprises 94 clinical pharmacists with adult oncology sub-specialisation. Of these, 17 (18%) expressed interest in PO pharmacy, but have no formal train-

ing in paediatric pharmacy. The African PO Pharmacy Group comprises 89 members; 38/49 respondents agreed that paediatric training should precede PO pharmacy training. Two pharmacists completed PO pharmacy fellowships in Ghana. Three non-certification courses in PO pharmacy were identified in Egypt, Morocco and Ghana, but there is no prerequisite to train in paediatric pharmacy. All participants agreed that Africa needed more paediatric and paediatric oncology pharmacists and would train further if the opportunity was available in Africa.

**Conclusions:** Demand for paediatric and PO pharmacy training exceeds available training opportunities in Africa. Pharmacists working in paediatric pharmacy do so without specific training. Many African pharmacists expressed interest in training in paediatric oncology pharmacy. Training and certification in both paediatric pharmacy and PO pharmacy should be relevant to the African setting.

EP642/#728 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### SYMPTOM TO DIAGNOSIS TIME INTERVAL FOR CHILDHOOD LEUKEMIA AND LYMPHOMA IN LOW-, MIDDLE- AND HIGH-INCOME COUNTRIES - A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background and Aims:** Barriers to timely diagnosis and treatment of childhood cancer are likely to be higher in low- and lower middle-income countries (L&LMICs) than upper middle (UMIC)/high-income countries (HICs). We aimed to compare the variation in symptom to diagnosis interval (SDI), defined as the length of time between symptom onset and diagnosis, by country income groups, for childhood leukemias/lymphomas.

**Methods:** A systematic search of literature for studies containing SDI data for childhood leukemia/lymphoma was conducted through Medline, PubMed, EMBASE and Scopus in Dec 2021. Studies with sample size <5, reviews, editorials and commentaries were excluded. We meta-analysed the median SDI, for each subtype of leukemia/lymphoma, with <sup>35</sup> studies and at least one study in each

country income group. Quality assessment was done with Aarhus checklist where appropriate.

**Results:** Of the 5364 studies screened, 71 studies (5 from LIC, 27 LMIC, 14 UMIC, 25 HICs) were included, representing 36 countries. The median SDI overall was longer for lymphomas compared to leukemias; longest being 18.47 weeks (95%CI 12.01-28.39) for Hodgkin lymphoma and shortest being 3.96 weeks (95%CI 1.84-8.52) for lymphoid leukemia. The median SDI in weeks for lymphoid leukemias (HIC 1.08, UMIC 3.61, L&LMIC 7.36), acute myeloid leukemia (HIC 1.45, UMIC 4.39, L&LMIC 6.36), Hodgkin's disease (HIC 9.95, UMIC 20.96, L&LMIC 32.97) and non-Hodgkin lymphoma (HIC 3.84, UMIC 7.24, L&LMIC 12.49), was shortest in HIC and longest in L&LMIC, and these all were statistically significant ( $p < 0.001$ ). Majority of the studies did not fulfil the Aarhus checklist criteria, but did provide clear definitions of the time interval to diagnosis.

**Conclusions:** The median SDI of leukemias and lymphomas is significantly longer in L&LMICs compared to HICs. This may partly explain more advanced disease at presentation and poorer outcomes in L&LMICs. We further plan to investigate factors leading to longer SDI.

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#### CREATION OF "GOLDEN CODE" A STRATEGY TO AVOID CHILDHOOD CANCER DIAGNOSIS DELAY IN A THIRD LEVEL HOSPITAL IN MEXICO CITY

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**Background and Aims:** Cancer delay still remains an important public health concern in middle income countries which impacts in overall survival. Centro Medico Nacional 20 de noviembre is the main reference hospital for governmental workers and we have previously published our main problems for cancer diagnosis delay (lack of cancer suspicion in first contact doctors and parents and late patient reception due to lack of communication between hospitals). We created an strategy for early referral to our institute a called "Golden Code".

**Methods:** Main delay factors were: lack of suspicion in parents and doctors and late referral to our hospital. We created 3 strategies: Parents (teaching cancer sign alert Doctors (cancer detection training course on line and creation of Golden Code which means "children with cancer suspicion" are sent immediately to our hospital. We trained health and administrative staff to avoid delay in oncologist assessment. There is an acceptance traffic light: green (children accepted in less than 7 days) yellow (between 7 and 14 days) red (more than 15 days).

**Results:** We received 64 new cancer cases in 2017, 73 in 2018, 93 in 2019, 55 in 2020, 73 in 2021 and 75 in 2022. Since the implementation

of the Golden code strategy for early reference around 80 percentage of patients (median) were accepted in our hospital in less than 7 days (green light), less than 10% of the patients were accepted in more than 14 days. The diagnosis was made in our hospital in 13.5 days (median).

**Conclusions:** The creation of the Golden code for cancer early reference at a middle-low income country has been a success. 80% of children and adolescents referred to our hospital are seen in less than 7 days. There is a significant trend for decreasing delays to diagnosis and treatment. We are still working to make it better

EP644/#1009 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### IDENTIFYING LYNCH SYNDROME IN PEDIATRIC ONCOLOGY PATIENTS WHO UNDERGO GERMLINE SEQUENCING

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**Background and Aims:** Lynch syndrome (LS), caused by heterozygous pathogenic variants in DNA mismatch repair genes *MLH1*, *MSH2*, *MSH6* and *PMS2*, is associated with a high risk of colorectal, endometrial, urothelial and other cancers. Until recently, LS has been considered an adult-onset cancer predisposition syndrome. With increasing availability of genomic sequencing in the context of childhood cancer, LS is being detected at earlier ages, but causality is still in question. Since 2020 all pediatric cancer patients in Quebec are offered paired germline and tumour sequencing as part of the *Signature* research initiative, providing a unique opportunity to determine prevalence of LS and its relevance in unbiased children and adolescents with cancer.

**Methods:** Patients 18 years of age or less with a range of hematologic and solid tumours (excluding brain tumours) underwent successful germline analysis including whole exome sequencing and a 424-cancer gene panel including mismatch repair genes. Patient-level phenotypic data (personal and cancer history, and family history) were abstracted. Germline variants were interpreted by ACMG/CCMG-certified molecular geneticists.

**Results:** Of 599 patients, three (0.5%) had heterozygous pathogenic germline variants in *PMS2*, *MSH6*, and *MLH1*. These previously healthy children were diagnosed with B-cell acute lymphoblastic leukemia (age 7 years), acute myeloid leukemia (5 years), and multifocal unilateral Wilms tumour (5 years), respectively. LS was not known in any family members, however two of three had relatives with gastrointestinal, genitourinary and other cancers. Loss of heterozygosity was detected

in leukemic cells in one patient; no somatic second hit was identified in the other patients.

**Conclusions:** This body of data adds to the very recent publication by Kratz *et al.* stating a 0.5% prevalence of LS in children and adolescents with non-brain tumour oncologic diagnoses. While these findings may be relevant in families, for now they appear to be incidental as evidence of causality is lacking.

EP645/#215 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### TREATMENT OUTCOMES FOR COMMON AND CURABLE CHILDHOOD CANCERS IN SUB-SAHARAN AFRICA - A REPORT FROM CANCARE AFRICA

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**Background and Aims:** The WHO Global Initiative for Childhood Cancer aims to increase survival to at least 60% for all children with cancer globally, with an initial focus on six common curable cancer types. Outcome and survival data from Sub-Saharan Africa is scarce. The objective of this study was to describe end-of-treatment outcomes of childhood cancer in sub-Saharan Africa.

**Methods:** We conducted a multi-centre, prospective, observational cohort study in five hospitals in Malawi, Ethiopia, Ghana and Cameroon. Patients younger than 16 years and newly diagnosed with acute lymphoblastic leukaemia (ALL), Hodgkin disease, Wilms tumour, retinoblastoma and Burkitt lymphoma were included. Outcome at the end of treatment was categorised as: alive without evidence of disease, death before treatment; treatment abandonment; death during treatment, or persistent disease. Details around death during treatment were documented to distinguish between a treatment or disease related cause.

**Results:** Between January 1<sup>st</sup> and September 1<sup>st</sup> 2022 we included 285 patients after the exclusion of seven patients with a misdiagnosis. The median age was 5.8, range 0.4–15.6 years, 60% male. The most common diagnosis was Burkitt lymphoma (84/285, 29%), followed by ALL (74/285, 26%), Wilms tumour (62/285, 22%), retinoblastoma (45/285, 16%) and Hodgkin disease (20/285, 7%). Of these 285 patients, 44% (126/285) completed treatment without evidence of disease, 2% (6/285) died before treatment, 19% (55/285) abandoned treatment, 17% (49/285) died during treatment, 5% (15/285) had persistent dis-

ease at the end of treatment and 12% (34/285) are still on treatment. At least eighty-two percent (40/49) of the deaths during treatment were considered treatment related.

**Conclusions:** Treatment abandonment and treatment-related deaths were important causes of failure in Sub-Saharan Africa. Interventions to prevent treatment abandonment and to improve supportive care need to be given priority to improve survival chances and achieve the 60% initial target of the WHO GICC.

EP646/#125 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### CHALLENGES AND OBSTACLES FOR YOUNG PHYSICIANS TO INTEGRATE RESEARCH INTO CANCER CLINICAL CARE -LOW AND MIDDLE INCOME SETTING

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**Background and Aims:** There are always multiple obstacles and challenges, pediatric oncologists and specially young physicians face in their career development. It has been attributed to many factors. Clinical care burden is not only the main indicator. Personal, economic and health system variants are the main attributing factors to the deficient research contribution in low and middle income countries. Disparities among pediatric cancer care institutions are also important to be targeted to improve the research opportunities for pediatric oncologists.

**Methods:** Checklists-Surveys were distributed among 120 clinical fellows and doctors including > Socioeconomic status, distance of accommodation, number of attended clinics per week, number of patients examined, number of inpatient shifts, outreach activities, number of publications per year, number of working hours per week and analysis was done regarding the impact of these factors on research contribution and research yield. The study was done for pediatric oncologists after 2 years workin as residents or fellows at the National cancer instiute and the children s cancer hospital Egypt 57357.

**Results:** The research contribution in the first 3 years of clinical fellowship was 20%, the median number of working hours per week was 45 hours. The socioeconomic status was analysed through SES scoring system, reflecting the score 0-4, Physicians with scores 3-4 had less contribution into research. The average median number of patients examined was not significantly affecting the number of clinical research -publications, lab work or outreach activities. However the number of workng hours, lack of funding, non orientation with research projects national and international adopted programs were encountered in 67% of the physicians.

**Conclusions:** Integration of research into clinical care is recommended to improve childhood cancer care. Solutions must be adopted including funded projects as well as scheduled orientation to physicians in low and middle income settings.

EP647/#1791 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
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**SITE-LEVEL CHALLENGES TO RECRUITMENT OF CHILDREN FROM FAMILIES WITH NON ENGLISH LANGUAGE PREFERENCE: A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP'S DIVERSITY AND HEALTH DISPARITIES COMMITTEE**

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**Background and Aims:** To ensure equitable clinical trial representation and improve generalizability of study findings, increasing diversity in recruitment within Children's Oncology Group (COG) trials is a high-priority. The resources available to COG institutions recruiting persons with non-English language preference (NELP) are unknown.

**Methods:** An electronic 20-item survey was distributed through RED-Cap® in October 2022 to all COG institutional Principal Investigators (PI) [N=266]. Responses were collected over a 6-week period. Our objective was to assess current institutional practices and available resources for recruiting and enrolling NELP consenting parents or patients onto COG trials, including translation of consents and interpretation services.

**Results:** Response rate was 57% (N=151); 70% (n=106) were from academic medical centers, and 73% (n=110) from mid-to-large size institutions (>50 new cancer cases/year). Seventy-eight (52%) reported that ≥10% of providers were bilingual/multilingual. However, only 35 (23%) endorsed having certified multilingual providers. The

most common NELP language was Spanish (78%), followed by Arabic (28%), and Chinese (18%). Consent short-forms were utilized at 62% (n=94) of sites. Among these, 43% (n=40) had them available in 10+ languages. Compared with larger sites (>50 cases/year), smaller centers used short-forms more frequently (47% vs. 25%, p=0.03) whereas larger centers required translation more often (56% vs. 41%, p=0.05). Forty-four percent (n=67) reported insufficient funding to support translation costs; 15% (n=22) had access to no-cost translation services. Level of difficulty recruiting NELP persons was reported as "somewhat difficult" or "very difficult" at 48% (n=72) of centers. The most commonly endorsed contributors were time constraints (37%), lack of resources (38%), and lack of in-person interpreters (40%).

**Conclusions:** COG institutions face multiple resource-specific challenges that may impede recruitment and consent of NELP participants onto clinical trials. These findings indicate an urgent need to identify strategies that reduce barriers recruiting NELP participants onto COG clinical trials to ensure equitable clinical trial representation.

EP648/#1210 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

**DEVELOPMENT OF CLINICAL RESEARCH CAPACITY AS A MEANS TO ACHIEVE WHO-GICC GOALS IN LMIC - A PAKISTAN SOCIETY OF PEDIATRIC ONCOLOGY (PSPO) STRATEGY**

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**Background and Aims:** Clinical trial methodology strongly impacted improvement in outcomes for childhood cancer in developed countries. Research capacity development is critical for similar improvements in LMIC. PSPO is utilizing this strategy to drive its mission towards achievements of the WHO-GICC goals.

**Methods:** Starting in 2021, PSPO developed physical infrastructure, established a workforce, and implemented national standard-of-care (SOC) protocols, with centralized data collection. Details include: Clinical Trials Unit: Physical workspace equipped with reliable

internet and power, laptops, server, and licensed software (REDCap<sup>R</sup>) for data collection and management. **Work Force:** Clinical Trials Coordinator/biostatistician (CTC), Data Quality Officer (DQO), and Administrative Officer (AO) were recruited centrally. CTC enables multidisciplinary teams in developing protocols, CRFs, and provides statistical analytics. DQO trains data entry officers at participating institutions, provides technical help, and conducts virtual/on-site audits. AO ensures financial and regulatory compliance. **Protocol Development:** Multidisciplinary professionals evaluated local practices, and international care-standards to develop SOC guidelines for the six, target cancers. Treatment was adapted to local capacity, including strategies to mitigate inter-institutional capacity variations. National consensus was reached through sharing and resolving differences. PSPO BoD approved all protocols. **Regulatory Approval:** Pakistan's National Bioethics Committee (NBC) and individual IRBs approve each protocol. **Protocol Implementation:** The first protocol was launched in July 2021, with subsequent phased deployment through September 2022. Institutions require IRB approval to participate in protocols.

**Results:** NBC approved the ALL protocol in April 2021 and all others by September 2022. Multiple institutions received IRB approvals. By 15<sup>th</sup> March 2023, 964 patients (ALL 711; cHL 195; RB 55; WT 2; LGG 1; NHL 0) have been enrolled. Data-management training for NHL is underway. Scheduled interim analysis of ALL data is identifying areas of data-driven improvement at individual institutions.

**Conclusions:** Research capacity building with deployment of national treatment protocols in LMIC is a feasible method for WHO-GICC goal achievement.

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#### MAPPING THE REFERRAL PATH – HURDLES IN CHILDHOOD CANCER DIAGNOSIS IN LOW MIDDLE INCOME COUNTRY

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**Background and Aims:** India has a substantial burden of delayed diagnosis of childhood malignancy. The health care system is poorly networked for timely referral of childhood cancers.

**Methods:** A cross-sectional observational study meticulously designed to delineate the referral path to a tertiary care Pediatric-Hematology-Oncology unit is presented. Children (<18-years) with cancers registered in the division (Nov2019-July2022) who consented to participate were enrolled. Patients with relapsed disease and partially treated prior to referral were excluded. A pretested case-record form including, a) Baseline socio-demographic details, b) the referral path to reach the hospital c) the family/oncologist perspective, was administered.

**Results:** A total of 100 children with cancer were enrolled. The study cohort included patients with hemato-lymphoid (73%) and solid

(27%) malignancies. Median age was 7-years (range:1-18) with M:F of 1.5:1. Fifty-eight percent were from rural-background, 45% being BPL and 69% remained undiagnosed at the time of referral. Median distance travelled from hometown to our centre was 160km (range:3-650). Median of 3 (range:1-6) medical-consultations was sought with an average expenditure of Rs 23,300 prior to referral. Initial consultation was by non-pediatric speciality (54%) including GP (35%) and alternate-system-medicine (7%). Mean total delay from symptom onset to diagnosis was 53.4 days (range:1-460) with healthcare seeking delay of 14.3 days (range:0-130) and health system delay (HSD) of 39.2 days (range:1-367). The factors influencing delay included rural-background ( $p=0.04$ ), economic-status ( $p=0.01$ ) and number of medical-consults ( $p=0.01$ ). Factors including gender, speciality first consulted and distance travelled did not influence. Family and treating oncologist felt a delay in referral/diagnosis in 47% and 41% cases, respectively. The felt needs of families included, financial constraints (54%), need for near to home cancer centre (53%) and support for local stay nearby treating centre (43%).

**Conclusions:** Without massive investments in improving infrastructure, we still can improve the efficiency of the existing system by strengthening the referral pathway and improving awareness among primary care physicians.

EP650/#1433 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### INCIDENCE, MORTALITY, AND CUMULATIVE RISK OF CANCER IN ADOLESCENTS AND YOUNG ADULTS (AYAS) IN SWITZERLAND

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**Background and Aims:** It has been acknowledged that cancers in adolescents and young adults (AYA) aged 15-39 years require specialized approaches to cancer research. Cancers in AYAs have distinct biological features compared to cancers diagnosed in children and older adults. Cancer is the leading cause of death in this age group in high-income countries. However, there is little research in Switzerland on this topic. This study aims to investigate trends in incidence and mortality rates and cumulative risk of cancer in AYAs in Switzerland.

**Methods:** Data on primary adolescent cancers (15-19 years) were obtained from the Childhood Cancer Registry (ChCR) and on young adult cancers (20-39 years) from the National Agency for Cancer Registration (NACR). Swiss population and mortality data were obtained from the Swiss Federal Statistical Office (FSO). We calculated age-standardized rates using the European standard population (1976), adjusting for regional differences in cancer registration. We will use NIH's Joinpoint regression software to investigate cancer incidence and mortality trends and estimate average annual percent changes (AAPCs). We will estimate cumulative risk for cancer up to the ages of 20, 30, and 39 years.

**Results:** A total of 73,932 new cancer cases occurred among AYAs in Switzerland between 1980-2019. Out of those, 41% were carcinomas, most often of the breast, thyroid, colon, skin, and genital sites (excl. ovary and testis). Testis tumors, melanomas, lymphomas, CNS tumors, leukemias, and sarcomas were also among the most frequent cancers. Preliminary analyses showed higher incidence and a stronger increase in incidence in females than in males during the study period (79.39 vs. 66.49 per 100,000 person-years; 1980-1989: 62.44 vs. 57.41, 2010-2019: 83.73 vs. 66.87).

**Conclusions:** This is the first nationwide Swiss study that focuses exclusively on cancer in AYAs, integrating all accessible cancer registry data and adjusting for regional differences in cancer registration.

EP651/#255 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### INCIDENCE OF SEPTIC SHOCK IN PEDIATRIC CANCER PATIENTS WITH FEBRILE NEUTROPENIA AFTER THE IMPLEMENTATION OF THE "GOLDEN HOUR" AT THE SALVATIERRA HOSPITAL

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**Background and Aims:** Febrile neutropenia is a complication of cancer patients receiving chemotherapy. The appearance of neutropenia associated with episodes of fever in cancer patients receiving chemotherapy is considered an emergency, it is vital that antibiotic therapy is started in the first hour after the onset of symptoms (golden hour), since it has been shown that the delay in the application of the antibiotic increases the risk of developing septic shock up to 60% and increases mortality by 7.6%.

**Methods:** Data were collected from all hospitalized patients and new admissions who presented febrile neutropenia to whom the "GOLDEN HOUR" was applied from November 2021 to January 2023, subsequently those who developed septic shock were evaluated.

**Results:** In the period from November 2021 to January 2023, a total of 35 patients presented an episode of febrile neutropenia in which the golden hour was applied, of these patients 2 developed septic shock which corresponds to 5.7%.

**Conclusions:** The use of the GOLDEN HOUR significantly reduces the risk of septic shock, so it is important to publicize and apply this type of action to reduce morbidity and mortality in pediatric oncology patients.

EP652/#1745 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### UNDERSTANDING REASONS FOR TREATMENT REFUSAL AND ABANDONMENT AMONG PAEDIATRIC CANCER PATIENTS IN CENTRAL INDIA

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**Background and Aims:** Treatment refusal and abandonment is the major cause of therapy failure in pediatric oncology patients. A variety of socio-economic and treatment-related factors underlies this problem. Interventions aimed at addressing these issues can bring tremendous improvements in cancer survival. Unfortunately, the burden of treatment refusal and abandonment is poorly defined in developing nations and in central India in particular. In this pilot study we analyze the factors responsible for treatment abandonment and refusal in a Pediatric Oncology centre in central India.

**Methods:** In this single centre retrospective observational pilot study, we interviewed parents of 28 children with cancer registered from April 2018 till October 2022 in Pediatric Hematology Oncology division, Department of Pediatrics, AIIMS Bhopal who refused or abandoned treatment. The questionnaire had demographic, socio-economic, personal and disease related factors affecting their decision.

**Results:** Male: female ratio was 2:3. The mean age was 7.4 years (SD 4.6). Two third of patients were from rural residence and 85% belonged to upper middle class. Financial reason alone was the most common cause (40%: mainly medical cost) followed by personal reason alone (14%). Four (14%) patients went for alternative medicine while social factors were seen in 4 cases. More than one reason was observed in 40% cases. Most of them died due to disease progression (75%) while 14% are alive with disease. Among the 3 who are alive in remission one patient is stage IV S Neuroblastoma and other two were B-ALL treated elsewhere few months after diagnosis.

**Conclusions:** Knowledge of burden along with various causes of abandonment and refusal of treatment can help in designing appropriate policies to improve survival of paediatric oncology patients. We have recently strengthened socioeconomic support through various

Governmental and non-Governmental resources effect of which to be seen.

EP653/#732 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

### CLINICAL DOCUMENTATION OF CONSTIPATION IS ASSOCIATED WITH DELAYED CLEARANCE OF HIGH-DOSE METHOTREXATE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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**Background and Aims:** High dose methotrexate (HD-MTX) is an essential component of acute lymphoblastic leukemia (ALL) therapy. While MTX is primarily renally eliminated, a small proportion is eliminated fecally. HD-MTX may overwhelm renal elimination in some patients, necessitating the increased elimination by non-renal routes. Delays in clearance can result in clinically significant toxicities including neurotoxicity, mucositis, neutropenia, and thrombocytopenia. We hypothesize that constipation possibly due to concomitant medications may alter gut motility, blood flow, and MTX elimination.

**Methods:** This retrospective cohort study identified pediatric patients with ALL who received HD-MTX (5 g/m<sup>2</sup>) between 2010 and 2020. We extracted demographic, clinical, and treatment information from electronic health records (EHR). A diagnosis of constipation was based on clinical documentation noted in the progress note or imaging within 48 hours of the start of each MTX infusion. Laxative medications received within the timeframe were also collected. Clearance was defined as the hours from infusion start to protocol-defined clearance, with delayed clearance as a serum MTX >0.4 μM at hour 48. Adjusted odds ratios (adjORs) for associations between clinical variables and methotrexate clearance were estimated using multi-level logistic regression, accounting for repeated MTX infusions within individuals.

**Results:** Patients (n=499; 1,780 infusions) were mostly male (58.9%), Latino (60.1%), and diagnosed at a median age of 9 years. Constipation was observed in 201 cycles (11.3%); however, only 37.3% of cycles with documented constipation received 1 laxative (n= 75). Documented constipation was significantly associated with delayed clearance (adjOR =1.45; 95% CI: 1.08-1.94; p=0.013), independent of age, sex, race/ethnicity, creatinine elevation, and MTX dose. Use of laxatives did not significantly affect this finding.

**Conclusions:** Patients with documented constipation in EHR had an increased likelihood of delayed HD-MTX clearance. Aggressive

constipation management may promote MTX clearance and thwart subsequent MTX-related toxicity.

EP654/#1424 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

### "ONE SIZE DOES NOT FIT ALL" - LESSONS IN ADAPTATION OF MULTI-COUNTRY RESEARCH: ASSESSING DOCTORS' ATTITUDES ON PALLIATIVE TREATMENT (ADAPT) STUDY IN ASIA PACIFIC (AP)

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**Background and Aims:** Approximately 50% of the world's children reside in AP, a large, socio-culturally diverse region with significant areas of scarce access to palliative care (PC). Building on the previously published ADAPT study instrument evaluating physicians' perspectives towards PC for children with cancer, we aimed to conduct this study across AP and examine adaptation needs required.

**Methods:** Champions from across AP were invited to modify the published mixed methods survey, considering contextual factors impacting PC delivery, as well as conceptual equivalence and relevance. Team meetings were conducted with collaborators from each of the 21 included countries to 1) understand the local provision of PC; 2) review eligibility criteria and develop an inclusive participant list; and

3) review study logistics including translation needs, ethics committee procedures, survey distribution, and engagement strategies.

**Results:** Minor modifications were made to the survey instrument, reflecting feedback considering locoregional norms around PC provision. Iterative meetings were conducted with each country team pre-launch. Although the study was exempt by the sponsoring institution's ethics committee, 13 countries required local ethics approval. Systems-driven challenges included generation of collaboration agreements specifying governance of data sharing and ownership, and in one country, creation of a legal agreement with the local study site. Two countries required IRB fees. Five countries requested translation of the survey into their native language with an additional country requesting the option for open ended responses in the native language. Initial success factors included committed, locally respected champions, existing communication channels, and alignment with national priorities.

**Conclusions:** Despite a well-established study design previously implemented in two global regions, unique challenges and success factors have been noted in the process of conducting this study across AP. Local partnership and context-specific solutions have been critical to success, establishing the foundation for data driven interventions that will be tailored to address loco-regional education and advocacy needs.

EP655/#983 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### THE EVALUATION OF PEDIATRIC HEMATOLOGY/ONCOLOGY MEDICAL FELLOWSHIP TRAINING PROGRAMS IN AFRICA: A ST. JUDE GLOBAL AND SIOP AFRICA COLLABORATION

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**Background and Aims:** A skilled workforce is the cornerstone of pediatric hematology/oncology and quality training programs are necessary to increase the global capacity to provide care. To enhance pediatric hematology/oncology training capacity for Africa, the Education Program Assessment Tool (EPAT) was used to assess existing fellowship programs.

**Methods:** EPAT is a systematically designed tool to assess pediatric hematology/oncology medical fellowships consisting of 196 questions, organized into 10 domains covering aspects of patient care,

infrastructure, and educational organization. EPAT was electronically distributed via REDCap to 22 fellowship directors at African and non-African programs that have historically trained pediatric hematologists/oncologists from African countries.

**Results:** EPAT was completed by 21 training programs in Africa (19/21; 9 countries), India (2/21), and Brazil (1/21). The numbers of fellows trained ranged from 1-4 fellows/year. In most programs, a sufficient volume of patients was cared for in the inpatient and outpatient settings, providing learning opportunities for trainees. Trainees were exposed to a wide array of diseases and have opportunities for diverse classroom-based learning. Nonetheless, in some programs the ratio of faculty to trainees may not always allow for sufficient oversight of trainees. Educational Infrastructure, the domain evaluating the resources to provide educational oversight, had the highest aggregate mean score (90%) across the cohort. Educational Culture, evaluating the existing support for trainees, and Graduate Impact, evaluating the effect of the program on availability of care and academics, had the lowest mean scores, 63% and 59%, respectively. Although participation in research is a requirement for most programs, infrastructure to support research projects are frequently lacking.

**Conclusions:** EPAT identified strengths and areas for improvement among African training programs using a structured, quantitative approach. As a next step, a regional co-design workshop with representatives from the institutions completing EPAT will be held in-person to brainstorm regional opportunities for synergy and collaboration.

EP656/#1165 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### ANALYSIS OF PATIENTS TREATMENT FOLLOW-UP IN A BRAZILIAN PEDIATRIC ONCOLOGY CENTER DURING THE PROFILE IMPLEMENTATION

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**Background and Aims:** The St. Jude Pediatric Oncology Facility Integrated Local Evaluation (PrOFILe) is a tool used to identify opportunities for health service delivery improvement. Its current active patient definition includes new patients with curative intent who started treatment during the calendar year, patients who started treatment in previous years and are still receiving disease directed therapy, patients with relapsed disease receiving cancer treatment for the



relapse, and patients under follow-up for end-of-life palliative care during any time of the evaluated year. Non-active patients are patients out of treatment in follow-up. In this analysis, patients receiving metro-nomic chemotherapy were included in the active patients group. The objective was to analyze outpatient visits over a period of 30 days, clas-sifying patients into active and non-active and to evaluate the rate of absenteeism in the service.

**Methods:** All appointments made in November 2,022 were classified according to the ProFILE definition.

**Results:** A total of 395 appointments were scheduled in the evaluated month, with an absenteeism rate of 17.7% (70 missed appointments). All appointments refer to 233 patients, 60% active patients, 35.6% non-active patients and 10 patients without classification due to lack of data (4.3%). The absenteeism rate among active patients was 13.8% and 29.6% among non-active patients. The average number of visits per month among non-active patients was 1.05 visits and the average among active patients was 2.12 visits (minimum of 1 and maximum of 6 visits per patient).

**Conclusions:** It was observed that most of the visits in the month referred to active patients in the year 2,022, and many patients were seen more than once in that month. In addition, it was observed that the abstention rate was higher among non-active patients. The results helps strategizing for better care of patients undergoing treatment and in the elaboration of follow-up strategies for non-active patients.

EP657/#1398 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### NATIONAL BREAST AND THYROID SCREENING AFTER A TREATMENT RECEIVED AGAINST A CANCER DURING CHILDHOOD A DENACAPST FRENCH COHORT

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**Background and Aims:** Radiotherapy associated with chemotherapy has significantly improve survival rates for childhood cancer, with current cure rates above 80%. However, 40-70% of former patients will have a disease- or treatment-related health problem. Cancer-related mortality from a secondary cancer is tenfold increased compared to the general population within 30 years. Existing recommendations for screening of secondary cancers like breast and thyroid cancers in these risk populations are difficult to realize without a targeted national program. The objective of this study is to evaluate the feasibility and adherence to screening recommendations in patients at risk for breast and thyroid cancer.

**Methods:** The DeNaCaPST study is a prospective, observational, multi-center study combining two cohorts of childhood cancer survivors: FCCSS (French Childhood Cancer Survivor Study) and LEA (Leukemia in Children and Adolescents). Additional patients could also be included by physicians during long term follow up consultations. Screening in this program began 8 years after radiation therapy for breast cancer and at least at the age of 25 years and 5 years after radiotherapy and at least at the age of 18 years for thyroid cancer.

**Results:** 289 patients participated to the study with a response rate to self-administered questionnaires of 71%. 24 people were screened for breast cancer, 147 for thyroid cancer and 89 for both. The participation of at least one of the screening was 90%. Most of the participants rather agreed to say screening didn't use lot of time (81,1%), lot of moving (74,6%) neither too much cost (85,4%). Three-quarters feels reassured with a regular cancer screening (78,6%).

**Conclusions:** This study showed screening of breast and thyroid cancers is globally well accepted with admissible inconveniences. In these risk populations, prevention of a secondary cancer is one of the priorities and should be more developed in order to treated the most earlier.

EP658/#1583 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### IMPROVING ACCESS TO HIGH-POTENTIAL PEDIATRIC PRECISION THERAPIES: A CHILD-TAILORED ASSESSMENT FRAMEWORK TO DETERMINE VALUE FOR FUNDING DECISIONS

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**Background and Aims:** Children and adolescents with refractory, relapsed and metastatic disease have the most to gain from promising oncologic precision therapies. However, these therapies are highly expensive. Furthermore, current funding evaluation methods do not fully capture childhood biological and psychosocial distinctiveness. The result is few funded precision therapies having pediatric indications. To inform funding decision-making, we developed a multi-criteria decision analysis (MCDA)-based value assessment framework (VAF) that is child-tailored.

**Methods:** We held four deliberative engagements with general public (n=45) to solicit views on criteria important to evaluating pediatric therapies. We constructed an additive MCDA model through a modified-Delphi process with key stakeholders (n=24), comprising two surveys and deliberations on feasibility, importance, and consistency. Criteria were weighted (1-20) by ranked importance. We developed guidelines for scoring nine precision drugs against standard-of-care in each criterion domain. Aggregate scores out of 300 (summed criteria weight\*score per drug) were mapped to funding recommendations. Two external clinicians and one study-team pediatric oncologist tested the VAF for usability and apprehensiveness in two rounds.

**Results:** Public engagement yielded 16 criteria; the 14 highest-ranked proceeded to the modified-Delphi stage. Synthesizing stakeholder and tester inputs culminated in 10 final criteria: effectiveness, child-specific health-related quality-of-life, disease severity, unmet need, therapeutic safety, equity, family impacts, life-course health, rarity, and fair-share-of-life. Aggregate scores ranged from 88 (gemtuzumab ozogamicin, mean=123) to 225 (blinatumomab, mean=217). The smallest difference between testers was 15 (blinatumomab) and the largest 105 (crizotinib). Four drugs were scored as "high priority" or "priority" for funding by all testers (dinutuximab, larotrectinib, blinatumomab, dabrafenib). Among testers, only one drug was scored as "low priority" (gemtuzumab ozogamicin).

**Conclusions:** A child-tailored MCDA-based VAF may confer transparency and cohesion in guiding funding decisions for pediatric therapies, including precision drugs. Validation with pediatric oncologists and decision-makers is underway. Acknowledgements: Funding provided by Terry Fox Research Institute and Canadian Institutes for Health Research.

EP659/#1487 | **Poster Topic: AS05 SIOP Scientific Program/AS05.r Epidemiology, Policy and Advocacy**

**ACCESS TO PROMISING NEW PEDIATRIC ONCOLOGY DRUGS: COMPARING INTERNATIONAL APPROACHES TO DRUG REGULATION AND REIMBURSEMENT**

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**Background and Aims:** Existing policies on drug regulation, value assessment, and funding mechanisms in most health systems rarely account for the unique needs of children, resulting in significant access constraints. The relevance of innovative, precision oncology therapeutics is rapidly expanding, as are rising costs of the same, exacerbating pre-existing challenges. Our study sought to understand the policy and regulatory challenges related to the evaluation and reimbursement of innovative cancer therapies for children.

**Methods:** Using qualitative methods including key informant interviews with clinical and policy experts, and analysis of policy documents, we identify, describe, and compare the policy, legislative and regulatory environments across Canada, the UK, the EU, and Australia. Attending to the assessment of therapeutic safety and efficacy, market authorization processes, and funding allocations for children and focusing on rare disease and pediatric oncology, we demonstrate where and how policy mechanisms impact access.

**Results:** Health systems globally are grappling with challenges presented by pediatric precision oncology therapies, namely uncertain benefit, and high costs. Policies and regulations that address the unique socio-biological, economic, and ethical considerations inherent in child health are lacking but many efforts are underway to innovate clinical research and evidence appraisal methods. We describe distinct approaches to shared challenges and identify how policy contexts (governance structures, processes of value assessment, stakeholder engagement) impact access. We highlight differences in policy priorities and attention, in the included sets of values and stakeholder voices, and in the value assessments and regulatory pathways created to meet the needs of novel pediatric therapies.

**Conclusions:** This work illuminates a shared set of challenges ripe for collaborative efforts at policy reform. We aim to provide policy-makers, healthcare providers, and childhood cancer advocates with evidence-informed recommendations for the design and implementation of policies to govern equitable and sustainable access to innovative therapies for children with cancer in a range of health systems.

EP660/#1220 | **Poster Topic: AS05 SIOP Scientific Program/AS05.r Epidemiology, Policy and Advocacy**

**CLINICAL PROFILE AND OUTCOME OF SIX INDEX CANCERS IN THE WHO GLOBAL INITIATIVE FOR CHILDHOOD CANCER AT A CANCER INSTITUTE IN DAVAO CITY, PHILIPPINES**

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**Background and Aims:** In September 2018, the World Health Organization (WHO) launched the Global Initiative for Childhood Cancer (GICC) to improve outcomes of children with cancer around the world. It aims to achieve at least 60% survival globally by 2030. The Philippines was designated focus country for the initiative in the WHO Western Pacific Region in September 2019.

**Methods:** This retrospective study included pediatric patients aged 0-18 years diagnosed with acute lymphoblastic leukemia (ALL), low-grade glioma, Burkitt lymphoma, Hodgkin lymphoma, retinoblastoma and Wilms tumor as index cancers at Southern Philippines Medical Center Children's Cancer Institute from January 1, 2018 to December 31, 2022. The overall survival rates were estimated using the Kaplan-Meier method.

**Results:** A total of 424 patients were included in the study. Majority were male ( $n=274$ , 58%) with mean age of 7 years old. Among the index cancers ALL ( $n = 268$ , 63%) was the most commonly diagnosed, followed by retinoblastoma ( $n = 80$ , 19%), Wilms tumor ( $n=47$ , 11%), Hodgkin lymphoma ( $n=18$ , 4%), Burkitt lymphoma ( $n= 7$ , 2%) and low-grade glioma ( $n = 4$ , 1%). The proportion of survivors include ALL, 42%; Retinoblastoma, 55%; Wilms tumor, 43%; Hodgkin Lymphoma, 40%; Burkitt Lymphoma, 42%; and Low-Grade Glioma, 100%. The proportion of patients who abandoned was 17%. The 1-year and 3-year overall survival rates were 63% and 44% respectively for patients diagnosed before the initiative.

**Conclusions:** This study served as baseline data for measuring the impact of GICC implementation in a cancer institute from a tertiary hospital in the Philippines.

EP661/#1173 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### COST-EFFECTIVENESS OF CANCER PREDISPOSITION SYNDROME IDENTIFICATION STRATEGIES IN SURVIVORS OF PEDIATRIC LEUKEMIA, BRAIN TUMORS, OR BONE/SOFT-TISSUE SARCOMAS

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**Background and Aims:** Cancer predisposition syndromes (CPSs) are responsible for almost 10% of childhood cancers and signify an excess risk of developing subsequent cancers. CPS identification can result in earlier cancer detection and improved outcomes. Recent efforts for universal CPS genetic screening among pediatric cancer survivors are hampered by its excessive cost. The McGill Interactive Pediatric OncoGenetic Guidelines (MIPOGG) was built to streamline genetic referral and testing. This study aimed to compare the costs and effectiveness of MIPOGG-based and universal genetic testing of pediatric patients diagnosed with acute lymphoblastic leukemia (ALL), bone/soft-tissue sarcomas (bone/STS), and brain tumors.

**Methods:** A decision model was used to compare the health and economic impact of the two strategies from a healthcare payer perspective. The effectiveness of referral with MIPOGG was extracted from clinical data from children with selected cancer types who underwent germline sequencing from multiple sequencing initiatives. Accrued referral and testing costs were sourced from administrative databases and from genetic test providers. Outcomes included total healthcare costs and the probability of CPS detection. We conducted probabilistic analyses using a Bayesian approach to address the uncertainty surrounding MIPOGG's sensitivity, specificity, and disease prevalence, considering subgroups of different primary cancer diagnoses.

**Results:** Compared with MIPOGG-based practice, the universal strategy increased the CPS detection probability by 1.2% and per-person costs by \$1,454 for pediatric patients with any primary cancer diagnoses. Subgroup analyses suggested that the universal strategy improved the probability of CPS detection by 0.3%, 1.9%, and 2.0% compared with MIPOGG evaluation, at the increased costs of \$1,482, \$1,449, and \$1,433 for patients with ALL, bone/STS, and brain tumor, respectively.

**Conclusions:** MIPOGG-based practice reduces costs in referral and testing, at the expense of sensitivity in identifying CPS cases. The trade-off will be better understood with improved knowledge of the overall clinical and economic impact of identifying CPS cases.

EP662/#1812 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### RESULTS OF BETA 3 PEDIATRIC ONCOLOGY FACILITY INTEGRATED LOCAL EVALUATION (PROFILE) FROM THE HOSPITAL INFANTIL TELETON DE ONCOLOGÍA IN MÉXICO (HITO)

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#### Background and Aims: Background:

ProFILE is a systematized evaluation of pediatric hematology oncology (PHO) services, which allows analysis care practices and processes in low- and middle-income countries and promotes changes in the culture of quality, as well as the implementation of improvement projects based on their results. HITO joined the Beta 3 cohort in August 2023, and we present our results of the PROFILE evaluation.

**Methods:** The process was developed in three phases. A multidisciplinary clinical team of 16 members was integrated, headed by a physician lead and a site coordinator. Information was collected in 12 modules with 26 formats and 6 improvement quality exercises, with subsequent validation and analysis of the information.

**Results:** The results of the 12 modules were reported with polar graphs, establishing from the center to the periphery as C if the results were less than 50%, B with a range of 50% to 75%, and A with a percentage greater than 75%. The results obtained by modules were in the national context 55%, facility and local context 78%, finances and resources 89%, personnel 81%, service capacity 90%, services integration 76%, diagnostics 93%, chemotherapy 86%, supportive care 86%, surgery 92%, radiotherapy 81%, patients and outcomes 90%. Our polar graph reports A in all the modules except the national context located in B. We identified in the quality exercises the need to strengthen multidisciplinary communication, improve the definition of our care processes, and integrate the different subspecialists in training.

**Conclusions:** The implementation and evaluation of PROFILE at HITO allowed us to perform a deep analysis of our processes and quality of care considering the perspectives of a multidisciplinary team, which helped us identify strengths and opportunities to continue and focus on improvement strategies.

EP663/#762 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### UNDERSTANDING EARLY MORTALITY IN PEDIATRIC ONCOLOGY CASES IN WESTERN KENYA

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**Background and Aims:** In Kenya, the survival rate for pediatric cancer is as low as 19% with up to one-fourth of deaths occurring in the first months of therapy. This study aims to describe the pediatric cancer population experiencing early mortality in western Kenya.

**Methods:** A descriptive study of pediatric patients with cancer aged 14 years and below with early mortality, defined as before or within 60 days of starting treatment, was conducted at Moi Teaching and Referral Hospital (MTRH) within the Academic Model for Providing Access to Healthcare (AMPATH) and Princes Máxima Center Partnership. Data was collected prospectively from August 2022 to March 2023.

**Results:** A total of 16 patients experienced early mortality out of 141 patients (11.35%). Eleven were male and the average BMI was 15.58 kg/m<sup>2</sup>. Fourteen patients were referred from an outside facility to MTRH with 12 living more than 100 km away. Among the 21 cases diagnosed with Burkitt lymphoma (BL), 5 had early mortality. Of the 18 cases with nephroblastoma, 2 cases experienced early mortality. Of the 29 cases diagnosed with acute lymphoblastic leukemia (ALL), only one patient had early mortality. The causes of death were primarily due to disease progression or treatment-related mortality (n=11), but also included tumor lysis syndrome (n=2), infection (n=2), and cardiorespiratory arrest (n=1).

**Conclusions:** The rate of early mortality in western Kenya among pediatric patients with cancer (11.35%) remains higher than HICs (<2%) but is consistent with prior observations in Kenya. Although early mortality rates for BL and nephroblastoma are similar to previously established data (24%, 11% respectively), the mortality for ALL was significantly lower than previously reported (3% compared to 20%, p=0.02). Three-quarters of children who died early were from >100 km, reinforcing a continued need for improving awareness of childhood cancer and systems for early referral in rural communities.

EP664/#1181 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

### CO-DESIGNING A QUALITY CONTROL PROCESS FOR DATA ENTERED INTO HOSPITAL-BASED CANCER REGISTRIES: A PILOT STUDY FROM THE SJCARES REGISTRY NETWORK

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**Background and Aims:** The SJCARES Registry is a standardized hospital-based cancer registry tool that is part of a 34-member global collaborative registry-based data ecosystem designed to support institutional quality improvement. To ensure data quality, we worked collaboratively with participating registry teams to co-design a quality control process.

**Methods: Design/Methods:** A multidisciplinary team approach was defined at the outset. SJCARES Registry and statistics teams met to first define the data-driven processes. Analytic reports of system-generated queries, missing or delinquent data, and potential duplicate records were created. Using these reports, a template to facilitate communicating data queries was developed. To launch the pilot, training was conducted via a webinar with Benjamin Bloom Children's Hospital (El Salvador) and Children's Hospital Lahore (Pakistan). Sites addressed queries and tested the practicality of the processes. After two weeks, follow-up to gather feedback and identify barriers was completed. The process was repeated, following a quality improvement approach, until procedures were optimized.

**Results:** In development of process, key design principles were identified: readability, usability, alignment of included data. Feedback from partner teams after the first round of testing included: (1) suggestions to improve the template formatting to make the process more user friendly for sites with higher query volumes; (2) requests for office hour sessions for teams to ask questions or report system issues. The pilot also led to the unexpected opportunity for site teams to share internal processes for tracking queries addressed in the template, representing an opportunity to identify best practices that can now be shared across network sites.

**Conclusions:** Data quality control processes are imperative to ensure reliable, actionable data are collected in the SJCARES Registry. Next steps include completing the pilot, continuing to adapt processes according to feedback, expanding the data quality control process to all sites in network, evaluating the co-designed quality control processes for sustainability.

EP665/#1068 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

### TRAINING COURSE THE WAY TO THE EARLY DIAGNOSIS OF CANCER IN YOUTH IN THE WEST OF PARANA- BRAZIL

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**Background and Aims:** Introduction: Childhood cancer is a rare disease, it represents the 2nd cause of death in the range of 5 to 19 years old. On the other hand, the cure rate can reach more than 75% if diagnosed early. The Cancer Hospital of Cascavel - UOPECCAN, in partnership with the Ronald McDonald Institute, through the early diagnosis program for child and adolescent cancer, is training health professionals and medical students from the municipalities of the western region of Paraná in the suspicion of cancer in children and teenagers. Objective: Train health professionals and medical students to recognize the main signs and symptoms of childhood cancer.

**Methods:** Methodology: In the period from 2008 to 2018, the training was on-site, in 2021 online, and in 2022 hybrid - on-line and on-site. Professionals received basic information related to various topics of child and youth oncology, mainly the signs and symptoms of suspicion and how to refer a suspected case for diagnostic investigation.

**Results:** from 2008 to 2022, 3099 health professionals were trained, of which 2833 were physicians, nurses, nursing technicians/assistants, community health agents, higher education and technical professionals and 267 medical students from several universities.

**Conclusions:** Comments: The training of these professionals with basic information on the recognition of the main signs and symptoms of cancer in children and adolescents is a strong ally in programs for early diagnosis of cancer in children and adolescents. Reduce the time between the suspicion of cancer and early referral for diagnostic investigation and treatment will certainly contribute to increase the expectations of cure.

EP666/#1088 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

### HORA DORADA - MINUTES THAT SAVE LIVES IN WEST PARANÁ BRAZIL

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**Background and Aims:** Introduction: The Hora Dorada collaborative is an international collaborative project in partnership with the Institute for Healthcare Improvement, St. Jude Children's Research Hospital and

85 hospitals in Latin America, which aims to improve the care of children and adolescents undergoing treatment, where they must receive intravenous antibiotics in less than 60 minutes after presenting with a fever. Objective: To evaluate the time between arrival and receipt of venous antibiotics in pediatric hematologic oncology patients with fever who arrive at the emergency department of the Cancer Hospital. **Methods:** Methodology: The data entered into the Simple QI system, in children under 19 years of age from April 2022 to March 2023. Gender, oncological diagnoses and the time between arrival at the hospital until receive the antibiotic.

**Results:** There were 68 patients, 54(79%) male and 14(21%) female. Most 45 (66%) diagnosed with Leukemia. There was a reduction from 151 to 37 minutes between arrival with a history of fever (temperature >/ 37.8C) and administration of antibiotics at the institution. As of January/23, we are maintaining the proposed index with more than 70% of patients receiving antibiotics in the first 60 minutes.

**Conclusions:** Comments: Streamlining care and ensuring prompt antimicrobial administration is critical to reducing infection-related complications, including sepsis and death. Children and adolescents undergoing treatment in western Paraná are already benefiting from the Hora Dorada project. The commitment and will to make it work strengthens us through the expectations of improvement in the care of children and adolescents with cancer in our region.

EP667/#224 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### INTRODUCTION OF A PEDIATRIC HEMATOLOGY/ONCOLOGY FELLOWSHIP MATCH-STYLE RECRUITMENT SYSTEM IN LATIN AMERICA

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**Background and Aims:** One of the biggest barriers to caring for children with cancer is the lack of trained oncologist, impacting access to care. In Central and South America, this lack of specialists has been reported as a hindered to the care of the pediatric cancer burden. For the past 20 years, St. Jude Children's Research Hospital has worked with pediatric hematology/oncology fellowship training programs in Latin America, seeking to regionally expand care capacity. Over the past years, the number of programs and positions have increased.

**Methods:** To optimize the available resources and positions, a match style system, mimicking the American National Residency Match Program, was developed for the programs in Latin America (Mexico, Guatemala, Brazil, Uruguay) for the first time in 2021. The application was process included 3 components: submission of documents, knowledge evaluation, and interviews.

**Results:** This process was completed for the 2022 and 2023 candidate classes. An application platform was created and distributed through institutions, universities, the Society of Latin American Oncology Programs (SLAOP), and the St. Jude Global Alliance. To evaluate medical knowledge, a pediatrics exam was developed, and candidates completed it virtually. For the interviews, these were done virtually as a panel interview, with the presence of program leadership as well as St. Jude representatives. For the 2022 academic year, 21 completed applications were received from Guatemala, Honduras, Haiti, Nicaragua, Colombia, Ecuador, Bolivia, and Costa Rica. 12 positions were offered, and 11 fellows started fellowship in 2022. For the 2023 academic year, 35 completed applications were received from Colombia, Peru, Honduras, Bolivia, Ecuador, Guatemala, Nicaragua, Dominican Republic, Haiti, and Belize, and 13 positions were offered and accepted.

**Conclusions:** Using a match style process, has allowed all programs to fill open positions and allow physicians training and returning to their home country with this knowledge where there are few to no Oncologists.

EP668/#1026 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### GLOBAL STATUS OF HEALTH SYSTEM POLICY ENABLERS FOR OPTIMAL DELIVERY OF CHILDHOOD CANCER SERVICES: 4-YEAR REVIEW OF PROFILE RESULTS

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**Background and Aims:** Our team developed a model of country roadmaps and facility tiers for childhood cancer care for the Lancet Commission, incorporating 15 policy enablers under five domains. We summarize the status of these policy enablers as collected through the Pediatric Oncology Facility Integrated Local Evaluation (ProFILE).

**Methods:** From 2019 to 2021, 112 institutions from 23 countries collected data utilizing the Abbreviated Version of ProFILE. This descriptive analysis of policy enablers included institutions located in low-income (6), lower-middle-income (34), upper-middle-income (55), and high-income countries (17). Institutions ranked the status of each policy enabler from less desired (Step 1) to optimal status (Step 4).

**Results:** For **stewardship and governance**, numerous institutions reported step 4 status for the National Cancer Control Program (40%) and legislation to protect children's right to essential treatment (54%). National accreditation of facilities and providers reached step 2 (38%). Under **financing**, most institutions reported step 3 status for funding sources for direct and indirect treatment costs (55%) and competing health priorities and capacity to address them (57%). **Health information** policy enablers were most frequently reported as step 3, including national registration of vital statistics (44%), pediatric population-based cancer registration (63%), and research activities and governmental support (55%). Step 3 status was also reported by most institutions for **service delivery**, including access to essential medicines and technologies (54%), continuity of care in general pediatrics (47%), healthcare Infrastructure (45%), and healthcare workforce training and retention (51%). Finally, regarding **care access**, 76% of institutions categorized awareness among health providers and the public about childhood under step 2. Only 22% of institutions considered that traditional medicine poses minimal risk for timely diagnosis, curative intent, or step 4.

**Conclusions:** The distribution of policy enablers varies globally, related to country-income level. As countries engage in the Global Initiative for Childhood Cancer, disparities in these enablers should improve.

EP669/#775 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### GLOBAL, REGIONAL, AND LOCAL PEDIATRIC HEMATOLOGY AND ONCOLOGY (PHO) CARE CONTINUUM PRIORITIES: A 4-YEAR REVIEW FROM THE ST. JUDE GLOBAL PROFILE PRIORITIZATION WORKSHOPS

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**Background and Aims:** PrOFILe helps stakeholders set priorities for PHO care improvement. Since its inception in 2019, 154 institutions have implemented PrOFILe. The Abbreviated version helps set priorities for collaborative work across institutions in a region or country, and the Full version set priorities at the institutional level. We aimed to describe priorities selected during PrOFILe prioritization workshops (PWs) and their status.

**Methods:** We retrospectively reviewed action plans generated following each PW and categorized priorities under the 12 PrOFILe modules. Structured interviews and a follow-up survey were used to identify the

status of chosen priorities. Cohort or institutional liaison was asked to rate their progress using a 10-point scale (1=initial implementation, 10=completed).

**Results:** A total of 241 priorities were identified during 22 PrOFILe workshops. Median number of priorities was 6 (range 4-13) for regional/country-based and 10 (range 8-16) for institutional workshops. Priorities most selected at the regional/country level were under the Patients and Outcomes (P&O) (17%), Diagnostics (DX) (13%), and National Context (13%) modules. Similar results were found during institutional workshops where P&O and DX were the most frequent modules (15% each), followed by Service Capacity (11%). Improving prospective data collection (24%) and diagnosis timeliness from first evaluation to diagnostic confirmation (29%) were the most frequent priorities for the P&O and DX modules, respectively. The Asia Pacific and Central and South America regions follow the previous pattern. The Eastern Mediterranean, Sub-Saharan Africa, and Euro regions included additional modules. Overall, 40% of the selected priorities were reported as active. The median progress rate for regional/country priorities was 3 (range 1-9), and 6 (range 1-10) for institutional priorities.

**Conclusions:** Although differences across regional programs exist, PrOFILe found common ground when comparing priorities between regional/country and institutional PWs. Our results can inform the development of future Global Packages, enabling future cohorts and institutions to implement identified PHO care priorities.

EP670/#1388 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### CONTEXTUAL FACTORS ASSOCIATED WITH THE SUCCESS OF THE GOLDEN HOUR MULTI-COUNTRY QUALITY IMPROVEMENT COLLABORATIVE

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**Background and Aims:** Contextual factors contribute to Quality Improvement Collaboratives (QIC) success in real-world settings. Between November 2021 and February 2023, 85 institutions from six Latin American countries participated in the 2<sup>nd</sup> Mexico in Alliance with St. Jude Golden Hour Collaborative (2<sup>nd</sup> MAS Collaborative) to reduce time to antibiotic administration to ≤60min among febrile pediatric hematology-oncology patients (fPHOP) presenting to the emergency department with varying results across institutions. This

study aimed to identify the contextual factors associated with the success of the 2<sup>nd</sup> MAS Collaborative.

**Methods:** This 18-month QIC followed the Breakthrough Series Model and two QI capability-building programs. We built a multivariate logistic regression model to assess the factors contributing to success: a. Dimensions of the Model for Understanding Success in Quality (MUSIQ: external environment, organization, QI support and capacity, microsystem, and QI team); b. Active participation in activities of the collaborative (60% learning sessions and coaching attendance); c. Key drivers worked on (1. Clinical and paraclinical reliability; 2. Learning systems; 3. Effective teamwork and communication; 4. Early fever identification; 5. Effective access to medicines and supplies), and d. Intervention exposure time; and e. Participation in the 1st MAS Collaborative. We defined success as having achieved their local aim or a proportion of 70% of fPHOP receiving antibiotics in  $\leq 60$ min

**Results:** The following factors were associated with success: active participation in activities of the collaborative (OR 3.8), having worked on driver 1 (OR 11.3) and driver 5 (OR 11.9), and having participated in the 1st MAS Collaborative (OR 3.3). Other factors were not conducive to success.

**Conclusions:** Understanding the contextual factors associated with the success of QICs in real-world settings is key to informing their design and implementation and determining the support institutions should provide to help them achieve and sustain results.

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## THE BURDEN OF ACUTE PEDIATRIC CRITICAL ILLNESS AMONG HOSPITALIZED PEDIATRIC ONCOLOGY PATIENTS IN LOW- AND MIDDLE-INCOME COUNTRIES: A SYSTEMATIC REVIEW

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**Background and Aims:** Pediatric oncology patients are at increased risk for critical illness. While pediatric intensive care outcomes for this population have been studied in high-income countries (HICs), data from low- and middle-income countries (LMICs) is lacking. The objective of this study is to describe the burden and outcomes of acute critical illness among hospitalized children with cancer in LMICs.

**Methods:** A systematic search was conducted in PubMed, EMBASE, Web of Science, CINAHL and Global Health databases for articles in English, Spanish, French, Russian, Arabic, Chinese and Portuguese describing mortality in children with cancer admitted to pediatric intensive care units (ICUs), intermediate care units (IMCU) or high dependency units (HDUs) in LMICs. Two reviewers independently assessed eligibility criteria, data quality, and extracted data. Primary outcomes included mortality rates, cause of critical illness admission, and cause of death in the ICU, IMCU and HDU.

**Results:** Out of 3,641 studies identified, 482 full texts were reviewed. A total of 22 studies were included capturing data from 4,389 critical illness admissions among pediatric oncology patients. Of these admissions, 1,094 resulted in mortality (25%), which ranged widely by study (range 0/27 to 363/674). Most studies were retrospective observational designs and, in its majority, represented the Asian region (72%).

**Conclusions:** Mortality among hospitalized children with cancer who develop critical illness is high in LMICs specially among those requiring mechanical ventilation and inotropic support. This study provides insight into the global burden of acute critical illness in children with cancer. Our findings highlight the growing need to improve oncocritical services and to appropriately allocate limited resources to improve survival and outcomes of critically ill children with cancer worldwide.

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## COMPREHENSIVE INSTITUTIONAL ASSESSMENT OF A CHILDHOOD CANCER REFERRAL CENTER IN THE PHILIPPINES UTILIZING THE PEDIATRIC ONCOLOGY FACILITY INTEGRATED LOCAL EVALUATION (PROFILE)

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**Background and Aims:** PrOFiLE is a 360-degree guided institutional self-assessment that allows multiple stakeholders to identify opportunities and strengths in service delivery. PrOFiLE helps care teams define strategies to improve capacity and quality of care for pediatric cancers. In August 2022, the Philippine Children's Medical Center Cancer and Hematology Division team joined the Full PrOFiLE Beta 3 Testing cohort. We aim to describe our findings, accomplishments, and experience.

**Methods:** PrOFiLE was implemented in three phases: preparation, assessment, and interpretation and action. We recruited our assessment team and selected two providers to complete the Institute for Healthcare Improvement Quality Improvement (QI) [GM1] Basic Certificate during the preparation phase. Objective and subjective data for the twelve PrOFiLE modules (26 forms) were collected. A total of six QI exercises were completed. Data validation and feedback for the short interval reports were submitted. Both score-based and descriptive reports were utilized to plan a local workshop and develop our division's short term and long-term action plans.

**Results:** A total of 19 interdisciplinary healthcare providers formed the assessment team. The physician lead (PL) and site coordinator (SC) attended 33 mentoring sessions and completed 14 educational videos. Our form completion rate was 78% for both objective and subjective data. Our site scored 69% for Context, 69% for Personnel, 66% for Diagnostic, 59% for Chemotherapy, and 77% for Patients and Outcomes modules. There were differences in the awareness level of institutional planning between the point of care staff and PL and SC. These were substantial in the Service Capacity, Supportive Care, Chemotherapy, and Surgery modules.

**Conclusions:** PrOFiLE enabled providers better understand the local health system by determining gaps in delivering and accessing pediatric oncologic care. We identified QI strategies that cut across crucial areas affecting pediatric cancer treatment. The implementation process was instrumental in the formulation of concrete action plans.

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## HIGH QUALITY CARE CLOSE TO HOME: THE POGO SATELLITE PROGRAM

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**Background and Aims:** Ontario, Canada's most populous province, is home to 2.8 million children and adolescents spread across a vast geography. Despite the province having five publicly funded specialized childhood cancer programs (SCCPs) in major metropolitan areas, many pediatric cancer patients and their families still face substantial geographic, financial, and logistical barriers in accessing timely, safe and appropriate care. The Pediatric Oncology Group of Ontario (POGO) created a formal system of satellite clinics to allow patients access to high quality care closer to home.

**Methods:** Provincially-funded POGO satellite clinics were established based on regional need, general pediatric expertise and capacity of hospitals to host these clinics. POGO partners with SCCPs to provide training to satellite physicians, nurses, and allied health professionals. An open access web-based manual provides procedural and evidence-based care guidance. Clinical trial participation is facilitated by local designated investigators, satellite-specific training, and a provincial Research Ethics Board. Ongoing quality assurance and improvement is supported by regular site visits, province-wide education events and indicator reporting. Program capture is defined as the percentage of eligible patients served in a satellite clinic.

**Results:** Currently, the POGO Satellite system includes 8 satellite clinics. From 2014 to 2019, over 55% of newly diagnosed patients lived in satellite catchment areas and over 800 newly diagnosed patients were seen in the system, resulting in more than 6,300 satellite visits on average per year. The program reach for all 8 satellite clinics was 66%, ranging from 33% for acute myeloid leukemia to 71% for patients with non-CNS solid tumours.

**Conclusions:** The POGO Satellite system provides a structured method of providing high quality care for patients closer to home, as well as data to examine access to and quality of care. Future efforts will include expansion to underserved regions and expanding therapies that may be safely administered in satellite to improve program reach.

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## ASSESSING THE NEEDS FOR A MOBILE APP FOR INDIVIDUALS LIVING REMOTELY WITH PEDIATRIC-ONSET CANCER PREDISPOSITION SYNDROMES

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**Background and Aims:** Cancer predisposition syndromes (CPSs) are genetic conditions that increase the lifetime risk of developing cancer. A predominant part of CPS management is cancer screening assessments. Individuals living at an increased distance from cancer centres

experience differences in access to, and usage of, cancer screening services. Mobile apps are increasingly being integrated into clinics to help patients access resources and manage their care. This study explored the experiences of caregivers of/patients with pediatric-onset CPSs who are followed in a cancer surveillance clinic located >20km from their home, and if/how a mobile app could help address barriers and improve their cancer screening care.

**Methods:** We recruited eligible participants who were served by the McGill University Health Centre cancer surveillance clinic and who lived >20km from the hospital. Participation included a demographic questionnaire and semi-structured interview in English/French asking about participants' feelings and perspectives towards their CPS management, what barriers they experience with their care, and their degree of interest and preferences for a hypothetical app to help with CPS management. Interview transcripts were studied using inductive thematic analysis with NVivo software.

**Results:** Fourteen caregivers and three patients aged >18 years participated in 15 interviews (December 2021-October 2022). Seven different CPSs were represented. All individuals considered that challenges in coordination of care was a barrier, though heterogeneous perspectives were given on the impact of distance/commute. Participants expressed interest in an app that could coordinate care (n=15, 100%), store health data (n=14), facilitate communication with health-care providers (n=15), and provide education (n=15). The utility of the app outweighed patient concerns (e.g., data security).

**Conclusions:** Main barriers towards cancer screening are related to care coordination (and may be independent of distance). An app could help patients and families with CPSs overcome these barriers and improve their overall cancer screening experience.

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#### GLOBAL LANDSCAPE OF MULTIDISCIPLINARY MEETINGS PRACTICES IN PEDIATRIC HEMATOLOGY ONCOLOGY FACILITIES: A SECONDARY ANALYSIS FROM PROFILE

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**Background and Aims:** Multidisciplinary care (MDC) meetings improve the quality of cancer care by providing a space for interdisciplinary communication. The Pediatric Oncology Facility Integrated Local Evaluation (ProFILE) assesses MDC meetings as part of the Service Integration module. We aim to evaluate the elements of MDC meetings at institutions that completed ProFILE.

**Methods:** From 2019 to 2021, 112 institutions from 23 countries collected data utilizing the Abbreviated Version of ProFILE. We describe a secondary analysis of collected data focused on the characteristics of MDC meetings stratified by income level.

**Results:** Hospitals included were in low-income countries (LICs) (6), lower-middle-income (LMICs) (34), upper-middle-income (UMICs) (55), and high-income countries (HICs) (17). Of 112 participating facilities, 79% reported formal MDC meetings. The existence of an MDC varied with income; 50% of LICs vs. 100% of HICs hosting MDCs. The frequency of MDC meetings also differed, with 100% of MDCs in LICs occurring weekly, while 53% of MDCs in HICs occurred monthly. Specialties regularly represented at these meetings consisted of hematology/oncology (93%), pathology (49%), radiology (58%), general surgery (56%), and radiation oncology (37%). All MDC meetings in LICs reported representation from these specialties. Surgical subspecialists, pharmacists, nurses, and psychosocial support were less frequently represented. Availability of relevant test results, reports, and studies varied with income level, 40% in LICs and 88% in HICs, as did including an assessment of patient preferences which were not reported to be considered in meetings in LICs, but were in 62% of the institutions in UMICs, and 59% of the institutions in HICs.

**Conclusions:** The existence and components of a functional and effective MDC meeting vary with income level. While certain components, such as access to tests, may be explained by differences in resource distribution, other factors can be optimized in all settings to foster effective teamwork and communication.

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#### IMPLEMENTING A HOSPITAL-BASED CANCER REGISTRY IN FIFTEEN MEXICO IN ALLIANCE WITH ST. JUDE (MAS) INSTITUTIONS: EXPERIENCE WITH SYNCHRONOUS MULTI-SITE IMPLEMENTATION

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**Background and Aims:** In Mexico, about 7,000 children are estimated to develop cancer every year. A national population-based cancer registry does not exist. In 2022, Mexico in Alliance with St. Jude (MAS) collaborating hospitals adopted the SJCARES Registry, a

standardized hospital-based cancer registry developed by St. Jude Children's Research Hospital (SJCRH), with support from an expert panel. We report our experience with synchronous multi-site implementation.

**Methods:** In early 2022, 23 hospitals were invited to join the cohort. We used the "Knowledge to Action" framework (K2A) and a "cohort-based implementation model" to conceptualize and operationalize our approach. The latter entailed synchronous engagement of all participating sites throughout the implementation steps to build an intra-cohort learning system. Sites identified their local team, attended biweekly meetings, completed online training in an educational platform (Cure4Kids), entered test case dummy data into a training portal, and participated in a pre-activation feedback meeting. Access to the registry platform was granted only after completing all steps. Over the next six months, sites will engage in semi-structured interviews on barriers and facilitators to implementation.

**Results:** Fifteen (65%) eligible hospitals joined the first cohort. Fifty-two team members completed training [mean time to completion: 6.4 months (4.7 - 8.2)]. As of March 2023, 15 meetings were held, all 15 sites completed the test cases satisfactorily, 9 are entering data with 3 about to start. Based on each institution's average annual new childhood cancer diagnosis, >800 patients are expected to be registered yearly, corresponding to 11% of the expected yearly incidence in Mexico.

**Conclusions:** Cohort-based implementation allowed optimization of the implementation timeline, human resources, and knowledge-sharing opportunities, creating a functional intra-cohort learning system and leading to timely, effective early implementation. Through upcoming interviews, we will generate implementation insights and inferences to inform implementation for future cohorts for this and comparable interventions.

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#### THE ST. JUDE GLOBAL POST-PROFILE ACTIVITIES: ACTION PLAN DEVELOPMENT, OUTCOMES, AND CHALLENGES AT A TERTIARY CARE HOSPITAL IN PAKISTAN

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**Background and Aims:** The Pediatric Oncology Facility Integrated Local Evaluation (ProFILE) tool helps facilities and care teams to define an improvement strategy for increasing childhood cancer survival rates. The Indus Hospital & Health Network (IHNN) participated in the ProFILE 3-phase implementation (preparation, assessment, interpretation & action) from August 2021 to May 2022. We

aim to describe the IHNN action plan development, outcomes, and challenges.

**Methods:** Our institutional ProFILE score-based report identified 198 improvement opportunities. We conducted a 2-day in-person prioritization workshop to define opportunities to include in our action plan. We delivered three Quality Improvement (QI) exercises: (1) building consensus utilizing a ranking system, (2) prioritizing using an impact-effort matrix, and (3) categorization of opportunities into a 3-year action plan.

**Results:** A total of 50 healthcare providers participated in the prioritization workshop. We narrowed it down from 120 to 15 opportunities by the end of the second QI exercise. Then, we categorized opportunities as "currently working on it" (Year 1) and "not working on it but important to start" (Year 3). Year 1 opportunities include increasing childhood cancer awareness among the public and healthcare providers, decreasing infection-related mortality by improving and implementing hand hygiene and other strategies, reducing treatment abandonment, improving the cancer registry and prospective data collection, and increasing accessibility to palliative care. Critical three years opportunities include increasing resource allocation for surgery, neurosurgery, nutrition, molecular testing, raising the proportion of children treated with curative intent, and starting home health services. Five task forces including ProFILE champions and hospital leadership have been activated. Lack of human resources, finances, administrative support, and the overwhelming patient volume are identified challenges to action plan implementation.

**Conclusions:** ProFILE helped IHNN identify and prioritize improvement areas and systematically approach the problem. ProFILE Champions and local leadership plan implement solutions through continuous follow-ups, collaboration, QI capacity building, and teamwork.

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#### CO-DESIGNING PROCESS MAPS TO SCALE-UP HOSPITAL-BASED CANCER REGISTRIES (HBCR) IN SOUTH AFRICA: A ST. JUDE GLOBAL AND SOUTH AFRICAN CHILDREN'S CANCER STUDY GROUP (SACCSG) COLLABORATION

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**Background and Aims:** Strengthening the SACCSG HBCR network was identified as a priority at a national stakeholder workshop in October 2021. To initiate implementation, the SACCSG convened a stakeholder meeting in September 2022 to co-design a process map and action plan.

**Methods:** Participants were identified by SACCSG leadership were asked to complete four exercises aligned with an implementation mapping approach, a method used when designing multi-level health interventions and strategies. Exercises incorporated co-design principles and included: 1) defining/redefining the goal of HBCR strengthening; 2) completing a logic model with inputs, outputs, and outcomes; 3) Identifying barriers and strategies; 4) creating a first post-workshop meeting agenda. Outputs were used to guide next steps.

**Results:** Ten stakeholders from the South African Department of Health, National Cancer Registry, Childhood Cancer Foundation (CHOC), and St. Jude Global participated. In exercise #1, the defined goal was "to strengthen the HBCRs with a minimum dataset that can be linked to the national cancer registry (NCR) using a data capture system to improve care and motivate capacity/funding." During exercise #2, the logic model established key inputs (i.e., evaluation of established electronic data platforms), activities (identify pilot sites), identify person (s) responsible to lead work, directed outputs (database creation, training, workflows) and both short/long-term outcomes (pilots completed/linkage with NCR). Potential barriers included regulatory uncertainty, funding, and staffing concerns (exercise #3). Strategies to address these barriers focused on identifying pilot sites to create a template operation procedure and demonstrate feasibility to all centers and potential funders. A draft agenda for guide first working group meeting was outlined (exercise #4).

**Conclusions:** Activities from the workshop helped South African stakeholders develop a process map and implementation strategy to support HBCR strengthening activities. Application of our participatory approach, built on implementation science methodologies, can serve as a template for others seeking to enact complex, multistakeholder initiatives.

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## MATERNAL USE OF HORMONAL CONTRACEPTION AND CHILDHOOD CANCER RISK: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background and Aims:** Using available studies, we conducted a systematic review and meta-analysis on the association of maternal use of hormonal contraception and childhood cancer risk.

**Methods:** Pubmed, Embase, Scopus, Cochrane, and Web of Science databases were searched up to March 1, 2022, for studies on the association between maternal use of hormonal contraception and risk of cancer in the offspring. A total of 24 case-control and 2 cohort studies were included for analysis. A meta-analytical approach was used to weight the study-specific adjusted log RRs by the inverse of their variance to obtain a pooled relative risk (RR) and its 95% confidence interval (CI) for each cancer outcome, according to maternal hormonal contraception use 1) up to and/or during pregnancy and 2) during pregnancy only.

**Results:** Maternal use of hormonal contraception up to and/or during pregnancy was associated with an increased risk of any cancer in children with a RR of 1.20 (95% CI, 1.10-1.30). For specific childhood cancer types, the risk estimates were statistically significantly increased for any leukemia (RR = 1.23; 95% CI, 1.03-1.47), lymphoid leukemia (RR = 1.18; 95% CI, 1.05-1.31), and SNS tumors (RR = 1.49, 95% CI, 1.01-2.02). For maternal use of hormonal contraception during pregnancy only, the risk estimates for any cancer, leukemia, lymphoid leukemia, and non-lymphoid leukemia were further increased, compared to estimates for use up to and/or during pregnancy. The same pattern was not observed for CNS tumors, SNS tumors, Wilms tumor, and other cancer types.

**Conclusions:** These findings indicates that maternal use of hormonal contraception may be associated with an increased childhood cancer risk. However, since studies in this field are few and often limited by study-design and self-reported data, more studies based on

prospective high-quality data are needed, with a focus on specific products and timing of use.

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#### TIME FROM SYMPTOM ONSET TO INITIATION OF THERAPY FOR CHILDREN WITH CANCER IN LOW- AND MIDDLE-INCOME COUNTRIES (LMIC): AN ANALYSIS FROM THE SJCARES REGISTRY NETWORK

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**Background and Aims:** Delays in diagnosis are a common cause associated with excess morbidity and mortality in LMICs. Using data from the SJCARES Hospital-Based Cancer Registry (HBCR) Network, we analyzed four time points along the continuum of cancer diagnosis, from symptom onset to the initiation of therapy.

**Methods:** All cases in the SJCARES HBCR Network from October 2021 to March 2023 were included in this report. Sites with fewer cases (<20) or with low quality of data were excluded. For each patient, timelines were calculated using four dates in the registry: initial onset of cancer-related symptoms; first medical assessment; confirmed diagnosis; definitive treatment started. As patients are entered on a rolling basis, only records with complete pairwise intervals were included. Descriptive statistics are used to summarize patient demographics and four timelines.

**Results:** A total of 3,181 patient records with a confirmed cancer diagnosis from 20 institutions in 18 countries were included in the analysis. Median age at diagnosis was 6 years (IQR=8 years), 58% (n=1856) cases were male, 70% (n=1711) of cases were diagnosed based on microscopic evaluation. Median time from onset of cancer-related symptoms to first medical assessment was 27 days (IQR=52 days); first medical assessment to confirmed diagnosis was 7 days (IQR=18 days), confirmed diagnosis to definitive treatment started was 3 days (IQR=13 days) and onset of cancer-related symptoms

to definitive treatment started was 45 days (IQR=78 days). Among parents/guardians with known education status, 25% (n=453) had grade school education and 24% (n=431) had high school education.

**Conclusions:** Most delays in median time from the onset of cancer-related symptoms to definitive treatment started occurred before their first medical assessment, though large variations in the IQR were reported. Collection of these data is only feasible through HBCRs and can serve as benchmark data from which to design quality improvement initiatives.

EP681/#1366 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
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#### LONG TERM FOLLOW-UP OF 107 PHYSICIANS TRAINED THROUGH THE AFRICAN SCHOOL OF PEDIATRIC ONCOLOGY (EAOP) PEDIATRIC ONCOLOGY DIPLOMA

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**Background and Aims:** To improve the skills and increase the number of pediatric oncology (PO) healthcare providers in Africa, the FrenchAfrican Group of Pediatric Oncology (GFAOP) established the African School of Pediatric Oncology (EAOP). This project is primarily supported first by Sanofi Espoir foundation and then by Foundation S (My Child Matters program). In 2014, the EAOP set up the "Diplome Universitaire d'Oncologie Pédiatrique" a program of formal PO training for physicians. We report on the follow-up of physicians trained from 2014 to 2022

**Methods:** A Training Committee was established. The French model was selected and was accredited by two universities to be a formal training program (University Mohammed V – Rabat Morocco and Paris Saclay France). The training was initiated in 2014. We followed the outcome through regular electronic messages, calls, or teleconferences with the participants.

**Results:** Over 8 years of training, we recruited a total of 107 candidates. Participants were from 20 Francophone African countries. Two participants are from countries where PO facility is still not available. Participants were from different specialties; most of them pediatricians (69) As of today, 61 (57%) out of 107 participants are still involved in childhood cancer care in their home countries, 5 participants created new pediatric oncology units (Benin, Gabon, Central Africa republic, Niger, Republic of Congo), and increased by 50% the number of Pediatric oncologists in the GFAOP PO units. 25 participants are involved in medical student training and research. The most important cause of

the drop off from PO was the absence of the possibility to be recruited by the government or reassignment to other departments or hospitals. **Conclusions:** The challenge will be the retention of trained physicians in hospitals where they can participate in the multidisciplinary care of Children with cancer. The Global Initiative for Childhood Cancer is an opportunity to retain trained healthcare providers

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### SPECTRUM AND OUTCOMES OF SOLID TUMOURS AT MBINGO BAPTIST HOSPITAL IN NORTHWEST CAMEROON

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**Background and Aims:** The WHO Global Initiative on Childhood Cancer aims for 60% survival for common and curable childhood cancers by 2030. Childhood cancer management is provided at MBH since 2006 and has improved over time with a growing multidisciplinary care team. The aim of this study was to report the types and outcomes of paediatric solid tumours.

**Methods:** This was a cross-sectional registry-based study. Records of children below 15 years with a solid tumour diagnosis from January 2016 to December 2020 were extracted from the Resonance Patient Center hospital-based cancer registry. Analysis was conducted on the cancer type, delay to diagnosis, treatment status and patient outcomes. Frequencies were reported and chi-square was used to compare outcomes between categorical variables.

**Results:** One hundred and fourteen solid tumours were recorded. The median age at diagnosis was 4 years [IQR: 2-5] with a female-to-male ratio of 1.3:1. Median delay from onset to diagnosis was 9 weeks [IQR: 3-17]. The most common types were neuroblastoma (52.6%); retinoblastoma (15.8%), brain tumour (11.4%) and rhabdomyosarcoma (9.5%). One-year survival for all types was 37.3%. This was significantly higher in children who completed treatment (76%),  $p = 0.001$ . The rate of treatment abandonment was 17.7%. Abandonment was higher in females (23.3%) than in males (7.1%), ( $p=0.026$ ). Duration of symptoms and age at diagnosis did not affect abandonment.

**Conclusions:** Good outcomes for paediatric solid tumours can be achieved in Cameroon with available treatment. Care providers must find solutions to socioeconomic challenges like esthetics, cultural beliefs, distance to treatment facility, and financial difficulties to reduce treatment abandonment, enable all children to complete treatment to achieve better survival rates.

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### DEVELOPMENT AND EXPANSION OF A CANADIAN SURVEILLANCE POPULATION HEALTH TOOL FOR CHILDREN AND YOUTH WITH CANCER

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**Background and Aims:** Capturing cancer trends in children and youth is vital to understanding cancer burden. The Cancer in Young People in Canada (CYP-C) maintains an interactive tool that presents data on cancer incidence, survival and relapse risk. It is the only pan-Canadian surveillance tool dedicated to childhood cancer. New developments include data on prevalence, mortality and potential years of life lost (PYLL). This abstract describes the statistics newly available in the CYP-C data tool.

**Methods:** Data were collected from the CYP-C program (2001-2020) and Canadian Cancer Registry linked to the Canadian Vital Statistics-Death Database (1992-2017; excludes Quebec). Prevalence estimates include children diagnosed before 15 years old and alive 5, 18, or 25 years after diagnosis. Mortality and PYLL rates include children who died before 18 years old. PYLL was estimated using life expectancies in the general population. Crude and age-standardized rates (ASRs) are included and stratified by sex, age, year, cancer diagnosis, region, and period.

**Results:** At the start of 2018, there were almost 15,000 individuals in Canada diagnosed with childhood cancer in the previous 25 years. Of these individuals, 25% were diagnosed in the previous 5 years. Over 20 years, the age-standardized 5-year prevalence increased (419.0 per million in 1997; 531.7 per million in 2017). Leukemias were the most prevalent. All-cause mortality among individuals < 18 years old was consistently 20.5 per million over the fifteen-year analysis period. Almost 11,000 potential years of life were lost yearly, most in males. CNS tumors accounted for one of the highest rates of PYLL (ASR 410.5 per million).

**Conclusions:** The CYP-C data tool aims to make childhood cancer epidemiology accessible. The expansion to include prevalence, mortality and PYLL allows users to explore more trends by several stratifiers. Future developments will include other childhood cancer indicators for continued surveillance of this population.

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**MAPPING PEDIATRIC ONCOLOGY CLINICAL TRIALS AND COLLABORATIVE RESEARCH IN ASIAN CONTINENT: A SURVEY-BASED STUDY BY ASIAN PEDIATRIC HEMATOLOGY AND ONCOLOGY GROUP (APHOG)**

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**Background and Aims:** The newly formed Asian Pediatric Hematology Oncology Group (APHOG) aims at promoting clinical trials and collaborative research across Asian countries. The aim of this study was to map the landscape of pediatric oncology clinical trials in Asia, identify barriers to clinical research and hence strategize a focused approach toward research collaborations within continent.

**Methods:** The APHOG conducted a baseline assessment survey to evaluate ongoing National Multicentric Clinical Trials (NMCT) and barriers to collaborative clinical research in the continent. The leading pediatric oncologists in all Asian countries, except three countries that are members of other continental branches of SIOP, were invited to participate through a survey monkey questionnaire. Participating countries were categorized by the World Bank income levels into high (HIC), upper-middle (UMIC), lower-middle (LMIC) and low-income countries (LIC) for further analysis.

**Results:** Of 47 invited Asian countries, 42 (89% response rate) participated in the survey. According to survey data, the sum of new cancer patients per annum in the participating countries was 123805. Twenty-two of 42 (52%) countries had national pediatric oncology societies and only 11 of these 22 have been actively running NMCT; 4/12 HIC, 4/10 UMICs, 3/18 LMICs and 0/2 LICs. The projected population of new pediatric oncology patients with no potential access to NMCT for middle eastern HICs, Non-middle eastern HICs, UMICs, LMICs, and LIC was 100%, 0.04%, 20.6%, 31.8%, and 100% respectively. ALL and AML are the most studied cancers, followed by neuroblastoma and lymphomas. The most notable barriers highlighted by survey participants were deficient research training and limited experience in conducting clinical trials, lack of insight into the importance of clinical research, and minimal opportunities to participate in international studies.

**Conclusions:** Based on our study findings, a customized need-based approach should be applied to address the barriers and strengthen collaborative research in Asian countries.

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**IMPACT OF FINANCIAL SUPPORT AND OUTCOMES OF CHILDREN WITH CANCER – INDIAN CANCER SOCIETY-CANCER CURE FUND (ICS-CCF)**

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**Background and Aims:** In absence of insurance-awareness and state-funding, dearth of finances for cancer treatment impacts outcomes in India. ICS-CCF, through 18 empanelled hospitals across India, provides financial assistance, the impact of which we evaluated on paediatric subset of beneficiaries.

**Methods:** A multi-step thorough Due-Diligent selection of beneficiaries with curative malignancies, treated with evidence-based streamlined strategies and optimal turnover, ensured provision of care throughout the course of treatment. A consented prospective longitudinal telephonic follow-up study was conducted to report outcomes.

**Results:** From 2011-2020, financial aid of USD 4.9 Million was provided to 2514 paediatric patients. The planned prospective phone follow up could be completed in 2173/2514 (86%) beneficiaries. At a median follow-up of 4.7 years, 1399/2173 (64%) were alive and disease-free. Outcome was better in Haematolymphoid malignancies 1137/1710 (66%) as compared to Solid tumours 262/463 (57%), Lymphoma 223/292 (76%) vs Leukaemia 914/1418(64%). Patients with Sarcomas fared particularly poorly 167/341 (49%). Age was a significant determinant for survival (0-5 years; 521/732 = 71%, 6-10 years;

444/666 = 67%, 11-15 years; 434/775 = 56%). Gender was not a significant factor for outcome.

**Conclusions:** Over a decade, ICS-CCF has demonstrated a sustainable model of significant impact delivery on a national level. While prospective long-term structured follow-up remains a significant challenge in Indian health-care system, our major achievement is the feasibility in the majority.

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#### DELAYS IN ACCESSING CHILDHOOD CANCER TREATMENT IN WESTERN KENYA

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**Background and Aims:** Awareness, and early referral, diagnosis and start of treatment are crucial to improve childhood cancer survival in resource-limited settings, such as Bungoma County in Kenya. This study aims: 1) to compare the annual number of diagnosed children with cancer from Bungoma County to the expected number in this region; 2) to explore diagnosis, treatment and total delay among these children; and 3) to determine patient characteristics that influence these delays.

**Methods:** This study combined a retrospective medical records review with an illustrative case report. Data on delays and socio-demographic and clinical characteristics of children from Bungoma County diagnosed with cancer between 2010 and 2016 at MTRH, a large academic hospital, were collected. Among these children, the researchers identified a 13-year-old child with Hodgkin's lymphoma. An interview was conducted in November 2022 with the parents of that child using a semi-structured questionnaire, after obtaining Informed consent.

**Results:** Between 2010-2016, 92 children were referred from Bungoma Country. The annual average of 13 children constitutes only 9% of the expected 150 children developing cancer in this region. Most common diagnoses were: non-Hodgkin lymphoma (17%), acute lymphoblastic leukemia (16%), rhabdomyosarcoma (12%). Median total delay was 108 (7-1731) days. Median diagnosis delay (97 days) was significantly longer than median treatment delay (3 days;  $P < 0.001$ ). Significantly longer total delay was associated with: referred from another facility ( $P = 0.008$ ), longer symptoms duration ( $P < 0.001$ ), solid cancer type ( $P = 0.013$ ), low stage at diagnosis ( $P = 0.036$ ). The case study highlights challenges encountered by families of children with cancer: health beliefs and fear of conventional medicine led to delayed seeking of appropriate treatment.

**Conclusions:** Delays in access to childhood cancer treatment are considerable. Several factors impact delays, such as referral from another

health care facility and solid cancer type. Increasing awareness is an important step towards reducing delay and ultimately improving childhood cancer survival.

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#### FINANCIAL COSTS OF PEDIATRIC CANCER MANAGEMENT IN AFRICA: SYSTEMATIC REVIEW

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**Background and Aims:** The high costs of cancer treatment and lack of investment in health care are significant obstacles to public health in the African continent. The objective of this study was to estimate the financial cost of treating children suffering from cancer in in Sub-Saharan Africa.

**Methods:** We systematically searched PubMed, Cochrane and Google Scholar to identify relevant studies between March 2000 and December 2022. We selected articles that specifically addressed the financial costs using in US dollars of childhood cancer in African countries. Medians and interquartile ranges (IQR) were calculated. The quality of economic studies was assessed using the CHEERS 2022 28-item checklist.

**Results:** A total of 17 studies met our eligibility criteria. The median (IQR) of total childhood cancer costs by region was 909.5 \$ (\$ 455.3 - \$ 1765). No significant difference ( $p < 0.05$ ) was observed for comparisons of the direct cost of childhood cancer between the Geopolitical zone sub-Saharan Africa. Differences in direct childhood cancer costs were significant for the different types of cancer ( $p < 0.05$ ). Costs for leukemia patients (\$1831.2) are significantly higher than costs for lymphoma patients (\$103.8).

**Conclusions:** The cost of treating childhood cancer is high in Africa in relation to the standard of living of individuals residing in this region.

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#### STRENGTHENING HEALTHCARE SYSTEMS THROUGH STANDARDIZING COMMUNITY HEALTH WORKERS' SERVICES FOR BURKITT'S LYMPHOMA IN WESTERN KENYA

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**Background and Aims:** Burkitt's lymphoma is a highly aggressive form of cancer that is prevalent in western Kenya, particularly among children. Community Health Workers (CHWs) play a vital role in delivering healthcare services in underserved communities in Kenya. The aim of this study is to develop a Standard Operating Procedure (SOP) for CHWs in western Kenya to improve the delivery of healthcare services, with a focus on Burkitt's lymphoma. The SOP provides a framework for the effective and efficient delivery of healthcare services by CHWs, with the ultimate goal of improving health outcomes in underserved communities.

**Methods:** A mixed-methods approach was used to develop the SOP. First, a comprehensive literature review was conducted to identify best practices in CHW programs worldwide. Next, key informant interviews were conducted with CHWs, community members, and healthcare providers to gather information on the current state of CHW programs in Kenya. A Delphi method was then used to obtain expert consensus on the content and structure of the SOP.

**Results:** The SOP includes the identification and selection of CHWs, training and supervision, community mobilization, health data management, and referral procedures. In total, 796 CHWs were identified and selected for training. The implementation of the SOP had success in some of its components, including recruitment, selection, and training, deployment and supervision, service delivery, and referral and coordination. However, further assistance is required in monitoring and evaluation indicators, as well as challenges in requesting incentives and motivation by the CHVs.

**Conclusions:** The implementation of the SOP will require collaboration among key stakeholders, including the government, non-governmental organizations, and community members, to ensure its successful implementation and sustainability. The SOP provides a framework for CHWs to operate in a structured and consistent manner, which can lead to improved health outcomes, increased community trust, and strengthened healthcare systems.

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#### PERILOUS STATUS OF PEDIATRIC CANCER TREATMENT IN KOREA: SUGGESTIONS FROM THE KOREAN SOCIETY OF PEDIATRIC HEMATOLOGY-ONCOLOGY (KSPHO) TO RESUSCITATE VANISHING MEDICAL INFRASTRUCTURE FOR CHILDHOOD CANCER

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**Background and Aims:** South Korea has the world-record lowest total fertility rate of 0.78 in 2022. Rapidly shrinking pediatric population has led to abrupt decline of application for pediatric residency from 113% for 2017 to 17% for 2023. This study aims to suggest several ideas from the KSPHO to implement better governmental policy for the sake of Korean children with cancer

**Methods:** Since April 2021 we have conducted extensive data searches, big data analyses on national health insurance claim, in-depth interviews, and reviews on medical and legal systems of pediatric cancer care from the US, Japan, and the Netherlands. To draw public attention, several articles have been written for press, and public hearings were scheduled.

**Results:** Korea has an 85 percent five-year survival rate for pediatric cancer patients. Currently, only 67 pediatric hematology-oncology specialists are actively working to cover whole country of 50 million population. There is an eccentric centralization of specialists to Seoul-metropolitan area, already leaving provinces without specialists. Moreover, 1/3 of them will retire within 10 years. Thus, the collapse of pediatric cancer management in out-side Seoul area is clearly evident. The government now seems to turn ears to petitions and press from the Society. Finally, Mr. President of Korea ordered a special consideration to rescue the pediatric hematology-oncology services, especially in local areas. Five regional centers will be designated, for which financial and personnel support from national and local governments will be provided. Epochal revision of medical reimbursement fees considering age factor, severity of care, localization, comprehensiveness of services is now under investigation.

**Conclusions:** We have proposed the evidence-based recommendations from KSPHO. Further steps are needed, such as amendment of laws, governmental investment to regional centers, sufficient rewards to personnels, to maintain and to further improve survival and quality fo life of pediatric cancer patients in Korea.

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#### RECORD LINKAGE OF TWO NATIONAL REGISTRIES FOR RETINOBLASTOMA IN SOUTH AFRICA BETWEEN 2012-2017

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**Background and Aims:** Incomplete data on the incidence of retinoblastoma in South African children results in limited ability to monitor interventions and evaluate outcomes. This study aimed to compare data from the National Cancer Registry (NCR), a pathology-based registry, and the South African Children's Cancer Study Group Tumour Registry (SACCSG-TR), a clinical registry administrated by paediatric oncologists.

**Methods:** All children, under 15 years old diagnosed with retinoblastoma between 2012-2017 were included in the study. Due to the lack of unique identifiers between the two registries, probabilistic record linkage was done between the two registries to determine the proportion of matched and unmatched cases.

**Results:** A total of 460 cases of retinoblastoma were diagnosed overall between 2012-2017. There were 279 cases registered in the NCR and 363 cases in the SACCSG-TR. The median age pre-linkage was respectively 2.4 years and 2.34 years for the NCR and the SACCSG-TR, while the male-to-female ratio was similar (respectively 1:0.84 and 1:0.82). There were 182 matched cases (39.6%); with 97 (21.1%) unmatched from NCR and 181 (39.3%) cases from SACCSG-TR. The median age of matched cases was slightly higher at 2.69 years and 2.58 years for the NCR and the SACCSG-TR respectively. Unmatched cases from SACCSG-TR were mostly (43.7%) International Retinoblastoma staging system stage I and II. Approximately 60% of retinoblastoma cases were missed by both registries. The cases missed by the pathology-based NCR were early-stage intraocular disease cases, managed without enucleation and with no pathology reports. Cases missed by the SACCSG-TR might be due to enucleation done without referral to a paediatric oncologist.

**Conclusions:** This study highlights the need to merge the two registries to increase the reporting of accurate retinoblastoma incidence data in South Africa in line with the WHO Global Initiative for Childhood Cancer, which prioritises retinoblastoma.

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### CLINICO-ETIOLOGICAL PROFILE OF INFECTIONS IN CHILDREN WITH FEBRILE NEUTROPENIA DUE TO HEMATO-ONCOLOGICAL DISORDERS IN A TERTIARY CARE HOSPITAL IN EASTERN INDIA

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**Background and Aims:** Febrile neutropenia (FN), a dreaded complication in children with hematological disorders. There is a paucity of studies in the Indian Subcontinent on FN. Aim of our study was to find Incidence of clinically detectable infection Incidence of microbiological isolate Correlation between clinical focus and microbiological isolate in children with febrile neutropenia.

**Methods:** This is a single center cross-sectional descriptive epidemiology study done in a tertiary care hospital in Eastern India. Study was conducted for 13 months. After Institutional Ethics committee approval children aged 3 months to 15 years with absolute neutrophil count < 1500 /mm<sup>3</sup> with underlying haemato-oncological disorder, were included. Relevant laboratory investigations were sent. Data was entered in excel sheet and analysed using SPSS.

**Results:** Total 93 children with haemato-oncological disorders were included. Focus of infection was detected in 84 out of 121(69.4%) instances of examination. Lower respiratory tract was the commonest (19.8%) followed by upper respiratory tract and skin infections and musculoskeletal (1.65%) was the least common focus of infection. Most common organism grow in blood culture was MRCONS (41.4%). Most common organism in urine culture was E.coli (5.5%). Fungal isolates were seen in 2/105 (1.9%) samples. Among the virus, commonest viral agent detected was CMV (62.5%) followed by parvovirus. Out of 55 specimens with positive growth (blood, urine, ear swab, ET aspirate), 33 of them belonged to patients with ANC <500/mm<sup>3</sup>(60%), 10 (18.18%) to patients with a count between 500-1000/mm<sup>3</sup> and 9(16.3%) to patients with a count of 1000-1500/mm<sup>3</sup>.

**Conclusions:** Respiratory tract was the most common focus in children with FN. Children can have multiple foci at same time or during different episodes. Increasing consideration must be given to viral etiologies especially Cytomegalovirus which will reassure the clinician

regarding etiology of fever and limit indiscriminate use of antimicrobials. Fungal and parasitic etiologies are not common in the studied demographic.

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### THE COST OF PEDIATRIC CANCER CARE: HACETTEPE EXPERIENCE FROM TURKEY

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**Background and Aims:** Several recent studies from predominantly lower-middle income countries have reported the costs associated with running pediatric hematology/oncology units. As limited data from upper-middle income countries are available, we report the comprehensive costs associated with managing childhood cancer at a large tertiary center in Turkey.

**Methods:** The total cost center expenditures for oncology, hematology, intensive care, radiation oncology, laboratories, pharmacy, pathology, radiology, nuclear medicine, blood bank, operating theaters (surgery, neurosurgery, orthopedics) as well as hospital overhead were obtained from hospital information system for 2017. For each cost center, a “pediatric cancer care cost ratio” was calculated using various proxy measures such as the number of patients, inpatient days, lab and radiology investigations, and operating room suite hours. The annual pediatric cancer care costs was estimated based on the summation across all hospital cost centers. 5-year survival was calculated from the Hacettepe hospital-based cancer registry.

**Results:** 328 new pediatric cancers were diagnosed in 2017 and 5 year overall survival rate were 74.5%. The aggregated total annual cost for pediatric cancer care was estimated at 3,792,100 USD, reflecting 9.50% of total budget for departments. The cost per patient was 11,600 USD. By cost center categories, costs were: 1,527,720; 403,034; 276,521; 214,326; 77,555; 61,052; 43,819; 255,790; 131,653; 58,664; 247,353 (146,391; 69,743; 31,219); 494,623 USD for Oncology, Hematology, Intensive Care, Radiation Oncology, Laboratories, Pharmacy, Pathology, Radiology, Nuclear Medicine, Blood Bank, Operational Theaters (Surgery, Neurosurgery, Orthopedics) and Overhead, respectively. The staff costs, fixed assets, medical supplies, non-medical supplies, Others, Medical waste, House keepings, Washing, Overhead Costs made 44.34%, 5.71%, 25.15%, 3.80%, 2.15%, 0.33%, 4.87%, 0.60%, 13.04% of pediatric cancer related costs.

**Conclusions:** This is the first study of pediatric cancer care costs from Turkey, an upper-middle income country. These data are critical to ensure sustained investments in childhood cancer are used by stakeholders in all World Bank income-level settings.

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### NATIONAL CHILDHOOD CANCER PLANS IN LATIN AMERICA AND THE CARIBBEAN

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**Background and Aims:** Governments and ministries of health are key stakeholders in the fight against childhood cancer. They lead public-funded national health plans and specialized programs that provide diagnostic and treatment services, and address inequities in care. National childhood cancer plans (NCCP) are documents that define the cancer agenda and guide the implementation of national interventions. This abstract describes the collaborative work between the Pan American Health Organization (PAHO), St. Jude Children’s Research Hospital (St. Jude), international partners, and technical teams in twenty countries in Latin America and the Caribbean to develop their NCCPs.

**Methods:** In 2017, PAHO and St. Jude began working with eight countries to identify common initiatives focused on improving childhood cancer care. In the 4th St. Jude Global Alliance Central America and Caribbean meeting in Costa Rica (2019), participants unanimously recognized the need for and committed to developing national childhood cancer plans. More countries joined the working group with the launch of the Global Initiative for Childhood Cancer. St. Jude and PAHO supported the writing process with technical and financial resources for prioritized interventions, access to tools for childhood cancer planning, trainings, executing regional workshops and biweekly meetings, and offering individual technical assistance upon country request.

**Results:** As of February 2023, one regional framework is in place, nine countries are currently implementing national plans or laws that include childhood cancer, and ten countries are writing new plans. Success factors include multi-stakeholder engagement, leadership of a technical team to write the plan, the exchange of best practices between countries, and support from international partners. Common challenges are securing resources for implementation, keeping childhood cancer on the public agenda, and obtaining reliable data for evidence-based decision-making.

**Conclusions:** The experience from Latin America and the Caribbean can be adapted to support other countries developing a childhood cancer plan and extended to other public health areas.

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### USING THE ABBREVIATED PROFILE TO IDENTIFY SHARED PRIORITIES IN BRAZIL: PRELIMINARY RESULTS FROM TWO COHORTS

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**Background and Aims:** The Pediatric Oncology Facility Integrated Local Evaluation (PrOFILe) Abbreviated Version supports institutions to map resources and opportunities in the care of children with cancer. Brazilian institutions used the tool to develop initiatives to improve access to treatment, quality of care, and survival.

**Methods:** Two cohorts applied the tool. During the preparation phase, virtual meetings were scheduled to present the tool and engage stakeholders. In the assessment phase, institutions collected data using paper (2019) and electronic collection forms (2019 and 2021). CDC Epi Info software was used for data entry and analysis for both cohorts. For the interpretation and action phase, the 2019 cohort joined an in-person workshop where working groups were created to implement the selected projects. The 2021 cohort assigned priorities to existing working groups from AMARTE Alliance, a Brazilian collaborative group, during a virtual workshop using Zoom and MURAL.com. Project status was rated in January 2023 using a 10-point scale (1=initial implementation, 10=completed). Technical support from St. Jude Children's Research Hospital and project management were available to all working groups.

**Results:** Twenty-six Brazilian institutions implemented the Abbreviated PrOFILe: 15 in 2019, and 11 in 2021 (two implemented twice). More than 185 stakeholders from multiple disciplines participated in the workshops and prioritized nine initiatives across four modules: Context (2), Workforce (3), Diagnostics (2), and Patients & Outcomes (2). Eight projects are active with recurring meetings and deliverables. The median progress rate was 5 (range 3-8).

**Conclusions:** Using PrOFILe, participants identified common priorities and collaborated on projects despite disparities in Brazil. Both cohorts followed the same implementation methodology, with minor adjustments for specific needs. Assigning projects to working groups ensured continuity and accountability. In 2022, nine institutions from the 2019 cohort joined AMARTE, which will use PrOFILe results as a baseline to monitor impact. Deliverables from working groups are available to all AMARTE members.

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### SCREENING WITH A QUESTIONNAIRE FOR PEDIATRIC CANCER IN A MIDDLE-INCOME COUNTRY. ARE WE MISSING THE RED FLAGS?

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**Background and Aims:** In Mexico, 3 out of 4 children with cancer are diagnosed in advanced stages. There are different factors for this delay in diagnosis, for example, the pathology and the patient, the environment and the family, and those related to the health provider. New programs are directed toward childhood cancer to increase early

diagnosis. During the last year, primary care physicians applied a 27-questionnaire screening tool to detect warning signs of pediatric cancer during the regular pediatric consult. Primary center patients with a “positive questionnaire” are referred to a tertiary center to rule out cancer. This health policy aimed to improve the early diagnosis of pediatric cancer.

**Methods:** We reviewed the record of the patients referred from this questionnaire, leading 189 pediatric patients with cancer suspicious to the pediatric oncology outpatient clinic.

**Results:** The 189 pediatric patients referred for cancer risk evaluated in the pediatric oncology clinic did not require a further oncology workup. The most common positive signs were lymphadenopathy, headache, nose bleeding, lower-limb pain, and hyporexia. At least five patients required a psychology consultation for anxiety derived from the suspicion of malignancy.

**Conclusions:** This screening tool did not refer a patient at risk of cancer; otherwise, any of the patients who had a high risk of malignancy was referred by a primary care physician using this tool. It is essential to evaluate the number of “negative” questionnaires to assess the effectiveness of this policy because, at the moment, it is not a useful screening tool. We should continue expanding awareness, mainly in the primary care office, to achieve a timely referral to pediatric oncologists.

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#### THE FEASIBILITY OF ESTABLISHING A POPULATION-BASED CHILDHOOD CANCER REGISTRY IN THE DAKAR REGION OF SENEGAL: A PILOT STUDY FROM THE FRANCO-AFRICAN PAEDIATRIC ONCOLOGY GROUP (GFAOP)

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**Background and Aims:** Estimates of childhood cancer incidence in Africa are based on population-based registries from 14 African countries covering 5% of the total population of Africa. In 2016 a Hospital Based Cancer Registry (HBCR) was developed in the Pediatric Oncology Unit (POU) in Aristide le Dantec Hospital in Dakar as part of GFAOP collaboration. In 2020, Senegal was selected by the WHO

for the development of a national Cancer Plan. Following WHO recommendations, using the Dantec HBCR data, we carried out a feasibility study to establish baselines and pathways to enable the development of a population-based childhood cancer registry for the Dakar region.

**Methods:** We contacted, medical, academic and governmental bodies to identify sources for completeness of registration of diagnosed children <18 years between 01 Jan. 2017 and 31 Dec. 2019. Data from HBCR in the POU was completed for comparison with data collected on site from 4 regional pediatric institutions susceptible to diagnose and treat children in the target area.

**Results:** The Dantec HBCR registered 452 patients. Place of residence was known for all 452 patients, 133 came from the Dakar region, 278 from 13/14 other regions of Senegal and 41 from neighboring countries. The 4 additional institutions identified 311 patients, 169 of whom never attended the POU, the place of residence, treatment and outcome was unknown for these patients. This group also included 13 CNS tumors from neurosurgical services and 9 patients with Burkitt lymphoma, never referred to the POU. Burkitt lymphomas historically low in the region was 6% even with the addition of other regional service.

**Conclusions:** We identified the need to extend coverage of additional sources, improve completeness by registration especially for CNS tumors and better characterize the patient pathways. The small numbers of Burkitt and CNS tumors previously noted in HRCR Dantec, need to be examined with regional population-based data.

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#### CARING FOR CHILDREN WITH CANCER EVACUATED FROM UKRAINE: HOW IS IT FELT BY PATIENTS?

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**Background and Aims:** Since the war in Ukraine started on February 2022, many pediatric oncology centers in Europe have received patients from Ukraine. To understand the needs of patients and families reaching our hospital, an anonymous questionnaire was developed to investigate the families' backgrounds, needs, feelings, and impressions about hospitality.

**Methods:** After a month of treatment, 20 items were investigated: how patients had reached Italy and from whom the help was received (logistically/economically); emotions on the condition of war refugees; knowledge, expectations, and opinions about Italy and Italians; quality of medical care received and relationship with health staff; suggestions to improve assistance

**Results:** Questionnaires were completed by 19/32 patient (age 1-17 years, median 11) parents in the time interval May-November, 2022. Tumors affected Central Nervous System in 10 cases, there were 5 osteosarcomas, 4 neuroblastoma, and 13 others. Most families had reached Italy (58%) and received medical care (95%) thanks to the help of voluntary organizations and the Italian health care system. Many of them (69%) were satisfied by assistance. Italian population appeared to most patients as friendly (95%) and generous (58%). Only a minority express criticism about slowness and disorganization of health activities (15%). could the improvement of their stay correlated with the cure of their children (15%), the presence of their whole family (15%), the end of the war (10%), and the overcoming of language barriers (10%)

**Conclusions:** Taking care of children from a different country who suffered the traumatic experience of war which is added to the equally traumatic condition of cancer disease, is a huge task. Our questionnaire appears a useful tool to better understand patients' and families' conditions, not only from a clinical point of view but also from a psychological and cultural one, to bridge the relational gap between them and healthcare personnel

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#### CHANGES IN STRUCTURAL QUALITY INDICATORS IN DESIGNATED AFFILIATED HOSPITALS OF PEDIATRIC CANCER IN JAPAN

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**Background and Aims:** In Japan 15 core hospitals (CHs) for pediatric cancer treatment were elected to consolidate pediatric cancer patients. However, consolidation of pediatric cancer patients into 15 CHs is limited to 40%. In order to achieve advanced medical care and support in the other 60%, the development of affiliated hospitals (AHs) will be essential. The purpose of this study is to identify changes in structural indicators in AHs.

**Methods:** Twenty-one indicators for AHs (10 structure, 8 process and 3 outcome index) were developed in 2020. The structure indicators in 2020 were compared with that in 2019.

**Results:** With respect to pediatric oncologists and pediatric oncology-certified surgeons at AHs, there are 0 fewer facilities in 2020 compared to 2019 (from 10 to 7, from 63 to 61, respectively). The number of AHs without certified palliative care doctors decreased from 25 to 21. By 2020, the number of children's hospitals without palliative care specialists had decreased from 8 to 5. In 2020, medical care support personnel (MCSP) consisted of CLSs (44; 51.2%), HPS-Js (29; 33.3%), and Child Care Staffs (14; 16.1%), and they were assigned to only 33.7% (35/104 hospitals) of AHs. This was in contrast to the 87.5% (91/104 hospitals) of AHs that had child care providers. Furthermore, the number of hospitals with no MCSP in 2020 compared to 2019 increased from 68 to 69, and the number of AHs with three or more personnel decreased from seven to four. This decrease occurred at university and general hospitals rather than at children's hospitals.

**Conclusions:** By calculating the QI over time, we have been able to visualize the quality of pediatric cancer care in Japan. The insurance system in Japan reveals that staffing related to pediatric oncology care is gradually progressing, leading to reimbursement. On the other hand, the assignment of MCSP reveals a trend toward regression.

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#### THE EVALUATION OF TASK SHARING PRACTICES FOR PEDIATRIC CANCER CARE IN PAKISTAN

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**Background and Aims:** Task sharing has been implemented as a pragmatic response to the shortage of pediatric oncologists in many settings, especially in low-middle-income countries. Importantly, how task sharing has been implemented has not been widely evaluated. This study sought to describe the roles and tasks assigned to non-specialists caring for children with cancer in Pakistan.

**Methods:** This multicenter study utilized a survey to identify the institution-specific models used to implement task sharing, defining the responsibilities that are routinely performed by non-specialists.

**Results:** Fifteen pediatric cancer units provided responses. These included general, pediatric, and cancer hospitals, ranging from secondary to quaternary level facilities. Of the professionals engaged in task sharing, resident medical officers (RMOs) and registrars were the most common, followed by general pediatricians. Task sharing professionals provided inpatient (n=12), outpatient (n=11), emergency room (n=15) and overnight coverage (n=14). They could decide on unplanned admissions such as febrile neutropenia (n=14). They participated in defining cancer diagnosis and risk-stratification (RMOs (n=2), registrars (n=7), pediatricians (n=6)), selecting initial chemotherapy plans (RMOs (n=1), registrars (n=2), pediatricians (n=4)), and modifying chemotherapy based on toxicities (RMOs (n=2), registrars (n=2), and pediatricians (n=2)). Under supervision of a pediatric oncologist, they could write intravenous chemotherapy (RMOs (n=6), registrars (n=7), pediatricians (n=4)), and prescribe oral chemotherapy (RMOs (n=5), registrars (n=6), pediatricians (n=6)). Procedures were also performed by task sharing physicians including lumbar punctures (RMOs (n=7), registrars (n=12), pediatricians (n=8)), administration of intrathecal chemotherapy (RMOs (n=7), registrars (n=9), pediatricians (n=4)), and bone marrow aspiration/biopsy (RMOs (n=5), registrars (n=8), pediatricians (n=4)). All patients seen by task sharing professionals were discussed with a pediatric oncologist (n=13).

**Conclusions:** In Pakistan, task sharing professionals are responsible for many essential steps in the pediatric cancer care continuum, spanning from initial diagnosis and risk stratification to the prescription of chemotherapy. Tiered training initiatives are being planned for this critical workforce.

EP700/#229 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
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#### EPIDEMIOLOGY OF PEDIATRIC HEMATOLOGICAL MALIGNANCIES IN KAZAKHSTAN: DATA FROM UNIFIED NATIONAL ELECTRONIC HEALTH SYSTEM 2014-2019

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**Background and Aims:** We aimed to investigate incidence, prevalence and all-cause mortality of hematological pediatric malignancies (leukemia and lymphomas, with their subtypes) and distributions, changes over time in Kazakhstan based on nationwide large-scale healthcare data from the Unified National Electronic Health System (UNEHS) for 2014-2019 year period.

**Methods:** Cohort included data of patients less than 18 years old with the diagnosis of hematological malignancies registered in the UNEHS (inpatient and outpatient registries). Descriptive statistics were conducted to indicate socio-demographic, medical characteristics of the cohort. Incidence, prevalence, all-cause mortality were calculated per 100,000 population. Cox proportional hazard regression analysis, Kaplan-Meier survival estimates were performed.

**Results:** The cohort population (n=2,348 of leukemia and n=1,275 of lymphoma) with mean age at diagnosis of pediatric leukemia is 7.2±4.6 years, whereas for lymphomas it is 9.8±4.8 years. Age-specific standardized incidence rates of pediatric leukemia is the highest for 0-5 years age group (7.9 per 100,000 in 2019). Patients with ALL (acute lymphoblastic leukemia) had higher incidence rate than patients with AML (acute myeloid leukemia) (3.2 and 0.9 per 100,000 in 2019, respectively). The incidence rate of HL (Hodgkin lymphoma) and NHL (non-Hodgkin lymphoma) was relatively similar which varied from 0.7 to 2.1 per 100,000 in 2014-2019. Prevalence rate of hematological malignancies increased from 9.5 to 49.6 per 100,000 between 2014-2019. All-cause mortality of pediatric hematological malignancies varied from 0.8 to 1.5 per 100,000 in 2014-2019, with the peak in 2019 (1.9 per 100,000). Younger age, male sex and Kazakh ethnicity are significantly associated with increased all-cause mortality.

**Conclusions:** Leukemia and lymphomas reported as the most common types of malignancies in children in Kazakhstan with increasing prevalence and mortality rates. For the future perspectives, there is a need for a separate registry for childhood tumors with detailed data on relapses, treatment effectiveness, short and long-term side effects of specific therapies.

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#### REIMAGINING GOVERNANCE TO IMPROVE PAEDIATRIC AND ADOLESCENT CANCER CARE IN SOUTH AFRICA: SOUTH AFRICAN CHILDHOOD CANCER STUDY GROUP AND ST JUDE GLOBAL MEDICINE CO-DESIGN EXERCISE

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**Background and Aims:** The coordination of paediatric and adolescent cancer care in South Africa is fragmented. Members of the South African Childhood Cancer Study Group (SACCSG) and St Jude Global Medicine held a workshop in 2022 to identify opportunities to strengthen the governance of the SACCSG.

**Methods:** Thirty participants from organisations involved in paediatric and adolescent cancer care in South Africa and St Jude Global attended a workshop. Participants worked in four groups (governance, clinical focus, administrative structure, and education) identifying opportunities to empower the SACCSG. The groups conducted a thematic SWOT (strengths, weaknesses, opportunities, threats) analysis of their focus area. A mission exercise involved defining the role and development of a mission statement. An organization design exercise was conducted to seek critical activities and functions required to achieve the new mission statement.

**Results:** Participants provided recommendations to strengthen the SACCSG recognizing a committed paediatric and adolescent cancer expertise group as a strength. Weaknesses included a lack of infrastructure, equity, and central funding. Identified opportunities for improvement were reimagining governance structures, multidisciplinary transformation in leadership, and refining research activities. Additionally, participants identified the need for increased outreach, resource-sharing, collaboration with other groups, and training in psychological, palliative, and long-term follow-up care. The outcomes from the workshop provide a roadmap for the SACCSG to enhance its structure, processes, and impact in paediatric and adolescent cancer care in South Africa.

**Conclusions:** Outputs of the SACCSG co-design exercises have been instrumental in driving organisational change. Considerable progress in redrafting the constitution and organogram defining membership and responsibilities. These outputs are crucial to ensure that the SACCSG is well-equipped to improve performance and provide high-quality paediatric and adolescent oncology services.

EP702/#1717 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
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## PEDIATRIC CANCER PREDISPOSITION REGISTRY: RESULT OF A PILOT STUDY FROM JAPAN CHILDREN'S CANCER GROUP (JCCG)

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**Background and Aims:** At least 10% of pediatric patients with cancer have germline pathogenic variants in cancer-predisposing genes. Our previous survey showed that 66% of children clinically diagnosed with or suspected of having genetic predisposition to cancer in Japan had not received genetic testing, mainly due to the lack of availability of genetic testing. The aim of this pilot study is to assess the need for the registry and its feasibility, to provide genetic testing and to accumulate the variant and clinical data at baseline and follow-up.

**Methods:** Eligible participants included (I) patients diagnosed with cancer under the age of 40 and clinically suspected of (or diagnosed with) a cancer predisposition syndrome or (II) relatives, at any age, of the patients who are genetically diagnosed with a cancer predisposition syndrome in this study. Each case was reviewed and discussed in multidisciplinary teams both before and after genetic analysis. The



analysis was performed using single-gene testing and/or multi-gene panel testing.

**Results:** Between January 2022 and December 2022, 72 cases were registered, 55 of whom met the criterion (I) and 17 who met the criterion (II). Of the 64 cases in which analyses were completed, 35 (54.6%) were genetically diagnosed with cancer predisposition syndrome including Li-Fraumeni syndrome (N=11), DICER1 syndrome (N=9), hereditary pheochromocytoma paraganglioma syndrome (N=3), von Hippel-Lindau syndrome (N=2), and others (N=10).

**Conclusions:** Over half of the participants were genetically diagnosed with cancer predisposition, and Li-Fraumeni Syndrome and DICER1 syndromes were most frequent. Our preliminary results demonstrate the need and promise for establishing a pediatric cancer predisposition registry with a multidisciplinary review board. We will confirm the registry's logistics, including updating family histories and other follow-up clinical data. Further analysis using whole-genome sequencing in cases of suspected cancer predisposition for which the underlying genetic causes have not yet been detected is planned.

EP703/#1432 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
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#### ORGANIZATION OF SHORT-TERM OBSERVERSHIPS FOR UKRAINIAN PEDIATRIC HEMATOLOGY-ONCOLOGY SPECIALISTS DURING WAR

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**Background and Aims:** Specialized training in pediatric hematology and oncology (PHO) is crucial to improve pediatric cancer care. In Ukraine, PHO training was severely compromised by the pandemic and Russian invasion. In collaboration with Supporting Action for Emergency Responses (SAFER Ukraine), Tabletochki Charity Foundation (Tabletochki) launched a short-term observership program to sustain and improve the competencies of PHO workforce in Ukraine.

**Methods:** An application form was developed and distributed within Ukrainian PHO network to select candidates. Selection criteria included: (1) Employment in the Ukrainian PHO system; (2) English proficiency; (3) Age under 45 years. Training hospitals were chosen based on educational need of the applicants and capacities of accepting institutions. Experience feedback forms were sent to observers and supervisors in accepting hospitals. Tabletochki covered all logistics expenses, while accepting hospitals absorbed the costs of the educational program.

**Results:** Out of 41 applicants, 23 were selected to participate and 22 (96%) completed 2 to 3 week observership (August - December 2022). Among the group, 64% were physicians and 36% laboratory specialists from four major Ukrainian PHO hospitals. Observers were accepted by hospitals in Netherlands, Poland, Germany, Czech Republic, and Spain. Feedback received from both observers and supervisors was positive. Identified areas for improvement include more precise matching of educational needs to facilities' areas of expertise, decreasing the number of trainees undergoing observership in the same facility simultaneously, improvement of observers' language proficiency. As a result of this initiative, enrollment, and retention in free English language courses provided by Tabletochki increased 164%. PHO specialists started to proactively reach out to Tabletochki with their educational needs, demonstrating increased interest in the program.

**Conclusions:** The experience of the Ukrainian PHO observership program demonstrates that despite challenges presented by war, clinicians remain motivated to improve their competency. The second round of observerships has already started with implementation of provided feedback.

EP704/#1490 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
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#### IMPLEMENTATION MAPPING TO ADDRESS SOUTH AFRICAN CHILDHOOD CANCER PRIORITIES: A ST. JUDE GLOBAL AND SOUTH AFRICA CHILDREN'S CANCER STUDY GROUP (SACCSG) COLLABORATION

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**Background and Aims:** In 2021, the South African Children's Cancer Study Group (SACCSG) collaborated with St. Jude Children's Research Hospital to identify national opportunities for collaboration using the St. Jude Paediatric Oncology Facility Integrated Local Evaluation (PrO-FILE) tool. To further refine priorities and plan next steps, a two-day strategic workshop was held in Johannesburg in 2022 among key stakeholders.

**Methods:** We applied a modified implementation mapping approach, an implementation science method used for designing multi-level health interventions and strategies. The workshop was attended by thirty participants representing twelve of thirteen public-sector institutions, the South African Department of Health, the National Cancer Registry, and foundations. Participants and any additional priorities were identified by SACCSG leadership and the heads of units. All workshop attendees participated in four structured co-design activities. These activities included prioritizing initiatives identified by the SACCSG, setting defined goals for each priority, co-designing project-specific logic models, reviewing potential barriers to implementation, and developing a post-workshop agenda.

**Results:** Three additional priorities were added to the twelve priorities identified from PrOFILE. Through structured discussion and voting, the participants identified six priority areas of focus: redrafting the organization's constitution; standardization of multidisciplinary reporting; development of protocols and treatment guidelines; establishing fever-management guidelines; strengthening chemotherapy safety practices; enhancing Hospital Based Cancer Registries. Each priority was assigned to a working group, with four of the six groups continuing their efforts six months after the workshop. The remaining two groups are collaborating with other global initiatives, such as Adapted Resource and Implementation Application (ARIA).

**Conclusions:** Using an implementation mapping approach enabled key stakeholders to develop actionable plans. The success of this approach is demonstrated by the active implementation of the identified priorities by focused working groups. This approach could serve as a model for countries with identified priorities but lack clear means to implement them.

EP705/#326 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
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## VACCINE ACCEPTANCE AMONG PEDIATRIC ONCOLOGY AND BONE MARROW TRANSPLANT PATIENTS: A FOCUS ON COVID-19

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**Background and Aims:** Vaccine hesitancy among immunocompromised populations such as pediatric oncology and bone marrow transplant (BMT) patients is complex and not well understood. This study aimed to determine the rate of vaccine hesitancy among pediatric oncology and BMT patients and to understand factors associated with vaccine acceptance for COVID-19.

**Methods:** Parents of patients ( $\leq 18$  years) who were treated for cancer or received a BMT were recruited from the Alberta Children's Hospital in early 2023. Patients on active therapy as well as post-therapy surveillance were included. Participants completed a modified version of the Parent Attitudes about Childhood Vaccines Survey which included questions specific to the COVID-19 vaccine. A COVID-19 vaccine hesitancy score (COVID-VHS) was scored from 0-18 (higher score indicates increasing vaccine hesitancy).

**Results:** Among 46 parents, the majority were female (63%) and at least college/university educated (77%). Regarding their children, the majority (76%) were patients with cancer (55% leukemia/lymphoma, 45% solid/CNS tumors) while 24% had received BMT. Most patients were undergoing active treatment (78%), with the remainder in surveillance. Only 24% of patients had been vaccinated against COVID-19. Vaccine hesitancy (32%) and ineligibility due to age (32%) were the top two reasons for not vaccinating patients against COVID-19. Only 14% of parents said they would "definitely vaccinate" their child if they became eligible. COVID-VHS was higher but not significant for patients with leukemia/lymphoma compared to solid/CNS tumors (mean 10.7 versus 7.2;  $P=0.06$ ), as well as for patients with cancer vs. post-BMT (mean 9.4 versus 5.8;  $P=0.05$ ). COVID-VHS was not significantly associated with any of the following factors: diagnosis, relapse status, active treatment vs. surveillance, or parental demographic factors (gender, education, income, child's school).

**Conclusions:** Vaccine hesitancy is common among parents of children with cancer and post-BMT. More research is needed to clarify factors associated with vaccine hesitancy among immunocompromised populations.

EP706/#92 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
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### RAPID DECREASE IN PEDIATRIC ONCOLOGY MEDICAL CAPACITY IN POLAND DUE TO WAR IN UKRAINE

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**Background and Aims:** Three days after the Russian invasion of Ukraine, the first Ukrainian refugee child with cancer arrived at a Polish Pediatric Hematology Oncology Center (PPHOC) seeking care. Poland, a neighboring country, rapidly became the main destination for over half of Ukrainian refugees. The goal of this study was to assess the changes in PPHOC capacity during the first eleven weeks of war.

**Methods:** This multicenter longitudinal analysis was conducted at all 19 PPHOCs. First, we measured each PPHOC capacity using annual cancer patient volume during the three preceding years, as well as patient-to-physician (PtP), patient-to-nurse (PtN) and patient-to-bed (PtB) ratios before and during the first 11 weeks of war. Finally, the effect of decreased medical capacity on PPHOC care was evaluated through the delay in access to complex medical procedures requiring general anesthesia.

**Results:** During the study period of 11 weeks, 237 Ukrainian refugee children with cancer were treated in the PPHOCs. Most patients (60%) arrived during the first 21 days of war. Depending on the PPHOC, this corresponds to a 42%-460% increase in the patient volume. The average PtP, PtN and PtB ratios in PPHOC were 0.76 (0.5-1) vs. 1.41 (0.96-1.78)  $p=0.001$ , 0.35 (0.27-0.55) vs. 0.81 (0.58-1.08)  $p=0.001$  and 0.36 (0.31-0.5) vs. 0.74 (0.5-1.11)  $p=0.001$  before and after the war, corresponding to a significant increase of 85%, 131% and 105%, respectively. Similarly, there was an increase in medical procedures delays after the war began, with 18.2% of procedures being delayed compared to 15% before the war ( $p=0.043$ ).

**Conclusions:** Cancer care in Poland has been significantly affected by the large influx of Ukrainian children with cancer fleeing the war, resulting in reduced PPHOC capacity. To ensure that standards of care are maintained, further patient referral to medical facilities around the world became necessary, which was facilitated by the SAFER Ukraine initiative.

EP707/#1646 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

### FIVE DECADES OF CHILDHOOD CANCER IN ESTONIA

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**Background and Aims:** In 2021 a new national Cancer Control Plan (CCP) was developed in Estonia, including for the first time a separate chapter for childhood and AYA cancers. Aiming to meet many strategic goals but foremost to ensure accurate and timely diagnosis by increasing awareness, twinning and setting up a monitoring system for families with genetic predisposition to cancer. Childhood cancer a rare disease per se together with the small population size of Estonia make it hard to understand the changes in cancer incidence. We therefore aimed to use all available cancer data to evaluate incidence trends through five decades.

**Methods:** Data on all malignant cases, diagnosed in children aged 0–14 between 1970–2019, were obtained from the Estonian Cancer Registry. Age-specific and age-standardised (World standard) incidence trends were evaluated by ICC-3 site groups, calculating annual percentage change with Joinpoint Regression Program.

**Results:** Within fifty years 1737 children received a cancer diagnosis, yielding an incidence rate of 130 per million. Lymphoid leukemia, astrocytoma and Wilms tumor were most often diagnosed sites with incidence rates of 25, 14 and 10 per million, respectively. Incidence increased from 115 in the first decade to 153 per million in the last (annual percentage change of 0.6%). Incidence increased for both sexes but was statistically significant only for boys.

**Conclusions:** During the observed period major political and health-care transformations took place in Estonia. Decrease in the number of unspecified neoplasms indicates improved diagnostics but statistically significant overall increase refers to an actual rise. Therefore, as stated in the CCP, to grant our children the best possible treatment and outcome, it is crucial to develop monitoring guidelines for families with genetic susceptibility, to increase the awareness of parents and primary healthcare workers and to set up collaboration with other pediatric oncology centres to provide accurate diagnosing for more complex and rare cases.

EP708/#733 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### IMPACT OF DEDICATED OUT-PATIENT PEDIATRIC CANCER GENETICS SERVICES ON THE DETECTION OF CANCER PREDISPOSITION SYNDROMES IN CHILDHOOD CANCERS

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**Background and Aims:** Integration of cancer predisposition screening into routine cancer-care can have far-reaching consequences, identifying patients and families eligible for therapy modification and early cancer surveillance, since family history and clinical phenotype are

absent in the majority. Pre-2021, patients suspected to have pediatric-Cancer Predisposition Syndrome (p-CPS) were randomly referred to hospital-Cancer Genetics Clinic (CGC) in our institute. We studied the impact of a dedicated pediatric-CGC in the outpatient department.

**Methods:** Pediatric-CGC started in September-2021 with a certified genetic counsellor. P-CPS-oriented proforma with details of target population eligible for testing, consent and assent were developed. Screened patients if eligible were tested post-counselling. Next Generation Sequencing (NGS)-26-gene Sophia panel and targeted TP53, NF-1, DICER, Rb sequencing were used initially, and 94-gene Illumina panel later. Post-test counselling included offer of extended-family testing and surveillance where required. We compared patients referred, tested at pediatric-CGC from October 2021-April 2022 (6months) to those who attended hospital-CGC in 2018-2019 (2years).

**Results:** One-hundred twenty patients were registered [diagnosis of first primary-64(53.3%), relapse/refractory-53(44.2%), second malignancy-3(2.5%)] in pediatric-CGC during 6months. Median age at registration was 5years (range,1month-37years). Positive family history of cancer was noted only in 13(10.8%), specific for CPS in 6(5%). Tumor characteristics dictated testing in 100(83.3%), patient characteristics in 38(31.7%), physical features in 15(12.5%). Of 91 samples tested, 31(34.1%) were positive for CPS (LFS-12, CMMRD-3, Lynch-2, FAP-1, DICER-1, NF1-2, NF2-1, RB-9), VUS-16(17.6%). Median time to reporting from testing was 47days. Hospital-CGC in 2018-2019 registered only 58 patients and tested 12 samples.

**Conclusions:** The availability of a dedicated and targeted cancer predisposition screening service in outpatient-clinic is a practical and feasible strategy in the developing world. This strategy detected CPS in one-third of the tested population in our clinic, asserting the need for the incorporation of genetic CPS screening services into routine cancer care to identify CPS beyond family history.

EP709/#1146 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### EARLY DIAGNOSIS OF CHILDHOOD CANCER: ATTITUDES AND KNOWLEDGE OF HEALTH AGENTS IN SIKASSO HEALTH CENTERS

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**Background and Aims:** BACKGROUND The situation of childhood cancer is alarmingly in sub-Saharan countries where the cure rate does not exceed 15 to 20 %. This is due to insufficient means of diagnosis, to the delay of treatment and especially to the lack of adapted chemotherapy protocols. The delay in diagnosis is based on a complex chain of factors and events complicated by the difficulties. Early diagnosis is a

fundamental objective in oncology. **AIM** The main aim is to evaluate the knowledge and attitudes of medical and paramedical personnel in the early diagnosis of childhood cancer in the health district of Sikasso.

**Methods:** **METHOD:** This is a prospective, descriptive, cross-sectional study conducted over 6 months in 2021 on a sample of 120 community health workers. Data collection was carried out using a previously tested structured questionnaire.

**Results:** **RESULTS** We interviewed 120 health workers and noted that 36.67% were general practitioners, 29.17% were nurses, 5.83% were pediatricians, 10.8% were midwives, and 17.5% were from other specialties. According to them, the first signs of cancer were adenopathy (90.8%), abdominal mass (89.2%), hepatosplenomegaly (75.8%) and 75.8% stated that there was a predisposition to cancer in children. In front of an abdominal mass 51.6% requested an abdominal ultrasound. 92.5% of the agents thought that management depended on early diagnosis.

**Conclusions:** **CONCLUSION** The lack of knowledge of the early signs of cancer leads to delayed diagnosis. It is necessary to develop strategies based on information, education and training of medical and paramedical staff in order to reduce the long delay in consultation and therefore in diagnosis. **ACKNOWLEDGEMENTS:** GFAOP Hospital of Sikasso.

EP710/#257 | **Poster Topic: AS05 SIOP Scientific Program/AS05.r Epidemiology, Policy and Advocacy**

#### EXPANDING THE IMPACCT MODEL ACROSS INDIA: LESSONS LEARNT OVER A DECADE

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**Background and Aims:** We have previously reported how the 'Improving Paediatric Cancer Care and Treatment' (ImPaCCT) foundation established in 2010 to offer holistic support to children with cancer at the Tata Memorial Centre (TMC), Mumbai led to a dramatic reduction in treatment abandonment from >20% to <5%. We report the impact of the expansion of the ImPaCCT model within TMC, Mumbai and at other TMC centres across the country.

**Methods:** The initial components of care provided by ImPaCCT at TMC were limited, but now expanded to include increased manpower, complete financial, nutrition and blood product support, and significant support for housing and survivorship care. This model was expanded at TMC, Mumbai and subsequently replicated strategically across five TMC centres in five states of India starting 2016. We assessed the

impact in terms of numbers supported, funds raised and rates of treatment abandonment (TxA).

**Results:** The ImPaCCT model has helped support the treatment of 28967 children with cancer since 2010, (21162 at TMC Mumbai and 7805 at other TMC centres), and employs 60 full-time support staff. A total of 37,740,000 USD has been raised from the government, non-governmental organizations, corporate and individual donors (75,000 USD in 2010 to 7,000,000 USD in 2022). TxA rates at TMC, Mumbai have been <5% since 2014 and <2% since 2021, and have dropped from >20% in 2018 to 12% in 2022 at other TMC centres. 1357 survivors have received funding for medical management and formal education.

**Conclusions:** The ImPaCCT model is a sustainable holistic support model, which has expanded in TMC to serve increasing numbers of children with cancer. Replication of this model to other TMC centres has led to improved support for treatment and decrease in TxA. The ImPaCCT model has potential to be adapted and implemented in other centres treating children with cancer across India and similar settings.

EP711/#958 | **Poster Topic: AS05 SIOP Scientific Program/AS05.r Epidemiology, Policy and Advocacy**

#### INTERNATIONAL BENCHMARKING OF CHILDHOOD CANCER SURVIVAL BY TUMOUR STAGE, FIRST RESULTS OF THE BENCHISTA PROJECT

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**Background and Aims:** Variation in tumour stage at diagnosis may explain international differences in childhood cancer survival. The BENCHISTA project aims to test this hypothesis and to encourage the application of Toronto Stage Guidelines (TG) by Population Based Cancer Registries (PBCRs).

**Methods:** Participating PBCRs collected TG at diagnosis for all cases of six paediatric solid tumours (Osteosarcoma, Ewing Sarcoma, Rhabdomyosarcoma – age 0-19yrs; Wilms Tumour, Neuroblastoma, Medulloblastoma – age 0-14 yrs) diagnosed in a 3yr window between 2014-2017. PBCRs submitted patient-level, depersonalized datasets with Tier 1 or Tier 2 staging information dependent on their clinical support and/or legally accessible clinical data sources. Online training followed by quality assurance tests were used for standardization. Three-years overall survival by tumour type and stage were analysed using standard Kaplan-Meier methods.

**Results:** PBCRs from Australia, Brazil, Canada, Japan and twenty-four European countries participated. Analysis of 7,674 cases received by Feb 2023 (~75% of expected total) showed stage completeness is highest for Wilms tumours (96%) and lowest for medulloblastoma (90%). The proportions with metastases at diagnosis were 18.2% for 1,615 Wilms tumours; 32%(M) + 9%(MS) for 2,048 neuroblastomas; 32%(M1-M4) for 1,106 medulloblastomas; 23% for 1,127 osteosarcomas; 31% for 757 Ewing sarcomas and 28% for 1,021 rhabdomyosarcomas. 3yr OS for all cases were respectively 93.4%(WT); 80.9%(NBL); 75.4%(MBL); 72.7%(osteosarcoma); 71.5%(Ewing); 73.2%(RMS). For all 6 tumours a gradient was present in 3-year survival by-stage; the largest differences were observed in the three sarcomas, which each had 3yr OS of 43% for metastatic disease compared to 94% for stage 'I' Rhabdomyosarcoma and, 82% and 85% respectively for localized osteosarcoma and Ewing.

**Conclusions:** PBCRs have successfully applied the TG to share data on stage at diagnosis. The BENCHISTA Project is strengthening collaborative relationships between PBCRs and clinicians to interpret geographic variations in childhood cancer outcomes. Funded by Children with Cancer UK, Italian Association Cancer Research (AIRC)

EP712/#1274 | **Poster Topic: AS05 SIOP Scientific Program/AS05.r Epidemiology, Policy and Advocacy**

#### INTERNATIONAL VARIATION IN CHILD HEALTH SURVEILLANCE AND ACUTE CARE PRACTICES: A MIXED METHODS ANALYSIS

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**Background and Aims:** Differences in pathways to medical attention and timely diagnosis for symptomatic children may partly explain variation in childhood cancer survival rates observed between countries. This study aims to assess current evidence in child health surveillance and acute care practices and to perform a descriptive comparative analysis of child health practices in countries participating in the International Benchmarking of Childhood Cancer Survival by Stage (BENCHISTA) Project.

**Methods:** Mixed methods approach comprising a) Literature review of articles published in the last decade using five databases, conducted according to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses); b) Semi-structured questionnaire, addressed to one general practitioner and one general paediatrician per country, to collect standardised data on child health prac-

tices and signpost data sources for national health policies and practice.

**Results:** 2,788 articles were screened; 30 articles met eligibility criteria for inclusion. Three main topics were highlighted as important for timely diagnosis: pathway to diagnosis, awareness of alarm signs/symptoms of childhood cancer (parents and professionals) and factors affecting the timely diagnosis of serious illnesses including lack of knowledge of risk associated to specific symptoms, variation in paediatric training of front-line practitioners, among others. The questionnaire was piloted, and vocabulary refined. Answers from 51 practitioners from 25 countries revealed a noticeable variation in child health surveillance practices, particularly in the number of universally offered check-ups with physical examination for children <5 years old (median: 10, range: 2-21). Validation against national published guidance was performed.

**Conclusions:** Marked variation is found between countries in terms of frequency of routine child health surveillance, direct access to assessment by a paediatrician for children with acute symptoms and availability of guidelines to raise awareness of serious conditions including cancer. These data are being used to categorise countries for interpretation of variation in tumour stage at diagnosis in the BENCHISTA Project. Funded by CwC\_UK, IACR.

EP713/#1164 | **Poster Topic: AS05 SIOP Scientific Program/AS05.r Epidemiology, Policy and Advocacy**

#### INCIDENCE AND PATTERN OF CHILDHOOD CANCERS IN CHENNAI, INDIA: AN ANALYSIS OF POPULATION-BASED CANCER REGISTRY DATA AND QUALITY ASSESSMENT

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**Background and Aims:** The incidence and pattern of childhood cancers in low-and middle-income countries (LMICs) like India are not well studied. Therefore, we analyzed the data from the population-based cancer registry (PBCR) in Chennai, India, to determine the incidence and percentage of childhood cancers and evaluated the data quality using data quality indices.

**Methods:** Data from the Chennai PBCR collected from 2002-2017 were analyzed based on age group, sex, and the international classification of childhood cancer, third edition (ICCC-3). The incidence was reported as the age-standardized rate per 1,000,000 population. Data quality indices were used to evaluate the completeness, validity, and reliability of the information.

**Results:** The study identified a total of 2749 cases of childhood cancer, with a higher incidence rate in boys (59%) than in girls (41%), and a male-to-female ratio of 1.4:1. The highest incidence was observed in the 0-4 age group, with 789 cases (29%), followed by the 15-19 age

group with 747 cases (27%). Leukemia was the most common childhood cancer, accounting for 53% of all cases, followed by lymphomas (18%), and central nervous system tumors (11%). For boys, the ASR was 18.26 per million for ages 0-4 years, 14.85 per million for ages 5-9 years, 11.62 per million for ages 10-14 years, and 13.41 per million for ages 15-19 years. For girls, the ASR was 12.27 per million for ages 0-4 years, 9.93 per million for ages 5-9 years, 7.93 per million for ages 10-14 years, and 8.70 per million for ages 15-19 years. The data quality indices showed good completeness (98%), validity (98%), and reliability (97%) of the data.

**Conclusions:** This study provides valuable information on the incidence and pattern of childhood cancers in Chennai, India. The data highlights a higher incidence of childhood cancer in boys and a higher incidence in the 0-4 age group.

EP714/#1201 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### EARLY MORTALITY IN MALIGNANT BONE TUMORS DURING THE COVID-19 PANDEMIC IN A MIDDLE-INCOME COUNTRY

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**Background and Aims:** The COVID-19 pandemic impacted the population's social and economic conditions and vastly affected health systems' capabilities for effective care delivery. In low-and-middle-income countries (LMIC), COVID-19's impact on childhood cancer mortality is unknown. We investigated COVID-19's effect on early mortality in children with bone tumors in ten cities in Colombia.

**Methods:** We prospectively collected data from children (<15 years) included in the Childhood Cancer Outcomes Surveillance System (VIGICANCER) from 2017 to 2021. The "COVID-19 pandemic period" included cases diagnosed 2020-2021. Children diagnosed with cancer during the study period were the exposed cohort (EC). Using Kaplan-Meier, we compared the cumulative mortality rate and survival in the EC with a historical cohort (HC; 2017-2019). We adjusted the hazard ratio estimates (HRa) for covariates using proportional risks multivariate regression.

**Results:** From 4197 children enrolled in VIGICANCER during the study period (EC 1692, HC 2505), 251 were diagnosed with a malignant bone tumor (EC 104, HC 147). Osteosarcoma was diagnosed in 63% (n=157; EC 70, HC 87), Ewing sarcoma in 31% (n=79; EC 26, HC 53),

and other in 6% (n=15; EC 8, HC 7). Ninety-three cases (37%) were metastatic, with no differences between cohorts (EC 41% vs HC 34%; p=0.29). Children with bone tumors in the EC showed an increased risk of death at 6 months post-diagnosis (HRa=3.4 95%CI:1.2, 10.1) and at 24 months post-diagnosis (HRa=1.7, 95%CI: 1.1, 2.8). The association of the EC with 6-months mortality decreased but persisted when including metastatic status (HRa=2.9 95%CI: 1.0, 8.7).

**Conclusions:** We found a three-fold increase in mortality risk at 6 months post-diagnosis in children diagnosed with bone tumors during the COVID-19 pandemic. This association remained in children with metastasis, suggesting other causal pathways to mortality. Next steps include investigation of COVID-19's effects in other tumors and follow-up analysis to assess long-term effects of COVID-19 on survival.

EP715/#1319 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### IS TREATMENT ABANDONMENT A DEAD END? A DEDICATED TASKFORCE FOR MISSED APPOINTMENTS CALL-BACK SYSTEM AT INDUS HOSPITAL, KARACHI

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**Background and Aims:** Abandonment of cancer treatment compromises the survival of approximately one in seven children worldwide. Abandonment of treatment is defined as either failure to initiate therapy or discontinuation of ongoing curative treatment for 4 or more weeks. The abandonment rate in Pakistan has previously been documented at 42%. Risk factors include financial limitations, long distances, lack of public transport, poor nutritional status and parental perception of disease. The Indus Hospital & Health Network (IHHN) in Karachi registers over 1200 children with malignancy annually, providing completely free of cost treatment, dedicated to improving treatment outcomes.

**Methods:** Following the PrOFiLE workshop at IHHN, a dedicated taskforce to reduce treatment abandonment was created in June 2022. A staff member was assigned for daily tracking of missed appointments and call-backs to document reason for absence. A rescheduled date was provided on call and those who failed to attend the second appointment or showed unwillingness to continue were referred for further counselling to social workers and their primary consultant. Financial assistance, residence and transportation facilities were offered to struggling families.

**Results:** From June 2022 to February 2023, a total of 1184 appointments were missed by on-treatment and off-therapy patients at a monthly average of 169±32.8. Over 55% of these patients returned to hospital to complete treatment following multiple call-backs from various team members. Unfortunately, over 25% of the registered contact

numbers were incorrect or not responding and these patients could not be convinced to return. 14% of patients returned by themselves at different dates before being contacted, however, remaining 6% of patients did not return due to personal reasons or unwillingness to get treatment despite multiple interventions.

**Conclusions:** Focused efforts for patient tracking is an effective way to reduce treatment abandonment in low-resource settings. It is also essential to create facilities for patients facing socioeconomic difficulties.

EP716/#1418 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

### A PUBLIC HEALTH APPROACH TO INCREASE ACCESS TO CHILDHOOD CANCER CARE IN LMICS; AN INITIATIVE OF IHHN, KARACHI

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**Background and Aims:** The practical difficulty of receiving cancer treatment at specialised centres away from home, remains a major concern in LMICs. Shared care is a collaboration between a specialised *hub centre* and smaller paediatric or *shared care* unit with a two way referral pathway. For many families in Pakistan, a cancer diagnosis translates to a long journey away from home with major financial implications. Increasing patient numbers have exerted an overwhelming burden on paediatric cancer services of Indus Hospital & Health Network (IHHN), Karachi, with around 1200 new cancer cases registered annually. To ease this burden and increase access to free-of-cost specialised care, IHHN initiated a unit in Quetta with support from the Government of Balochistan, creating the first facility for cancer care in the province.

**Methods:** Following fulfilment of legal processes and allotment of appropriate space for unit, a team including a paediatric oncologist, medical officers, nurses, psychosocial personnel, infection control practitioner, clinical pharmacists, data officer and other support staff were hired and monitored by relevant departments at IHHN. With the aid of the My Child Matters (MCM) grant, training courses for physicians, nurses, infection control, pharmacists, psychosocial personnel and data officers were conducted for all new inductees.

**Results:** From August 2021 to December 2022, a total of 2,631 patient visits have taken place in the Quetta unit. The level of care has progressed from Level 1 to Level 2 and is expected to become a full-fledged Level 3 facility by the end of 2023. Over 480 childhood cancer patients have been seen in this duration, with over 50% patients registering in Quetta directly.

**Conclusions:** IHHN is focused on expanding this shared care network across Pakistan. This initiative is essential for developing the local healthcare infrastructure, increasing access to childhood cancer care and achieving the WHO GICC goal for boosting overall survival by 2030.

EP717/#1465 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

### STREAMLINING PEDIATRIC ONCOLOGY BED MANAGEMENT: INSIGHTS FROM STAKEHOLDER ANALYSIS AND ENGAGEMENT STRATEGIES AT A CANCER CENTER IN JORDAN

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**Background and Aims:** Pediatric oncology bed management is a critical aspect of delivering high-quality care for children with cancer. King Hussein Cancer Center (KHCC) is a 352(46 pediatric)-bed hospital in Jordan, where adults and children with cancer are managed. The need for inpatient beds has consistently increased in, and outpaces the ability to add more inpatient beds, so effective bed management strategies are urgently needed.

**Methods:** A comprehensive, multilevel approach was implemented to identify key stakeholders involved in pediatric oncology bed management and the barriers to involving stakeholders in priority setting governance, and implementation. Then, through surveys, interviews, and meetings, we determined level of interest and influence of each stakeholder. Stakeholders were categorized based on their level of interest and influence, to develop a communication plan considering their needs and expectations. Finally, regular engagement with stakeholders throughout the project to address any concerns and ensure their support for the project was planned.

**Results:** Hospital administration was identified as the most powerful stakeholder, while patients and their families, medical staff, and oncologists were identified as highly interested and influential stakeholders. Insurance providers have moderate levels of interest and influence, as they are primarily concerned with the quality and cost-effectiveness of healthcare services. Government agencies and regulatory bodies were identified as highly powerful. A series of targeted engagement strategies and prioritization approaches were then developed to improve communication and collaboration among stakeholders, including regular meetings, clear communication protocols, and involvement of patients and their families in care decisions and prioritization panels. Inpatient length of stay for chemotherapy admissions averaged 5.5 days prior to the program and the target is planned to decrease to 3.5 days after implementing the strategies identified by influential stakeholders.

**Conclusions:** Stakeholder analysis followed by targeted engagement strategies are critical tools for improving pediatric oncology bed management. By identifying and engaging with all stakeholders involved in the care of these patients, healthcare providers can streamline patient



flow, and ultimately improve the quality of care delivered to children with cancer.

EP718/#1510 | Poster Topic: *AS05 SIOP Scientific Program/AS05.r Epidemiology, Policy and Advocacy*

### IDENTIFYING AND ADDRESSING OPPORTUNITIES TO IMPROVE PEDIATRIC HEMATOLOGY AND ONCOLOGY (PHO) CARE IN A CANCER CENTER IN JORDAN: PROFILE ACTION PLANNING EXPERIENCE

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**Background and Aims:** The Pediatric Oncology Facility Integrated Local Evaluation (ProFILE) assists PHO teams in establishing an institutional improvement strategy and enhancing local capacity for quality improvement. The King Hussein Cancer Center (KHCC) team participated in the ProFILE implementation from August 2021 to May 2022. We describe our experience identifying gaps and developing an institutional and national action plan using ProFILE.

**Methods:** ProFILE was implemented in three phases: preparation, assessment, and interpretation/action (I&A). Using the provided score-base and descriptive reports during the last phase, we conducted a 1-day local prioritization workshop to generate consensus and develop an institutional and national 3-year action plan. We carried out three exercises to prioritize identified gaps. The subsequent phases involve ongoing monitoring and progress reporting.

**Results:** A total of 30 interdisciplinary healthcare providers participated in the local workshop. We narrowed down 107 opportunities to 60 using a ranking table. Then, we prioritized three opportunities per ProFILE component using an impact-effort matrix (total 15). Institutional opportunities were classified into three categories. The final prioritization exercise informed the development of an action plan for Year-1 priorities addressing pre-existing focus areas we were actively working on, Year-3 included opportunities identified by ProFILE that we considered essential to work on, and Year-5 had opportunities that are important that we need to wait to address them. Challenges limiting the ability to address opportunities in the short term were also defined. The 3-year action plan includes developing a National Cancer Control Plan, improving pediatric oncology registration, enhancing PHO capacity and services, improving access to diagnostic and therapeutic modalities in children, and enhancing childhood cancer awareness among the public and health care workers.

**Conclusions:** ProFILE implementation was feasible in KHCC. The tool helped our team identify our strengths, prioritize opportunities amenable for improvement, and inform a national and institutional 3-year action plan.

EP719/#593 | Poster Topic: *AS05 SIOP Scientific Program/AS05.r Epidemiology, Policy and Advocacy*

### INITIAL OUTCOMES FROM IMPLEMENTATION OF A HOSPITAL-BASED PEDIATRIC CANCER REGISTRY NETWORK WITHIN THE AMARTE ALLIANCE IN BRAZIL

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**Background and Aims:** Although most children diagnosed with cancer live in low- and middle-income countries (estimated 90%), most face a lower survival probability than those in high-income countries. Cancer registries provide essential evidence to develop interventions to address these inequities. In Brazil, most reference centers in pediatric oncology are general hospitals without trained and dedicated staff to the proper registration of pediatric cancer. In 2019, thirteen Brazilian

pediatric oncology centers founded the AMARTE Alliance with the support of the St. Jude Children's Research Hospital. From the beginning, AMARTE members prioritized quality of data collection. This study aimed to report initial outcomes of the hospital-based cancer registry network to monitor actions developed by AMARTE.

**Methods:** Aspects of data collection, workforce, and legal compliance were identified upfront. All institutions agreed to use SJCARES Registry data collection standards in REDCap. Each institution nominated 1 data manager and 1 medical monitor and completed SJCARES global training in CURE4Kids and REDCap training. A working group was formed to support implementation work flows within each hospital and met regularly via virtual meetings. Governance structures in AMARTE ensured review and compliance of data collection with the norms for sensible data consent form, in accordance with Brazilian data protection law.

**Results:** Thirty-seven meetings were held, with an average of 14 participants per meeting. All participants were trained in the use of the chosen tools. In 2022, 1,154 new cases (851 malignant) were registered. There was a loss of 123 cases (deaths and follow-up loss). In September 2022, 12 additional hospitals joined AMARTE Alliance and began to receive the established training. Together, it is estimated that the 25 institutions will account for approximately 3,000 new cases/year.

**Conclusions:** The data presented show the feasibility of implementing a real-time pediatric cancer surveillance system that can guide interventions to improve clinical outcomes in low- and middle-income countries.

EP720/#765 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### IMPLEMENTING THE PEDIATRIC ONCOLOGY FACILITY INTEGRATED LOCAL EVALUATION (PROFILE) IN A PEDIATRIC ONCOLOGY CENTER IN GUATEMALA

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**Background and Aims:** The Pediatric Oncology Facility Integrated Local Evaluation (ProFILE) is a dynamic 360° assessment of health services that helps teams and institutions define a quality improvement strategy over five components (context, workforce, diagnostics, therapy, and patients & outcomes). The National Pediatric Oncology Unit (UNOP) is Guatemala's only comprehensive pediatric oncology center in the country. UNOP participated in ProFILE Beta 3 cohort

implementation from August 2022 to May 2023. We aim to describe our experience and results.

**Methods:** ProFILE was implemented in three phases: preparation, assessment and interpretation, and action. During the preparation phase, UNOP's leadership was involved upfront and a multidisciplinary assessment team was recruited. A total of 12 modules were completed by the Site Coordinator (SC) and 14 forms by Point of Care (POC) staff using DatStat. The Physician Lead (PL) approved the objective data entered by the SC. Six Quality Improvement exercises were completed, and three assessment team members completed the Institute for Healthcare Improvement Open School Basic Certificate in Quality and Safety. Score-based and descriptive reports were provided to facilitate a prioritization workshop and a 3-year action plan development.

**Results:** Twenty-four healthcare workers and one administrative staff participated. The overall form completion rate was 100%. A polar graph was created with a score calculation for each module. The highest score was for the Finances and Resources module, with 86%. The lowest scores were for the National Context and Surgery modules, with 45% and 48%, respectively, due to a lack of a National Cancer Plan and a dedicated surgery room at UNOP. All other modules scored between 62% and 76%. The highest discrepancy between objective data (SC & PL) and subjective data (POC staff) was in the Chemotherapy module.

**Conclusions:** Conducting ProFILE provided insightful information to staff members and helped stakeholders to develop a 3-year action plan on key improvement opportunities.

EP721/#568 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### IMPLEMENTING THE ST. JUDE PEDIATRIC ONCOLOGY FACILITY INTEGRATED LOCAL EVALUATION (PROFILE) TOOL AT ROYAL HOSPITAL, EXPERIENCE OF A TERTIARY CARE INSTITUTION IN OMAN

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**Background and Aims:** Pediatric Oncology Facility Integrated Local Evaluation (ProFILE) is a tool developed by St. Jude Global Metrics and Performance unit to guide institutional self-assessment and allow stakeholders to identify challenges in service delivery and prioritize solutions to improve Pediatric Hematology and Oncology care locally. Royal Hospital participated in the third beta testing ProFILE cohort. We aim to describe our implementation experience.

**Methods:** We implemented ProFILE through a three-phase process from August 2022 to May 2023. During the preparation phase, an interdisciplinary assessment team was recruited. Three selected members completed the Institute for Healthcare Improvement Basic Quality Improvement (QI) Certificate. In the assessment phase, participants electronically filled out the forms using the DatStat platform. Objective data was collected by the Site Coordinator, reviewed, and approved by the Physician Lead. Subjective data was entered by the rest of the assessment team. A total of twelve modules, twenty-six electronic forms, and six QI exercises were completed. The final report was generated following data validation. A local workshop is being conducted, and a 3-year action plan is being developed during the implementation and action phase. The ProFILE team guided the implementation via weekly online mentoring sessions.

**Results:** Seventeen interdisciplinary healthcare providers completed objective and subjective data with a rate of 100% and 91%, respectively. The twelve modules scored between 43 - 76%. Service Capacity, Chemotherapy, Radiation Therapy, and Patients & Outcomes modules scored above 70%, while the Facility and Local Context module scored the lowest at 43%. Opportunities prioritized during the workshop included but were not limited to developing a National Cancer Control Plan, integrating molecular studies into solid tumor diagnostics, and developing clinical pharmacy service.

**Conclusions:** Conducting ProFILE highlighted the areas of strength and opportunities for improvement and the local workshop aimed at prioritizing these opportunities and framing an action plan.

EP722/#441 | **Poster Topic: AS05 SIOP Scientific Program/AS05.r Epidemiology, Policy and Advocacy**

#### IMPLEMENTING THE PEDIATRIC ONCOLOGY FACILITY INTEGRATED LOCAL EVALUATION (PROFILE): EXPERIENCE OF A PEDIATRIC ONCOLOGY CENTER IN ALEXANDRIA, EGYPT

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**Background and Aims:** ProFILE is a 360-degree evaluation of health service delivery and helps teams to develop a quality improvement (QI) strategy. In August 2022, Borg El Arab University Hospital (BAUH) Pediatric Oncology Center joined the third Full ProFILE Beta Testing Cohort. The main goal was to identify opportunities amenable for improvement and develop an action plan.

**Methods:** ProFILE tool was implemented in three phases: preparation, assessment, and implementation and action. A multidisciplinary team was formed. During the preparation phase, three members were selected to complete a Basic QI certificate; then, six QI exercises were conducted throughout the assessment phase. The 360-degree evaluation is achieved by gathering data for the twelve modules of the five main ProFILE Components: Context, Workforce, Diagnostics, Therapy, and Patient and Outcomes. Objective and subjective data were gathered. The data was then validated, and a score-based report and a descriptive report were received, whereafter, we conducted our local workshop to prioritize and develop the action plan.

**Results:** The form completion rate was 100%. All twelve modules scored between 22% and 80%. BAUH- Pediatric Oncology Center scored 22% for National Context. While a score above 75% was given for Service Capacity. The rest of the modules scored between 50% and 75%. There was no significant difference in the score-based comparison between objective and subjective data except in the Service Integration module. Team awareness of improvement plan availability was low in most modules (0-43%).

**Conclusions:** The multidisciplinary assessment team was very effective in conducting the 360-degree evaluation. Several (QI) exercises and courses supplied by ProFILE empowered and motivated the team throughout the evaluation process. ProFILE descriptive and score-based reports helped our institution define and prioritize improvement areas and develop an action plan.

EP723/#1184 | **Poster Topic: AS05 SIOP Scientific Program/AS05.r Epidemiology, Policy and Advocacy**

#### ACUTE LEUKEMIA RESEARCH AND CARE NETWORK FOR LATIN AMERICA (ALRCAN LATAM): ONE YEAR OF EXPERIENCE

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**Background and Aims:** Despite advances in the treatment and supportive care of patients with acute leukemia worldwide, disparities in resources and training persist in low and middle-income countries (LMIC). To improve care and outcomes of pediatric patients with acute leukemias in Latin America, a virtual multi-country professional network was created.

**Methods:** A group of regional experts in pediatric acute leukemia, leaders in national pediatric oncology societies from Argentina, Brazil, Colombia and Mexico were brought together to form a steering committee that organizes a weekly online meeting to discuss clinical cases, research findings, and health system issues in adult and pediatric leukemia. Lectures are maintained in a searchable repository. All sessions are free to attend and open to everyone.

**Results:** Since March 2<sup>nd</sup>, 2022, 51 one-hour weekly sessions in Spanish and Portuguese were held with a median of 98 attendees (range: 40-147) from 17 countries of North, Central and South America. The steering committee hosts coordinate the speakers as well as the topics to present including different aspects of diagnosis, treatment and supportive care. Patients in active treatment are discussed together to get expert opinions regarding diagnosis and treatment options. All sessions are recorded and stored in a digital platform along with associated educational content at <https://networks.resonancehealth.org/networks/all-rcan-latam>. Healthcare professionals involved in childhood cancer care can freely access the network after registration.

**Conclusions:** ALRCaN LATAM successfully delivered more than 5000 person-hours of educational content and created a platform for networking and information exchange across Latin America. ALRCaN LATAM offers a free online space for healthcare professionals involved in the care of patients with acute leukemia in Latin America, highlighting the importance of multi-national collaboration to improve outcomes of patients with cancer and proposals to solve administrative issues in resourced-limited settings.

EP724/#1760 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

## FACILITATORS AND BARRIERS TO RECRUITING CHILDREN OF PARENTS WITH NON-ENGLISH LANGUAGE PREFERENCE TO CLINICAL TRIALS: QUALITATIVE REPORT FROM COG DIVERSITY AND HEALTH DISPARITIES COMMITTEE

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**Background and Aims:** Improving clinical trial inclusiveness is a Children's Oncology Group (COG) priority to improve for result generalizability and equitable translation. Our aim was to identify facilitators and barriers of COG institutions' capacities and practices for recruiting children to trials when parents have non-English language preference (NELP)

**Methods:** We distributed a 20-item online survey to site Principal Investigators (PI) at COG institutions (N=266.) Items focused on recruitment practices, interpretation resources, and consent document translation. The analytic dataset included responses to five open-ended items. We used a qualitative deductive descriptive approach to analysis. We initially analyzed the data in pairs (one pair per item) to code responses to each open-ended item, then as a group (6) to collate codes across items into themes and link identified barriers, facilitators, and improvement strategies.

**Results:** Respondents (n=152, 57.1%) identified influential parent characteristics, institutional facilitators and regulatory barriers. Parent characteristics included: cultural, attitudes/beliefs about research, preferred primary language, general and health literacy, immigration status, and preference for in-person interpreters. Institutional facilitators included: availability of forms in parents' preferred language, funding (translation, interpretation), and coordinated workflows for recruitment. Regulatory barriers included: lengthy translation approval process, document complexity and emphasis on toxicity, inflexibility related to timing of consents, ineffective training in informed consent process for individuals with NELP, requirements that providers read entire documents aloud with an interpreter, need for "wet signatures", and time constraints. Recommended strategies included: patient-friendly translated consents and information sheets, funding for translation and interpreter services, effective education (parents, research staff, providers), standardized recruitment processes, flexibility about timing of consent, and IRB members who understand complexities of consenting persons with NELP.

**Conclusions:** We identified barriers and facilitators to recruiting individuals with NELP. PIs suggested investments in translation, interpretation and education, as well as standardization of recruitment to improve inclusiveness in COG trials.

EP725/#1159 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### REGIONAL DRUG PRICE VARIATION IN LATIN AMERICA AND IMPACT ON COST ESTIMATION OF ESSENTIAL MEDICINES FOR PEDIATRIC CANCER CARE IN PERU

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**Background and Aims:** Inequitable access to essential medicines contributes to inferior outcomes for children with cancer living in low-and-middle-income countries. Prior work in collaboration with the Peruvian Ministry of Health (MOH) and the Pan American Health Organization shows that the pediatric cancer medicines budget in Peru amounts to only 4% of national cancer expenditure and is 47% less than expected when compared with international reference pricing. In this analysis, we aim to compare Peruvian drug pricing with two Latin

American countries to assess regional pricing variation that may inform future opportunities for pooled procurement.

**Methods:** FORxECAS is a pediatric cancer-specific model that projects required drug quantity and cost for 18 common pediatric cancers, drawing on internationally adopted standard treatment protocols. We customized model inputs for Peruvian incidence, stage at diagnosis, and per-unit drug prices provided by the Peruvian MOH. For comparative analyses, aggregate costs adapted for Peruvian incidence were calculated utilizing drug prices in two Latin American countries.

**Results:** FORxECAS projects the Peruvian cancer medicines budget to be USD\$1.7 million annually. All 15 medicines assessed are cheaper on a per-unit basis in Peru relative to regional comparators. Per-unit drug pricing based on Regional Comparators #1 and #2 would lead to an overall budget of \$5.1 million and \$9.8 million, respectively, based on Peruvian incidence. Containment of the cost of intravenous methotrexate and asparaginase appear to be key to keep Peruvian costs from rising.

**Conclusions:** The cost of procuring accurate quantities of essential pediatric cancer medicines to meet Peruvian population-level need would be significantly higher if in-country prices rose to levels seen elsewhere in Latin America. Factors that may impact intraregional cost variability include inflation, political context, and drug supplier differences. Future analyses may be performed utilizing different known medication suppliers to determine whether sources with higher perceived quality result in significant changes to overall budget predictions.

EP726/#1135 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### DIAGNOSTIC AND TREATMENT JOURNEY OF PATIENTS WITH NEUROFIBROMATOSIS TYPE 1 IN CANADA: AI BASED ANALYSIS

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**Background and Aims:** Neurofibromatosis type 1 (NF1) is a rare genetic disorder having multiple manifestations including tumours. This research aimed to provide a deeper understanding of paediatric patients' NF1 journey in Canada from the patients' and caregivers' perspective.

**Methods:** In this social listening research, a total of 3,035 messages on NF1 from 835 Canadian patients and caregivers were collected from domestic and international social media (2017-2022). Multilingual artificial intelligence and deep semantic analysis of anonymised patients'/caregivers' messages were used to identify demographics and patterns in NF1 symptoms, diagnosis, referral patterns, treatment experiences, and quality of life (QoL).

**Results:** Of the 835 patients and caregivers identified, 185 were children (0 – 18 years old). Gender was indicated in 177 children (94 males, 83 females). Top-5 mentioned symptoms in children were hyperpigmentation (18%), neurofibromas (12.2%), neoplasm (11.7%), neurodevelopmental abnormality (10.8%), pain and brain neoplasm (5.9% each). Café-au-lait spots most commonly triggered diagnosis (50% cases). Pain, however, appeared to be the most burdensome. Over 85% of cases were diagnosed in childhood, mostly between 6 and 10 years. Patients and caregivers highlighted challenges with referrals to specialists; paediatricians and neurologists were mentioned as most accessible. The treatment options most discussed for children were surgery (59.6%) and pharmacological therapy (31.9%; including protein kinase inhibitors, chemotherapy, mTOR inhibitors and anticonvulsants). Treatment-related messages highlighted a strong need for effective pain management.

**Conclusions:** These data highlight experiences and challenges faced by paediatric patients with NF1 and their caregivers in Canada and provide an opportunity to improve the patient journey to ensure better and timely care for these patients.

EP727/#1686 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### RISK FACTORS ASSOCIATED TO HYPOVITAMINOSIS D IN MEXICAN PEDIATRIC PATIENTS AT CANCER DIAGNOSIS

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**Background and Aims:** Vitamin D is an essential hormone for bone metabolism, growth, and immune system regulation. Vitamin D deficiency, also known as hypovitaminosis D, have been associated with the survival of cancer patients, as well as the appearance of adverse reactions to chemotherapy. In this cross-sectionally study, the aim was to explore the prevalence of hypovitaminosis D in Mexican pediatric patients at the diagnosis of any type of cancer and the risk factors associated.

**Methods:** Newly diagnosed cancer patients at Hospital Infantil de México Federico Gómez from February 2021 to July 2022 were invited to participate. A blood sample prior to the start of chemotherapy was taken to determine Vitamin D levels by measuring plasma calcidiol using a competitive ELISA kit (ab213966, abcam, Cambridge, UK). Patients with calcidiol levels below 10 ng/mL (25 nmol/L) were considered to have hypovitaminosis D. In addition, sociodemographic information was obtained from medical records. Plasma calcidiol levels are shown as median and interquartile range (IQR),

while the prevalence of hypovitaminosis D is shown as the number of patients and percentage. Odds Ratios (OR) were calculated with confidence intervals at 95% (95%CI) to determine hypovitaminosis D risk factors.

**Results:** Fifty-seven patients were included in the study. The median plasma calcidiol concentration was 5.85 ng/mL (IQR= 7.82) and 37 (65%) patients had hypovitaminosis D. Patients under 5 years old (OR= 13.0, 95%CI 1.6 to 107.4) had a higher risk of hypovitaminosis D at the time of cancer diagnosis, while sex, socioeconomic status, nutritional status, tumor type, and season were not.

**Conclusions:** Mexican pediatric patients with cancer have a high prevalence of hypovitaminosis D, particularly patients under 5 years old.

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EP728/#1734 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### AIM, DESIGN AND FIRST RESULTS FROM DEDICA, A WHO/IARC TOOL TO ASSESS COUNTRY-SPECIFIC BARRIERS TO TIMELY DIAGNOSES AND TREATMENT

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**Background and Aims:** Striking inequalities in childhood cancer (ChC) survival rates are observed between high- and low-income countries (survival >80% vs <30%). The WHO Global Initiative for Childhood Cancer aims at narrowing this difference and achieve a survival rate of at least 60% for all children with cancer by 2030. Delayed diagnosis and delayed treatment strongly affect survival in low and middle income countries. To help country to address this, WHO and IARC are piloting in the European Region a tool to evaluate country-specific determinants of late diagnosis/treatment of cancers (DEDICA tool). Such a tool has been successfully piloted for adult cancers

**Methods:** The tool consist in questionnaires for guardians of oncopediatric patients, and adapt to the common types of pediatric malignancies. It has been developed in collaboration with leading pediatric oncologists and translated into several European languages. Local interviewers have been trained by WHO/IARC and at least 50 patients are recruited in each pilot country. The study was approved by both national and IARC ethical committees. REDCap-based platform is used to collect data.

**Results:** The barriers identified span from financial, logistic, geographic, psychologic, and socio-cultural ones to those related to pathways of care, quality and organisation of the health care. Once barriers are identified and their magnitude measured, the need and the

priorities for action appears clearly. More detailed quantitative results will be presented at the conference.

**Conclusions:** The WHO-IARC DEDICA tool is both an advocacy tool - embarrassing statistics are efficient at prompting action- as well as a guide for policy-makers and cancer professionals about opportunities and priorities for interventions. The findings obtained thanks to this tool are expected to improve our understanding of the determinants of delayed diagnosis and treatment in individual countries as well as globally.

EP729/#103 | Poster Topic: *AS05 SIOP Scientific Program/AS05.r Epidemiology, Policy and Advocacy*

#### CHILDHOOD AND ADOLESCENT CANCER CARE AT A TERTIARY HOSPITAL IN NORTHERN TANZANIA: A RETROSPECTIVE STUDY

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**Background and Aims:** Each year, there are over 400,000 newly diagnosed children with cancer around the world, with over 80% of these children residing in low- and middle-income countries (LMICs). This study aims to summarize the epidemiology and care patterns of newly diagnosed childhood cancer cases in Northern Tanzania.

**Methods:** For this cross-sectional study, data from all children and adolescents (0-19 years old) with newly diagnosed cancers were collected from the Kilimanjaro Cancer Registry located at the Kilimanjaro Christian Medical Centre (KCMC) from January 2016 through December 2021. Descriptive statistical analysis was performed to determine the distribution of diagnosis, treatment, and demographic information over time and by age. Chi-square statistics were calculated to compare all variables across year of admission ( $p < 0.05$ ). Secondary analysis was conducted on the subset of children for whom the information on stage at diagnosis was available.

**Results:** We found a total of 417 newly diagnosed cancer cases between 2016 and 2021, with a significant increase by year. Overall, more than half of the children were under the age of ten years

(59.2%) and male (57.8%). Among all participants, 40% were from the Kilimanjaro region and 60% traveled from other regions. Most of the cancer cases were hematological malignancies in the overall sample (45.8%) and among children diagnosed at stages III and IV (30.7%). From a subset analysis of patients with available stage data ( $n=101$ ), chemotherapy was the most common treatment (87.1%), compared to radiotherapy (13.5%) and surgery (20.8%).

**Conclusions:** Our study fills crucial gaps in the literature related to the burden of disease and survival for children and adolescents with cancer in the Kilimanjaro region. Furthermore, our results can be used to understand the regional needs and guide research and strategic interventions to improve childhood cancer survival in Northern Tanzania.

EP730/#801 | Poster Topic: *AS05 SIOP Scientific Program/AS05.r Epidemiology, Policy and Advocacy*

#### DESCRIPTIVE REPORT OF PEDIATRIC LEUKEMIA IN ARMENIA

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**Background and Aims:** The 2019 Armenian Childhood Cancer Registry project prompted longitudinal, nationwide, oncology data collection. We conducted a descriptive study of pediatric patients diagnosed with leukemia: acute lymphoblastic (ALL), biphenotypic acute (BAL), acute myeloid (AML), unspecified acute (AL), chronic lymphoblastic (CLL), and chronic myeloid (CML). We aimed to define the population and preliminarily investigate known risk factors.

**Methods:** The study population included individuals aged 0-19 years diagnosed with leukemia who visited one of Armenia's two pediatric hematology centers between 1995 and 2021. In the accumulated patient files, common elements across years and facilities were isolated and recurring files were consolidated. We used descriptive statistics to investigate associations between socioeconomic status and blood type as risk factors in diagnosis. Gender was compared to the national population's overall mean of that age group, with blood type distribution being compared to the national population.

**Results:** There were 841 patients among 922 files, of which 92 relapsed post-treatment. Males comprised 59.7% of cases (national: 47.0%). There were 673 ALL (80.0% of total cases), 122 AML (14.5%), 22 AL (2.6%), 5 BAL (0.6%), 3 CLL (0.4%), and 16 CML (1.9%) cases. The mean age, height, and weight at diagnosis were 7.5 years, 122.8 cm, and 27.2 kg, respectively. Population blood type distribution differences were negligible except for the A- group: 40.9% A+ (national: 46.3%), 7.7%

A- (3.7%), 11.2% B+ (12%), 2.1% B- (1.0%), 6.3% AB+ (5.6%), 1.0% AB- (0.4%), 25.8% O+ (29.0%), 5.1% O- (2.0%). No marked difference was observed in hospital visits per patient by parental employment status.

**Conclusions:** Efforts to improve cancer surveillance and strengthen registry data collection in Armenia should be considered for expansion. Childhood cancers remain a public health threat in Armenia, and registry information could facilitate the identification of emerging trends in pediatric cancer incidence and inform targeted interventions for prevention and control.

EP731/#838 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

### EARTHQUAKE DISASTER AND ITS' ACUTE EFFECT ON PEDIATRIC HEMATOLOGY AND ONCOLOGY İN TÜRKİYE; TURKISH PEDIATRIC ONCOLOGY GROUP-TPOG QUESTIONARE STUDY

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**Background and Aims:** The earthquake disaster that occurred in 11 provinces of Turkey on February 6, 2023, affected all life. Patients with special needs like chilhood cancers and their doctors also affected. Our goal is to understand what we have lived, as PHO, how we handle the problems and understand special needs to be stronger and prepare such disasters.

**Methods:** A questionnaire has been send to TPOG members with 17 questions related to themselves and their families health conditions, their home, hospitals, patients, working and living conditions after 1 month of erthquake. Beside received their recommandations to be stronger and ready for the future possible disasters as PHO.

**Results:** Forty one Pediatric Hematologist/Oncologist (PHO) responded the questionnaire from 18 cities. 50% of the PHO that living outside of the earthquake cities have family members living at the earthquake region. Nine doctors that living at the earthquake region were able to quit their home while 1 had diffuculty to goout. Three of the doctors had damage at their homes. Seven of the doctors accommodated at tents, cars, hospitals or the their friends home. Eight of the doctors hospitals were damaged/collapsed. One of them worked at tent while others worked at solid buildings of the hospitals. Five doctors told they lost some patients while 60 % did not loose any and 30% did not know yet. Five doctors referred their patients to the other centers outside of the earthquake region or some bigger/solid hospitals near by themselves. 72% of the centers have received referral patients. Some of these patients accomadated at the hospitals, tents, dormitories and/or with their relatives.

**Conclusions:** As pediatric hematologist and oncologist, taking care of patient with special needs, we have to be prepared for disasters. For better coordination, we have to take place in the emergency management plan groups as PHO.



EP732/#712 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

### FACTORS ASSOCIATED WITH A DELAYED CANCER DIAGNOSIS IN THAI CHILDREN

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**Background and Aims:** Despite advances in pediatric oncology, cancer remains a leading cause of death in children. Diagnosis of childhood cancer as early as possible is crucial to reduce mortality. This study aimed to identify delayed diagnosis and factors associated with pediatric cancer patients in King Chulalongkorn Memorial Hospital, Thailand.

**Methods:** This cross-sectional study included 258 patients aged 0-18 diagnosed with cancer at our institute. Data was collected by interviewer-administered structured questionnaire from the primary caregiver, OPD, and IPD chart review from June 2018 to May 2021. Diagnosis delay was considered significant when it was more than 28 days. Binary logistic regression analysis was used to test associations between the determinant factors and the dependent variable.

**Results:** Of 258 patients, 151 (58.6%) had delayed diagnoses. The median time to diagnosis was 30 days (ranging from 1 day to 1095 days). Brain tumors were four times more likely to get delayed than other malignancy types. (AOR:4.63; 95%CI= 2.42-8.88, P<0.001) The first clinical presentation with lump and weakness had a significantly high risk for delay diagnosis (AOR:4.92; 95%CI= 1.96-12.34, P=0.001) and (AOR = 4.4; 95%CI = 1.26-15.41, P=0.02). The first doctor, the General doctor, and other specialists had a significantly higher risk for delay diagnosis than the pediatrician (AOR:4.72; 95%CI= 1.63-13.64, P=0.001) and (AOR=6; 95%CI =2.13-16.91) respectively. There were significant associations between the non-delayed diagnosis and type of cancer: acute leukemia (P=0.008) and presenting symptoms of fever (P=0.02)

**Conclusions:** Delayed childhood cancer diagnosis is related to cancer type, Initial health worker, and presenting symptoms. Thus, every effort should be made to promote public and parental awareness of childhood cancer.

EP733/#179 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

### A CORE OUTCOME SET TO MEASURE QUALITY OF CARE FOR CHILDHOOD CANCER - A JOINT INTERNATIONAL CONSENSUS STATEMENT FROM THE INTERNATIONAL CHILDHOOD CANCER OUTCOME PROJECT

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**Background and Aims:** The aim of treating childhood cancer remains to cure all. However, with improving survival rates, long-term health outcomes increasingly define quality of care. Outcome-based evaluation of care emphasizes measuring what is most important to patients, survivors and their families. The International Childhood Cancer Outcome Project aimed to develop a set of core outcomes for most types of childhood cancers involving relevant stakeholders to balance survival with quality of survival, with the ultimate goal to facilitate assessment of institutional progress and allow benchmarking with other organizations to improve the quality of care.

**Methods:** A survey among healthcare providers and focus groups with survivors resulted in unique candidate outcome lists for 18 types of childhood cancer. In a two-round Delphi survey, core outcomes were prioritized and harmonized definitions were developed. Measurement instruments were selected for all prioritized physical and (neuro)psychological outcomes.

**Results:** Potentially relevant outcomes were identified through a survey (n=87 healthcare providers with 17 professional backgrounds) and four online focus groups (n=22 survivors). Candidate outcomes were categorized into 67 physical and (neuro)psychological conditions. The 18 Delphi surveys, which included 457 participants from 70 institutions internationally (response rates, round 1: 70-97%; round 2: 65-92%), resulted in the selection of four to eight physical core outcomes per pediatric cancer subtype (e.g., heart failure, subfertility, and subsequent neoplasms) and three aspects of quality of life (physical, psychosocial, and neurocognitive). This corresponded to 26 unique outcomes in total including endorsed definitions. Measurement instruments consist of medical record abstraction, questionnaires, and linkage with existing registries.

**Conclusions:** This International Childhood Cancer Core Outcome Set, including proposed measurement instruments, represents outcomes of value to patients, survivors, families and healthcare providers which together with survival rates facilitates the implementation of outcome-based evaluation of care.

EP734/#231 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

### CLINICAL EPIDEMIOLOGY OF PROVEN INVASIVE FUNGAL DISEASE IN CHILDREN WITH HEMATO-ONCOLOGIC MALIGNANCIES IN MEXICO

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**Background and Aims:** Invasive Fungal Disease (IFD) causes a significant burden of complications among immunocompromised children, which greatly influences the outcomes of these patients. Most of the evidence regarding the epidemiology of IFD is obtained from studies in adult patients, currently, there is no published evidence regarding the local epidemiology of IFD in Mexican children, other than single case reports.

**Methods:** We conducted a retrospective single-center cohort analysis, at the Hospital Universitario "Dr. José Eleuterio González" in Monterrey, México between September 2017 and October 2022, Patients aged 0–18 years with hematological or solid tumor malignancy with proven IFD were identified by medical record and included. Standard definitions of IFD established by the Infectious Diseases Group of the European Organization for Research and Treatment of Cancer and the Mycoses Study Group were used to classify cases.

**Results:** We identified 27 cases of proven IFD over a 5-year period, of which 21 (77%) were caused by filamentous fungi and 6 (23%) were yeast infections. The median age at IFD diagnosis was 6.6 years, with younger children diagnosed with documented yeast infections in comparison with mold infections (2.8 vs 8.2 years accordingly). Among the mold infections, there was a predominance of *Fusarium spp.* in six cases (28%) and *Aspergillus spp.* in the same frequency (28%), the anatomical sites most frequently involved were sino-palatal in thirteen cases (62%), pulmonary in four cases (19%), skin in three cases (14%) and disseminated in one case (5%). All the yeast infections were central venous catheter-associate infections by *Candida spp.*

**Conclusions:** We found a higher incidence of IFD caused by molds than previous reports in similar populations, with a predominance of sino-palatal involvement among these. These findings provide valuable information on the epidemiology of IFD in children with malignancies in Mexico and warrant further study.

EP735/#804 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

### DETERMINANTS OF DIAGNOSTIC TIME IN PEDIATRIC CANCER IN GUATEMALA, IDENTIFYING BARRIERS AND OPPORTUNITIES TO IMPROVE EARLY DETECTION AND REFERRAL PATHWAYS

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**Background and Aims:** The reduction of diagnostic time (DT) and referral time (RT) can reduce advanced disease, and treatment toxicity, improving long-term survival in pediatric cancer. We aim to identify the factors that influence DT and RT at the Unidad Nacional de Oncología Pediátrica (UNOP).

**Methods:** We designed a survey to determine the DT (time -days- from detection of first cancer-related symptom to diagnosis confirmation) and RT (time from first consult to a healthcare provider -HCP- to the arrival to UNOP), and its variance regarding epidemiologic, economic, socio-cultural, and disease-related factors. After the ethics committee approval, the caregivers of all patients newly diagnosed with cancer in March-August 2022 at UNOP were invited. The DT and RT were analyzed using ANOVA test for independent variables in Rstudio.

**Results:** From 224 confirmed cases, 10/224 (4%) were excluded (6 early deaths, 4 palliative care) and 208 caregivers accepted to participate, whose children were diagnosed with leukemia/lymphoma in 119/208 (57%). The median DT and RT were 52 and 21 days respectively. The DT was longer ( $p < 0.05$ ) in patients with the diagnosis of solid tumors, the first disease-related symptom was leukocoria or a painless mass/lymphadenopathy, were indigenous race, lived far from central/metropolitan region or in rural areas, in extreme poverty, or with illiterate father or non-Spanish-speaker mother. The RT was longer when patients consulted with painless mass/lymphadenopathy, history of a performed biopsy, or required payment for diagnostic studies higher than Q.1000.00 (~125 USD). Caregivers reported misdiagnosis in 81/208 (39%) and >3 HCP's visits before referral in 133/208 (69%) cases, increasing the DT. Patient's gender, age, caregiver's occupation, type of HCP visited, use of natural/alternative medicine (58/208, 28%), and religious/ritual practices (130/208, 62%), didn't significantly prolong the DT.

**Conclusions:** Non-disease-related factors significantly impacted timely access to care, and strategies to mitigate them should be

implemented in early detection-referral guidelines for primary/secondary care, avoiding misdiagnoses and multiple medical visits.

EP736/#628 | Poster Topic: *AS05 SIOP Scientific Program/AS05.r Epidemiology, Policy and Advocacy*

### THE NEED FOR MANDATORY FOOD INSECURITY SCREENING FOR PEDIATRIC ONCOLOGY PATIENTS AT GOVERNMENT HOSPITALS IN INDIA

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**Background and Aims:** Food insecurity is a lack of consistent access to healthy or adequate food. Malnutrition can occur as a result of food insecurity and/or due to catabolic diseases like cancer. If food insecurity occurs in the milieu of childhood cancer, it can worsen the child's nutritional status and may impact overall treatment outcomes. Given the robust association connecting food insecurity with poor health outcomes, The American Cancer Society calls for mandatory food insecurity screening in cancer treatment.

**Methods:** In June 2022, Cuddles Foundation (CF) administered the Hunger Vital Sign™, a commonly validated screening tool for evaluating risk of food insecurity in CF beneficiaries across 29 partner hospitals and garnered 339 responses. CF evaluated whether the beneficiaries were at risk for food insecurity a year prior to receiving monthly ration bundles through the CF's FoodHeals™ programme.

**Results:** The results showed that 77% of beneficiaries worried that they would run out of money to buy food before the end of the month. The results also indicated that 74% of beneficiaries actually ran out of food and did not have the means to buy more. Overall, 82% of beneficiaries were deemed at risk for food insecurity a year before they started receiving the monthly ration bundles. A qualitative exploration of how beneficiaries procured food or resources to procure food, indicated they sold livestock, sought help from relatives, worked multiple jobs, purchased low-cost pantry staples, or had one meal/day.

**Conclusions:** A substantial majority of CF beneficiaries screened at 29 centres across India were at risk of food insecurity even before starting cancer treatment. Continuing food insecurity may contribute to cancer distress, which can lead to treatment non-adherence and poorer treatment outcomes. Therefore, food insecurity screening with a validated tool at the earliest visit can become the first crucial step towards providing vital nutrition assistance.

EP737/#433 | Poster Topic: *AS05 SIOP Scientific Program/AS05.r Epidemiology, Policy and Advocacy*

### EXPERIENCE IN IMPLEMENTING THE PAEDIATRIC ONCOLOGY FACILITY INTEGRATED LOCAL EVALUATION (PROFILE) AT A TERTIARY PAEDIATRIC HOSPITAL IN BRAZIL - HOSPITAL DA CRIANÇA DE BRASÍLIA-

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**Background and Aims:** As a St. Jude Global Alliance member and partner in improving childhood cancer survival, Hospital da Criança de Brasília joined the third ProFILE Beta cohort. ProFILE is a dynamic 360-degree evaluation that allows the Pediatric Hematology-Oncology (PHO) units to identify the impact of non-biological factors and helps PHO care teams define a quality improvement strategy. We describe our ProFILE implementation experience.

**Methods:** We implemented ProFILE from August 2022 to May 2023, guided by the ProFILE team through educational training modules, weekly virtual mentoring sessions, and IHI Open School courses. A multidisciplinary team (21) was invited to complete the 12 ProFILE modules (26 electronic forms) using the DatStat platform. Objective data was collected by the Site Coordinator (SC) and reviewed and approved by the Physician Lead (PL). Subjective data was entered directly by a pool of Point of Care staff. Six quality improvement (QI) exercises were conducted. Final score-based and descriptive reports were produced. Strengths and opportunities for improvement were identified for each module. The team will conduct a local 2-day prioritization workshop to define a 3-year action plan.

**Results:** The form completion rate for objective data was 100%, and 93% for subjective data. The QI exercises strengthened data collection and assessment of practices and processes at our unit. The score calculation was >75% in 5 modules and 50-75% in 7 modules. Patient and Outcomes and Service Capacity modules scored the highest (85% and 83%, respectively). Radiation Therapy and Service Integration modules scored the lowest (53% and 50%, respectively). In the impression section, 138 opportunities for improvement were highlighted.

**Conclusions:** PrOFiLE is a window of opportunity for “out-of-box thinking based on a detailed examination of what is in the box.” It promotes collaborative experience and fosters a culture of quality and systematic evaluation of our data. It helps to plan and prioritize feasible improvements.

EP738/#395 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### EARLY DETENTION PROGRAM FOR PEDIATRIC CANCER IN COLOMBIA. THE EXPERIENCE OF THE GOLDEN CLINICS (CONSULTORIOS DORADOS)

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**Background and Aims:** Early diagnosis of cancer and referral to cancer centers are key to improve oncologic pediatric patients' outcomes. Since February 2022, an initiative called Consultorios Dorados (Golden clinics) was implemented in the Department of Cordoba in Colombia to improve early detection by primary care providers and timely referral to pediatric cancer centers.

**Methods:** This is a cross-sectional study to evaluate early diagnosis and time to referral to a cancer center after the implementation of Golden Clinics, using a color-grading screening tool provided by the Pan-American Society of Health (AIEPI).

**Results:** A total of 34 Golden Clinics were instituted within the department of Cordoba. Health care personnel and primary care physicians were trained in the detection of early signs of pediatric cancer. From February 2022 to December 2022 a total of 113 patients were evaluated, of which 96 (85%) were classified as “possible cancer-severe disease-RED” and 22 (15%) as “some risk of cancer-YELLOW”). Bone pain was the most common symptom (38.1%), followed by headaches (22.1%). The median time from the beginning of symptoms to evaluation at the Golden Clinic was of 121 days (39-352). The median time from the evaluation at a Golden Clinic to evaluation at a pediatric cancer center was of 27 days (IQR: 13-51). A total of 2 cases were confirmed to have an oncologic diagnosis (Burkitt lymphoma and immature teratoma). The time to diagnosis for those patients was of 10 days and 1 day respectively. Both patients were clinically stable at the time of diagnosis and did not have advanced stages of disease.

**Conclusions:** The implementation of an early pediatric cancer program in Colombia is feasible as it provides a system for screening that can be easily implemented in primary care clinics in urban and rural areas and more importantly provide a clear path for referral to a pediatric cancer center.

EP739/#1754 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### CARE OF ADOLESCENT AND YOUNG ADULTS WITH CANCER IN LATIN AMERICA: A SURVEY FROM THE AYA - SLAOP CHAPTER

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**Background and Aims:** Treatment and care of adolescents and young adults (AYA) with cancer is challenging all around the world. However, little is known about AYA care in Latin America. We aim to describe the state of development of AYA care in Latin America. Treatment and care of AYA is challenging all around the world. However, little is known about AYA care in Latin America. We aim to describe the state of development of age specific AYA care in Latin America.

**Methods:** We conducted a survey among health care professionals in Latin America to assess the availability of services and resources specific for AYA. The survey was distributed through the Latin American Society of Pediatric Oncology (SLAOP) in May 2022.

**Results:** A total of 119 respondents from 19 Latin American countries completed more than 80% of the survey (75 pediatric and 25 adult hemato-oncologists, 6 psychologists, 5 nurses, 3 non-governmental organizations, 2 government representatives, 2 hospital teachers and 1 nutritionist). Half of the respondents work in public institutions. Most respondents reported seeing 10-20 new AYA patients/year (35%), 29(24%) more than 30 and 11(9%) between 20 and 30. AYA care was provided either by pediatric (44%) or adult (13%) hemato-oncologist or both (35%). More than half (61%) reported having access to a specific clinical space for AYA care. AYA were either referred by a physician or self-referred (57% by a friend and/or family, 56% after multiple failed health care visits and 78% through the internet) The main perceived difficulties in caring for AYA patients was the lack of specific AYA

protocols (60%), lack of adequate space (39%) and adherence to treatment (33%).

**Conclusions:** Only one-third of the respondents report that pediatric and adult oncologist work together in the care of AYA. Most AYA self-referred, pointing to a deficiency of the health care systems and difficulties to share care between pediatric and adult oncologists.

EP740/#802 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### ASSESSMENT OF SAFEGUARDS TO DISCOURAGE P-HACKING ON THE PEDIATRIC CANCER DATA COMMONS DATA PORTAL

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**Background and Aims:** Data for the Common Good developed a Kaplan-Meier survival analysis tool for exploring pediatric cancer data within the publicly-available Pediatric Cancer Data Commons data portal. To address concerns that the tool could be misused through the practice of “p-hacking,” safeguards were implemented. Uncertainty regarding the extent to which the tool would be misused and the effectiveness of proposed safeguards led to formal assessment. We aimed to (1) identify and analyze cases of suspected misuse of the tool (i.e., “p-hacking”), (2) understand how users utilize the tool, and (3) understand users’ perceptions of the implemented safeguards.

**Methods:** Data were collected through review of server log files, qualitative user survey, review of data requests, and feedback from participating disease-based consortia. A mixed-method quality-improvement approach was used for analysis.

**Results:** Among 356 active users over 9 months, 28 (8%) utilized the survival analysis tool. The range of survival analyses performed was 1-9 per user. Participating consortia did not identify any cases of suspected misuse of the tool during review of project proposals received during the data collection period. Eleven data portal users responded to the survey, 8 of whom used the survival analysis tool. Of 2 respondents who submitted data requests, one indicated that the survival analysis tool informed the data request. Among 7 users who responded regarding the appropriateness of safeguards, 3 felt they were “too restrictive” and 4 felt they were “just right.”

**Conclusions:** Early data have not demonstrated evidence of misuse of the tool in the form of p-hacking. A continuing review process and development of automated methods for detecting p-hacking are planned to ensure users continue to explore data responsibly. Developers of online analytic tools should be aware of the risks inherent in open data exploration and develop methods to mitigate those risks.

EP741/#1256 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### PRIORITY SETTING IN PEDIATRIC HEMATOLOGY ONCOLOGY SERVICE THROUGH SWOT ANALYSIS: EXPERIENCE OF 10 COUNTRIES

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**Background and Aims:** In partnership with over 40 medical institutions from 15 countries, St. Jude Children’s Research Hospital Global Euro Regional Program works to improve childhood cancer survival rates in Europe and Central Asia. Over the past 3 years, pediatric cancer care in the region has been challenged by the COVID-19 pandemic and war. This study describes current priorities and activities to improve childhood cancer care in 10 countries of the regions.

**Methods:** From November to December 2022, a standardized interview-based priority assessment was conducted in 10 countries (Azerbaijan, Armenia, Belarus, Kazakhstan, Kyrgyzstan, Moldova, Mongolia, Serbia, Tajikistan, Uzbekistan) using SWOT (Strengths, Weaknesses, Opportunities and Threats) analysis conducted with regional collaborator. The interviews included SWOT analysis, main structural and legislative changes in pediatric cancer care, and current country priorities.

**Results:** This analysis identified 3 primary areas of strength: support of charitable foundations (50% of countries), government support (50%), centralized cancer care (50%). Most participating countries reported

unstable geopolitical situation as a threat to provision of childhood cancer care (70%) and highlighted detrimental effect on cancer medication procurement (75% reported as weakness, 60% as a threat). In addition, 60% highlighted limited educational opportunities and lack of qualified personnel as a weakness or threat. Through further discussion and analysis of SWOT data across countries, opportunities for enhancement of cancer care services included: Improvement of education in pediatric hematology-oncology, expansion of cancer care services capacity, strengthening collaboration and research, and stabilizing procurement of cancer medications.

**Conclusions:** Natural and man-made crises, such as pandemics and geopolitical conflict, affect multiple areas of pediatric cancer care such as medication procurement, workforce capacity, and education. Through national and international collaboration, sustainability in childhood care delivery in Central Asia can be accomplished through joint efforts in capacity building and regional research to improve outcomes for children with cancer.

EP742/#1082 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### IMPLEMENTATION AND FINDINGS FROM THE ST. JUDE EDUCATION PROGRAM ASSESSMENT TOOL (EPAT) AT THE UNIVERSITY OF GONDAR HOSPITAL (UGH)

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**Background and Aims:** In 2018, University of Gondar Hospital (UGH) (catchment area of 7 million) in northern Ethiopia (population 125 million), in collaboration with Aslan Project (USA), developed and implemented a pediatric hematology/oncology fellowship (PHOF) program. One pediatric oncologist and more than 10 pediatric oncologists from Aslan project oversee two fellows caring for more than 160 children diagnosed with cancer annually. Our team implemented the St. Jude Children's Research Hospital Program Assessment Tool (EPAT) to identify strengths and opportunities to guide and track program development.

**Methods:** The EPAT, an assessment survey, has ten domains covering aspects of patient care, infrastructure, and educational organization across PHO programs. Numerical score calculations within each domain include three levels of maturity: developing (<50%), perform-

ing (50-75%), and optimal (>75%). Recommendations are provided to identify opportunities for improvement.

**Results:** The overall status of the education program was optimal (79%). Hospital infrastructure (58%), patient care (60%), program basics (74%), educational culture (70%), and graduate impact (55%) modules were at the performing stage. While education infrastructure (85%), clinical exposure (92%), theoretical curriculum (96%), research (100%), and evaluation (100%) modules were at optimal stages. No module was at a developing stage. Examples of areas of opportunity included expanding ambulatory services to create more significant learning opportunities, improving the ratio of faculty to trainees to allow for sufficient trainee oversight, and supporting trainees to present at conferences and complete peer-reviewed manuscripts. The evaluation acknowledged that as a new program, large elements of graduate impact could not be measured at this time.

**Conclusions:** UGH is committed to training quality pediatric hematologists/oncologists, which requires assessing all aspects of the training program to identify areas for improvement. The EPAT documented current program strengths and opportunities. As a next step, the fellowship program administrators will meet with stakeholders and collaborators to prioritize local interventions based on the opportunities identified.

EP743/#1627 | Poster Topic: AS05 SIOP Scientific Program/AS05.r  
*Epidemiology, Policy and Advocacy*

#### COUNTING THE UNSEEN: ESTIMATING DISTRICT-LEVEL RATES OF UNDIAGNOSED PEDIATRIC CANCERS IN MALAWI

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**Background and Aims:** Models of total cancer incidence in African children estimate over half of all cases are undiagnosed. We conducted a study to estimate undiagnosed cases in the catchment area of a pediatric cancer program at Kamuzu Central Hospital (KCH) in Lilongwe, Malawi, representing the northern and central regions of the country.

**Methods:** We adapted a model from the International Agency for Research on Cancer (IARC) that estimated the country-level total cancer incidence in children 0-14. Aggregate counts of cancer diagnoses by district for the year 2022 were obtained from KCH. Cancer incidence estimates for the 15 districts that comprise the catchment area for KCH were calculated using the IARC model and compared to observed counts.

**Results:** The population of children in the catchment area was 4,525,187, and the estimated number of cancer cases was 804 (177.7 cases per million person-years). The observed cases were 178

(39.3/million; 22% of the total estimate). There were an estimated 240 cases of leukemia and 35 observed (15%), 202 estimated cases of lymphoma and 48 observed (24%), 347 estimated solid tumors and 79 observed (23%), 219 estimated central nervous system tumors and 16 observed (7%), and 17 estimated cases of retinoblastoma and 16 observed (92%). Among the top three most populous districts closest to KCH, in Lilongwe, there were 207 estimated cases (178.4/million) compared to 58 observed (49.9/million; 28% of total), in Kasungu, 71 estimated (177/million) and 22 observed (55/million; 31%), and in Dedza, 68 estimated (177.8/million) and 17 observed (44/million; 25%). **Conclusions:** A high proportion of the expected retinoblastoma cases were identified at KCH. Lower proportions of other cancer types were observed. While we need to further assess the accuracy of these estimates, they suggest that most pediatric cancer cases are undiagnosed in Malawi, even in central districts with higher access to subspecialty cancer care.

EP744/#1701 | **Poster Topic: AS05 SIOP Scientific Program/AS05.r Epidemiology, Policy and Advocacy**

## ROLE OF CIVIL SOCIETY IN IMPROVING CHILDHOOD CANCER CARE IN LATIN AMERICA

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**Background and Aims:** Childhood cancer (CC) is a devastating disease that requires significant resources, and its outcomes depend on the economic realities of the country and/or the family of origin. In Latin America (LA), there is great inequality between countries in terms of diagnosis and access to adequate and timely treatment; civil society (CS) has a crucial role to play in addressing these disparities, and has been strengthened to play a more prominent role in service delivery, awareness raising, and advocacy. The GICC promoted by the World Health Organization (WHO), and other key stakeholders, provides an opportunity for states to work with CS to implement best practices in CC control and improve survival rates among children and teenagers.

**Methods:** Information was collected from the contributions of the different organizations and a bibliographic review to have the evidence that shows the work of CS in the region.

**Results:** The contributions of the CS are varied, more frequent is the provision of support in psychosocial areas to allow more expeditious access to treatment and/or improve the quality of life. Some organizations also deliver diagnostic and treatment strategies and education on timely cancer diagnosis. Progress has been made in strengthening the CS in fundraising and capacity building with organizations in several countries playing an important role. Honduras, Dominican Republic, Colombia, Mexico, Brazil, Panama, Uruguay, Argentina and Chile, among other countries, have organizations that have played a very important role in improvements in this field. Professionalism in

all organizational areas is necessary to support more children and be considered by decision makers and resource providers. The ENLACE program has had a significant impact.

**Conclusions:** In all the countries of our region, the SC contributes to give better opportunities to children with cancer from different areas, psychosocial, medical, school, education, hospital infrastructure, among others.

EP745/#700 | **Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship**

## IMPROVING THE OUTCOME OF CHILDHOOD CANCER WITH NUTRITION IN NIGERIA. BY RACHEL NOYEM NWOKORO

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**Background and Aims:** The study aims to identify nutritional status (NS) evaluation as a modifiable prognostic factor that can be intervened upon as a standard management to improve the clinical outcome of childhood cancer, treatment of alterations in nutritional status promptly, collaborations between multidisciplinary sectors on nutrition and cancer friendly diets like ready to use therapeutic foods all encompassing as nutritional support in the management of childhood cancer.

**Methods:** 53 children on chemotherapy and survivors of childhood cancer (29 males and 24 females) ages 5 years to 14 years of age with their parents from October 2022 to November 2022, participated in a semi structured interview carried out in the pediatric oncology ward of Lagos University Teaching Hospital, Idi Araba, Lagos State, Nigeria

**Results:** We successfully interviewed 53 parents whose children were undergoing cancer treatment or were survivors of cancer and were asked questions regarding nutrition during their child's treatment and after including whether they received support from a health professional, if their children experienced weight loss or multimodal treatment side effects and if they believed that their children were receiving adequate nutritional support for recovery. The study showed that 90% (48 Children) of the parents did not receive adequate information or guidance on the importance of nutrition and support during their child's cancer treatment from health care providers, while 10% (5 Children) who received guidance from online reviews and researches gave reports of better outcome. Those who had no nutritional support were at high risk of having poor outcomes

**Conclusions:** Nutritional status evaluation from the onset of diagnosis should be a standard management, diet implementation and nutritional follow up should be incorporated as an integral part of the care pathway. It is vital that the children with cancer receive prompt

and appropriate nutritional support especially in developing and low income countries like my country Nigeria

EP746/#1355 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

### IMPROVING EMPOWERMENT AND BETTER EXPERIENCE IN LONG-TERM FOLLOW-UP CLINICS: A SOUTHCENTRAL ENGLAND REGIONAL EXPERIENCE OF THE EFFECTIVENESS OF READY STEADY GO HELLO TRANSITION PATHWAY

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**Background and Aims:** Background Over 60% of childhood cancer survivors (CCS) and children with chronic illnesses experience a lifelong risk of increasing morbidity and mortality into adulthood due to multimodal treatment related complications. Evidence suggests that effective transition encompassing education and empowerment improves long-term outcomes. Transition planning continually needs quality improvement for benefiting survivors. Children's Hospital Southampton (UHS), a tertiary subspecialty centre, created a 4-stage transition programme, *Ready, Steady, Go, Hello (RSGH)* across all childhood subspecialties, including oncology. RSGH, starting at 11-12 yrs with 'Getting Ready' and finishing when the CCS arrives at adult services with 'Hello', is a traffic light-based questionnaire tool implemented in our long-term follow-up (LTFU) clinics. **Aims** Assess the feasibility and attitudes of patients, parents, and healthcare professionals towards RSGH. Evaluate the timeliness, ease of use, delivery, and efficacy of the RSGH programme across subspecialties including oncology.

**Methods:** In this Quality Improvement Project, we interviewed 17 CCS aged 12-24 yrs, 15 parents and 15 healthcare professionals (HCP) regarding their experience in LTFU clinics with RSGH, via age-appropriate questionnaires in 2022. We analysed their responses qualitatively and quantitatively. We compared ours with the published nephrology and endocrinology evaluations to make recommendations. **Results:** Both CCS (76.8%) and parents (82.7%) expressed positive attitudes to RSGH. We measured statistically significant increase in 'strongly agree' responses in all aspects from CCS in the initial "Ready/Steady" stages compared with final "Hello" stage ( $p=0.023$ , two sample T-test). All HCP across subspecialties including oncology had positive opinions to RSGH.

**Conclusions:** RSGH improves the experience, the engagement in shared decision making with education and better compliance of CCS and children with chronic illnesses. RSGH is structured and adaptable across childhood subspecialties. Ongoing areas for advancement include

better support for mental health, tailoring for learning difficulties, discussions around fertility and enabling online delivery of a National RSGH programme.

EP747/#1410 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

### PSYCHOLOGICAL STATUS OF ADULT SURVIVORS OF CHILDHOOD CANCER: AN INSTITUTIONAL CROSS-SECTIONAL ANALYSIS OF 236 SURVIVORS

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**Background and Aims:** Psychological disorders are common among survivors of childhood cancer, with scarce data from low-middle income settings (LMIC). This study estimated the prevalence of anxiety, depression, low self-esteem, perceived low/moderate social support and sexual dysfunction among adult survivors of childhood cancer from LMIC setting.

**Methods:** Consenting adult survivors (current age  $\geq 18$  years and cancer free  $\geq 2$  years) of cancer diagnosed  $\leq 21$  years were consecutively recruited from survivorship care clinic at our centre between December 2020-January 2023. Hospital Anxiety and Depression scale was used with score  $\geq 11$  and 8-10 representing mild and severe anxiety/depression respectively. Rosenberg self-esteem scale was administered with score  $< 15$  indicating low self-esteem. Multi-dimensional scale of perceived social support was administered with score between 1-2.9 and 3-5 considered as low and moderate perceived social support respectively. Sexual dysfunction questionnaire-19 (SDQ-19) was administered to willing survivors who were married/in stable relationship for 1 year and score  $< 45$  indicated sexual dysfunction. Predictors of psychological disorders were assessed by logistic regression analyses.

**Results:** Among 698 survivors attending the clinic during the study period, 236 were included (Median age 22 years, 173 (73.3%) male, 155 (65.7%) haematological malignancies). Median age at diagnosis was 14 years with median off treatment duration of 7.5 years. The prevalence of severe anxiety, mild anxiety, severe depression and mild depression was 54 (22.9%), 94 (39.8%), 44 (18.6%) and 148 (62.7%) respectively. Fifteen (6.4%) survivors had low self-esteem. Five (2.1%) and 24 (10.2%) survivors perceived low and moderate social support respectively. SDQ-19 was administered to 116 survivors and 3 (2.6%) survivors had sexual dysfunction. Solid cancer survivors had lower self-esteem (11.1% vs 3.8%, OR=3.10,  $p=0.038$ ) with no other factors predictive of any other psychological disorders.

**Conclusions:** Depression and anxiety are common among childhood cancer survivors. Low self-esteem is more likely among solid cancer



survivors. Psychological care should be an integral part of survivorship care.

EP748/#947 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

### ASSESSMENT OF TREATMENT SEQUELAE AND QUALITY OF LIFE AMONG SURVIVORS OF HEAD AND NECK EWING SARCOMA

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**Background and Aims:** Head and neck Ewing sarcoma (HN-ES) accounts for 1-9% of ES cases and have favourable treatment outcomes. No prior data exist on functional and cosmetic morbidity among survivors. This study examines quality of life (QOL) and sequelae in HN-ES survivors.

**Methods:** This prospective study included survivors of paediatric HN-ES registered at our centre between 2003-18 aged >15 years at enrolment. Baseline clinicodemographic details were compiled. QOL was assessed using the EORTC-QLQ-C30 and H&N-35 tools. Reference values were obtained from the EORTC Reference Values Manual (2<sup>nd</sup> Ed) and a Swedish general population cohort for QLQ-C-30 and H&N-35 respectively. A score difference from reference values of 5 was considered significant. For dental assessment, the clinical oral dryness (CODS) index; the decayed, missing, and filled permanent teeth (DMFT) index; and mouth opening were recorded. A comprehensive ophthalmologic was performed.

**Results:** Fifteen survivors [13 males; median age at diagnosis: 12 years] were enrolled. All subjects received neoadjuvant chemotherapy followed by local treatment (surgery alone: 2/15, surgery plus radiotherapy: 3/15, radiotherapy alone: 9/15). At enrolment, 11/15 (73.3%) had graduated college or were continuing education. The survivors had worse self-reported cognitive functioning than the reference cohort [mean (SD): 80 (27.6) vs 86.1 (20)]. However, overall health-related QOL (HRQOL) was unimpaired [78.9 (15.0) vs 71.2 (22.4)]. On H&N-35, the domains of local pain [8.9 (12.4) vs 3.4 (9.3)], swallowing [8.3 (19.2) vs 1.6 (6.5)], social eating [7.8 (10.2) vs 2.6 (8.9)] and teeth-related symptoms [24.4 (29.4)] were impaired among survivors. Dental evaluation showed that 6/15 (40%) of patients had moderate-severe oral dryness, 5/11 (43.6%) had moderate-to-severely impaired DMFT, and 5/12 (41.7%) had trismus. Five of 12 (41.7%) had cataract,

2/12 (16.7%) had glaucoma and 8/16 patients (50%) had abnormal tear film breakup time.

**Conclusions:** This is the first study that objectively assesses treatment consequences in HN-ES survivors, who had impaired daily functioning due to dental and ophthalmologic sequelae. Better recognition of survivor issues will allow early referral for specialised care, thus enriching the survivorship experience.

EP749/#335 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

### SUPPORTIVE CARE NEEDS OF AYAS AND THEIR PARENTS 5 YEARS FOLLOWING CANCER

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**Background and Aims:** Adolescents and young adults (AYAs) who have been treated for cancer are at great risk of physical, psychological or social consequences of cancer and associated treatments (Zabih, 2020; Nicklin, 2019). However, compliance to the long-term follow-up is low (Knighting, 2020). One possible explanation is that follow-up care fails to answer to the AYA survivors' and their families' expectations. The aim of this study is to explore specific supportive care needs (SCN) of AYAs and their parents in follow-up, five years post-diagnosis.

**Methods:** Exploratory interviews were conducted with fifteen AYAs aged 15 to 25 years old and twenty-two parents. Thematic analyses were realised in order to highlight SCN categories.

**Results:** Fertility and reassurance were the two categories of needs most reported by AYA survivors (each mentioned by 66.7% of AYAs), followed by the need for functional care, follow-up coordination and pluridisciplinarity (60% of AYAs each). Most parents reported the need for follow-up coordination (77.3%), for psychological care (72.7%) and the need for information about the cancer repercussions (63.6%). AYA and parent participants also reported needs regarding social relationships, administration and finance, academic and professional domains. A large majority of these expressed needs were declared unmet.

**Conclusions:** SCN are still present in AYA survivors and their parents 5-years post diagnosis. As unmet needs highlight defaults in offered care in follow-up, a better understanding of AYAs' and parents' SCN and unmet needs enable us to adapt long-term follow-up care, but also to improve compliance and comprehensive quality of life.

EP750/#1238 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

### ESTABLISHMENT OF END-OF-TREATMENT DAY HOSPITAL FOR ADOLESCENTS AND YOUNG ADULTS WITH CANCER

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**Background and Aims:** 2300 cases of cancer/year are diagnosed in France among AYA. This population has been specifically targeted, leading to the development of dedicated structures. The occurrence of cancer in this period leads to specific problems, and the transition from the end of treatment (EOT) to the follow-up remains sensitive. We therefore hypothesize that a multidisciplinary EOT day hospital (DH) would improve the quality of life of former patients.

**Methods:** The DH is scheduled after the evaluation of EOT. It consists at least of an interview with a psychologist, a social worker and an oncologist. The objectives of the medical consultation are to summarize the pathology, the treatments and to develop a personalized plan after cancer. The physician carries out both a clinical assessment and a comprehensive assessment of the patient. The psychological interview assesses future care needs and directs the patient to external management if necessary. The social interview guides the patient towards possible social assistance. Some consultations may be added if necessary (dietary consultation, APA, etc.).

**Results:** Created in January 2022, this DH has been proposed to 77 AYA. 66 have been achieved, resulting in a participation rate of 86%.

**Conclusions:** The goal of this DH is to reduce the impact of cancer. Although many recommendations are written, few devices exist allowing this multidisciplinary and expert management from EOT. A study is in progress assessing the feasibility and acceptability of this DH, as well as its impact on the quality of life.

EP751/#919 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

### FEASIBILITY AND POTENTIAL EFFECTIVENESS OF A NOVEL NURSE-LED VIDEO-COACHING FATIGUE INTERVENTION FOR CHILDHOOD, ADOLESCENT, AND YOUNG ADULT CANCER SURVIVORS: THE REVIVER FATIGUE STUDY

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**Background and Aims:** Twenty-four percent of childhood, adolescent, and young adult (CAYA) cancer survivors experience cancer-related fatigue, negatively impacting their quality of life. This study aimed to assess the feasibility and potential effectiveness of the REVIVER fatigue intervention, a nurse-led video-coaching intervention designed to reduce cancer-related fatigue in CAYA cancer survivors.

**Methods:** We used a single-group mixed methods design. CAYA cancer survivors, aged 16-54 years,  $\geq 5$  years post-treatment with fatigue defined as a score  $>35$  on the Checklist Individual Strength, participated in 3-5 nurse-led video-coaching sessions based on cognitive behavioural therapy. We assessed feasibility on demand, adherence, acceptability, practicality, integration/implementation, and reported results descriptively. Qualitative data was collected using semi-structured individual and focus group interviews with a subset of participants and involved healthcare professionals. We performed paired sample t-tests to assess changes in self-reported fatigue, quality of life, lifestyle, self-management, and self-efficacy at baseline (T0), post-intervention (T1), and at 6 months follow-up (T2).

**Results:** Fifteen CAYA cancer survivors were included (median age of 32 [21-53] years, 53.3% females). All feasibility criteria were met with a high demand (71.4% participation rate) and adherence to the sessions (100%). The intervention was acceptable with a mean score of 8.5 and 7.5 (scale 1-10) given by survivors and healthcare professionals, respectively. Regarding potential effectiveness, total fatigue and severity of fatigue scores were significantly lower at T1 vs. T0 ( $p=0.012$ ,  $p=0.004$ , respectively) and T2 vs. T0 ( $p=0.003$ ,  $p=0.005$ , respectively), whereas reduction in activity was significantly improved at T1 and T2 vs. T0 ( $p=0.031$ ,  $p=0.012$ , respectively). Concentration problems ( $p=0.033$ ), decreased motivation ( $p=0.016$ ), cognitive functioning ( $p=0.049$ ), social functioning ( $p=0.035$ ), and perceived control over health scores ( $p=0.020$ ) were also improved at T2 compared to T0.

**Conclusions:** The REVIVER fatigue intervention was found feasible and potentially effective to reduce fatigue, improve quality of life and self-management outcomes in CAYA cancer survivors.

EP752/#1819 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

### DISPARITIES IN HEALTH-RELATED DISTRESS AND BEHAVIORS IN PARENTS AND SURVIVORS OF CHILDHOOD CANCER

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**Background and Aims:** Describe health behaviors, health status perceptions and health-related distress amongst Hispanic parents and survivors of pediatric cancer.

**Methods:** Utilizing survey data collected from the multi-institutional Survivorship and Access to Care for Latinos to Understand Disparities (SALUD) cohort, responses to a 56-item bilingual survey assessing health behaviors, health status perceptions and perceived late effect risk were compared. Responses were scored on a Likert scale from 1-5. A t-test was used to analyze differences in mean scaled responses by self-reported ethnicity, respondent type, survey language, and time from diagnosis.

**Results:** Survey respondents included 119 survivors and 107 parents. Of 226 respondents, 104 self-identified as Hispanic, 117 as non-Hispanic, and five chose not to respond. Hispanic respondents indicated heightened concern for treatment late effects compared to non-Hispanics ( $p=0.04$ ). Hispanic respondents also reported poorer overall health in the preceding three months ( $p=0.03$ ) and experienced higher frequency of worry about their or their child's overall health ( $p<0.01$ ). Hispanic respondents indicated greater concern for developing illness or identifying a new health condition at a routine medical visit when compared to non-Hispanics ( $p<0.01$ ). No differences in health behaviors or perceptions were observed by survey language; however, only 24 Spanish surveys were completed. Despite a higher likelihood for poorer health and greater health-related concerns, Hispanic respondents were not more likely to seek routine ( $p=0.23$ ) or cancer-related medical care ( $p=0.52$ ) when compared to non-Hispanics.

**Conclusions:** Hispanic survivors and parents report poorer overall health and higher health-related distress after treatment than non-Hispanic survivors and parents, perceptions that did not align with a change in health-related behaviors. These results are suggestive of ethnic disparities in quality of life and health-related worry amongst survivors of childhood cancer and their families. Application of qualitative methodologies may elicit factors underlying these differences and how they impact patterns of survivor engagement in primary and cancer-related medical care.

EP753/#342 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

#### THE PSYCHOSOCIAL IMPACT OF DISEASE RELAPSE ON YOUNG ADULT SURVIVORS OF CHILDHOOD CANCER

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**Background and Aims:** Pediatric cancer survivors are at risk for psychosocial late effects even decades after treatment. A recent study (Chow et al., 2019) found cancer recurrence increased the risk for psychosocial sequelae in pediatric brain tumor survivors; the current study examined this association in young adult survivors across pediatric cancers.

**Methods:** Young adult survivors of pediatric cancer aged 18-40 enrolled on a local cohort study (Project REACH) completed the Brief Symptom Inventory-18 (BSI-18) assessing anxiety and depression, a suicidality checklist, and the Short Form-12 (SF-12) measuring quality of life.

**Results:** The 285 participants were 50% female; 86% White, Non-Hispanic, with mean age of 24.90 years ( $SD=5.48$ ); mean age of diagnosis = 10.50 years ( $SD=5.67$ ). Forty-three survivors (15%) experienced relapse; mean time from relapse to survey = 12.69 years ( $SD=6.15$ ). Relapse was not associated with any demographic variables but was more common in brain tumor survivors (22.5%) than other survivors (10.3%;  $p=0.005$ ). Among brain tumor survivors ( $n=111$ ), relapse was associated with significantly higher depression scores ( $d=0.49$ ,  $p=0.037$ ) and anxiety scores ( $d=0.53$ ,  $p=0.029$ ), but not associated with SF-12 scores. Brain tumor survivors who relapsed more commonly reported suicidal ideation, but this association was not significant ( $OR=2.54$ ,  $p=0.089$ ). Among non-brain tumor survivors ( $n=174$ ), relapse was not associated with any measured variables.

**Conclusions:** Among pediatric brain tumors survivors, data show relapse increases risk of psychosocial sequelae even many years later in young adulthood. No such relationship was found in survivors of other pediatric cancers. Clinicians caring for pediatric brain tumor survivors should be aware of the long-term psychological risks of relapse. To improve identification and treatment for these survivors, future research should examine how factors such as treatment exposures and fear of cancer recurrence may mediate this risk.

EP754/#590 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

#### THE COMPARISON OF SLEEP QUALITY BETWEEN ACUTE LYMPHOBLASTIC LEUKEMIA SURVIVORS AND SIBLINGS VERSUS CAREGIVERS'

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**Background and Aims:** While evidence on sleep in children with cancer during treatment is well-known, information on these subjects off

treatment is very limited. There is also sparse knowledge on their siblings and caregivers. Our study aimed to evaluate sleep patterns and to compare acute lymphoblastic leukemia survivors (ALLs) with siblings and caregivers.

**Methods:** Eighty-six participants (ALLs, n=33; siblings, n=20; caregivers, n=33) were enrolled to the cross-sectional study. ALLs and siblings completed Children's Sleep Habits Questionnaire (CSHQ). Caregivers filled Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS).

**Results:** Both 27 (81.81%) ALLs and 10 (50%) siblings had poor sleep according to the CSHQ results (score >41). The total scores of CSHQ in ALLs were significantly worse than that of siblings (54 vs 45: respectively  $p = 0.001$ ). Caregivers had poor sleep according to PSQI and ESS scores (12 % and 15%, respectively), and there was a significant correlation between them ( $r = 0.424$ ;  $p = 0.014$ ). No relation was found between ALLs, siblings, and caregivers in sleep quality ( $p > 0.05$ ).

**Conclusions:** In our study, it is found that the prevalence of sleep disturbances in ALLs off therapy is very high. Although siblings were found to have disturbed sleep, it is not as high as ALLs. However, in comparison to children, the caregivers had significantly good sleep quality. Future studies should be focused on both ALLs and their siblings on the management of poor sleep quality.

EP755/#405 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

#### FRAILITY AND ITS ASSOCIATION WITH NEUROBEHAVIORAL OUTCOMES IN SURVIVORS OF CHILDHOOD CANCER

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**Background and Aims:** Emerging evidence is supporting the role of "premature aging" in functional impairment among patients with cancer. Like physical and cognitive frailty, "premature aging" might contribute to elevated vulnerability to psychological stressors. We evaluated the association of frailty and neurobehavioral outcomes in survivors of childhood cancer.

**Methods:** We recruited 97 survivors (male 48.5%; current age 28.9 [SD=6.9] years) of childhood leukemia (n=59, 60.8%) and solid tumors (n=38, 39.2%) from an academic hospital in Hong Kong. Survivors self-reported their neurobehavioral functioning using the validated Achenbach System of Empirically Based Assessment (ASEBA) Adult Self-report Checklist. Survivors also underwent a clinical evaluation

and bioelectrical impedance analysis, and were classified as "non-frail", "prefrail" or "frail", respectively defined as  $\leq 1$ , 2 or  $\geq 3$  of: muscle wasting, muscle weakness, low energy expenditure, slow walking speed, and exhaustion (Fried's frailty phenotype). General linear modeling was conducted to evaluate the association between frailty and neurobehavioral scores, adjusting for age, sex and cancer type.

**Results:** At 18.8 (SD=7.6) years post-diagnosis, a minority of survivors reported significant depressive (13.4%), anxiety (9.3%), and somatic (13.4%) problems, as well as inattention (5.2%) and sluggish cognitive tempo (16.5%). Overall, 25.8% (n=25) were classified as "pre-frail" and 28.8% (n=28) were classified as "frail". As compared to "non-frail"/"pre-frail" survivors, "frail" survivors were more likely to have developed a chronic condition (53.8% versus 25.0%,  $P=0.034$ ) and were younger at cancer diagnosis (8.3 versus 12.5 years;  $P=0.029$ ). Multivariable analysis showed that as compared to "non-frail" survivors, "frail" survivors (Est.=4.14, standard error[SE]=1.97;  $P=0.039$ ) reported significantly more withdrawal symptoms. "Frail" survivors also demonstrated more depressive symptoms (Est.=3.26, SE=1.59;  $P=0.049$ ), and more sluggish cognitive symptoms (Est.=3.63, SE=1.92;  $P=0.042$ ).

**Conclusions:** Our study suggests that physiologic aging processes might affect psychological and behavioral outcomes in survivors. Future work should investigate targeted interventions that mitigate physiological and behavioral effects of aging, such as exercise and lifestyle modification programs.

EP756/#699 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

#### PRIORITIES OF LONG-TERM CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA SURVIVORS ENROLLED IN EORTC CLG STUDIES: ASSESSING QUALITY OF LIFE ACROSS A RANGE OF MEASURES

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**Background and Aims:** Survivors of childhood cancer can sometimes suffer from long-term sequelae or a decline in quality of life (QoL). Hence, investigations into long-term survivorship are increasing, and critical consideration and selection of outcome measures become more important. The aim of the study was to investigate priorities of survivors of childhood Acute Lymphoblastic Leukaemia (ALL) and their QoL issues as measured across three different QoL outcome measures. **Methods:** Childhood ALL survivors enrolled in EORTC studies in Belgium and France between 1971 and 1998 were invited (n=507) to complete QoL questionnaires, including the Short Form Health Survey (SF-12), the Impact of Cancer for Childhood Cancer Survivors (IOC-CS), and the Quality-of-Life Systemic Inventory (QLSI – assessing priorities). Relationships between these measures were examined to assess whether these QoL measures are comparable. More specifically, Pearson correlations were used to explore associations among the different subscale scores of the IOC-CS and SF12, and scales of the three measures were compared.

**Results:** A total of 183 survivors provided QoL data, with a median age at follow-up of 26.1 years (range 18.1-52.8) and a mean time since diagnosis of 20.5 years (range 12.9-41.6). The majority of subscales/domains between SF12 and IOC-CS showed negligible (<0.3) to moderate ( $0.30 \leq r < 0.45$ ) correlations, indicating complementary assessment of QoL domains. Priority areas of QoL identified by the QLSI included questions about overall physical health, interaction with family/friends, peace of mind, self-esteem and love life. The latter three of these domains were not represented in the other two questionnaires.

**Conclusions:** Our findings suggest that the measures complement each other but fail to cover all priority issues for ALL survivors. Using a cancer survivorship measure, combined with additional items covering selected priorities might provide a more holistic picture of the QoL outcomes of long-term adult survivors of childhood cancer.

EP757/#1773 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

#### FERTILITY PRESERVATION IN CHILDHOOD AND ADOLESCENTS CANCER PATIENTS: EXPERIENCE OF A TERTIARY HOSPITAL

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**Background and Aims:** Childhood cancer treatments can affect fertility and produce gonadal dysfunction. Due to the pressure of prompt cancer treatment many patients remain uninformed on the potential gonadal damage. The aim is to explore the utilization of fertility preservation methods in our hospital.

**Methods:** Retrospective descriptive study by medical record review of pediatric cancer patients (hematological and solid malignancies) diagnosed in our hospital between 2019 and 2022. We recorded and analyzed clinical characteristics and fertility preservation procedures.

**Results:** Over this period, 161 patients with childhood cancer (0-17 years old) were diagnosed in our hospital. Gender distribution was 90 boys (55.9%) and 71 girls (44.1%) with an average age of 7.8 years. Fertility preservation was advised to 42 patients (26%) and was performed in 33 of them (13 sperm cryopreservation, 6 testicular tissue cryopreservation, 9 oocyte cryopreservation, 5 ovarian tissue cryopreservation). Most of the techniques were performed before treatment (30 patients). Of the 115 prepubertal patients, fertility preservation was done in 11 patients as part of an investigational project. Among the 119 patients who were not offered a fertility preservation plan, 67 (73.9%) were boys and 52 were girls. The 6 postpubertal males who were not offered semen preservation, had terminal cancer or received a non-gonadotoxic treatment. Among the 10 postpubertal women, 2 had acute lymphoblastic leukemia and 8 other type of cancers that did not require gonadotoxic treatment. In our hospital there is no fertility preservation protocol for acute leukemias. All the techniques were done locally in our center.

**Conclusions:** The percentage of patients counseled for fertility preservation is low but given that the study is based on reviewing medical records, it is likely that fertility has been discussed with a larger number of families. It is however important to create a fertility preservation care plan for all our patients.

EP758/#1302 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

#### IS FERTILITY PRESERVATION BEING DISCUSSED AND OFFERED TO CHILDHOOD CANCER PATIENTS IN THE U.K.?

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**Background and Aims:** As childhood cancer survival rates increase, long-term treatment sequelae, including impaired fertility are an increasing concern. Patients and families desire information about fertility, and discussing fertility has a positive psychological impact. It is recommended that fertility should be discussed with all childhood cancer patients and fertility preservation (FP) offered to eligible patients. We undertook a Children's Cancer and Leukaemia Group (CCLG) led audit, aiming to clarify whether this standard is met in the U.K.

**Methods:** The CCLG's 20 principle treatment centres were invited to participate in a national audit, collecting six months of data relating to fertility on all patients <18 years, newly diagnosed with cancer. Fully anonymised data was analysed centrally.

**Results:** Nine centres submitted data on 348 patients, diagnosed at median age of 6 years (range 0-17). Fertility was discussed in 230/348 (66.0%) cases; 62/230 (26.8%) patients were involved in the discussion, with patients  $\geq 10$  years old more likely to be included ( $p < 0.0001$ ; Fisher's exact test). FP referrals were offered to 75 patients and accepted by 52, with potential treatment delay the most common reason for declining. Fertility was discussed with 148/242 patients scheduled to receive low/medium risk treatment, compared to 79/90 for high/very high risk ( $p < 0.0001$ ; Fisher's exact test). The most common reason for clinicians not offering FP was low risk of treatment-induced subfertility (182/348, 52.3%); others included urgency to start treatment (11.8%), patient age (7.5%), and palliative intent (2.9%).

**Conclusions:** We show that fertility is not being discussed with all childhood cancer patients, contrary to guidance. FP is more likely to be offered to patients receiving higher risk treatment, whilst urgency to start treatment is a barrier for patients/families and clinicians. In order to optimise access to FP for eligible patients,

fertility must be considered and discussed following cancer diagnosis.

EP759/#912 | **Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship**

### MULTI-SITE IMPLEMENTATION OF A SURVIVORSHIP SURVEILLANCE DATABASE: LESSONS LEARNED FROM PEDIATRIC ONCOLOGY GROUP OF ONTARIO (POGO)'S PROVINCIAL AFTERCARE PROGRAM

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**Background and Aims:** In Ontario, five tertiary pediatric oncology programs and two adult cancer centres collaborate with the Pediatric Oncology Group of Ontario (POGO) to create an integrated provincial system of AfterCare for survivors of childhood cancer (SCC). Here we describe the development of the POGO AfterCare Database, which supports system planning, program reach and preventive screening among SCC followed in the POGO AfterCare Program.

**Methods:** POGO conducted an environmental scan to determine the evolution of SCC and care providers' information needs. Between 2020 and 2022, a new database was custom developed at POGO using Microsoft SQL Server and the MS. Net Core Framework having optimized performance and high level data security in compliance with the Ontario Personal Health Information Protection Act (PHIPA). The Database was developed in consultation with stakeholders to streamline and standardize data collection for survivor surveillance, to reflect the information needs of SCC and care providers and to enable care teams to access important patient demographics and clinically relevant trends.

**Results:** Implementation of the database occurred over 6-months with data sharing agreements completed for each centre. Fiscal year 2023 analyses to date showed N=1614 patient visits, 12 high-risk breast cancer screening results, 195 cardiac screening results, and 435 specialist referrals. Feedback on database functionality, layout and essential data fields was positive. Data quality and completeness were achieved by implementation of strict data validation rules,

regular data quality reviews and the prevention of free-text entry to optimize multi-institutional data collection efforts. Capturing comorbidities remains challenging due to the variable provision of healthcare outside the aftercare setting, where data capture are variable and likely incomplete.

**Conclusions:** The creation of a multi-site SCC database will enable long-term and standardized data collection and reporting, which can provide dynamic resources for providers and inform funding, policy and targeted interventions in pediatric cancers.

EP760/#290 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

NEUROCOGNITIVE SEQUELAE OF CHILDREN TREATED FOR CENTRAL NERVOUS SYSTEM TUMOR: ABOUT 27 PATIENTS

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**Background and Aims:** The overall survival of children treated for a tumor of the central nervous system have improved markedly over the last decades, which has given rise to a population of long-surviving patients at risk of developing neurocognitive long-term sequelae. The objective of our work was to study the neurocognitive deficit of a series of patients treated at the Salah Azaiz Institute in Tunisia, and to identify the various predictive factors.

**Methods:** We conducted an analytical cross-sectional study, involving 27 patients treated for a CNS tumor at an age of less than 18 years between 2003 and 2018 with a minimum follow-up of 3 years. we have evaluated the following neurocognitive domains: Global efficiency, IQ, Short term memory (STM), Long terme memory (LTM), Mental flexibility, attention, Information processing speed (IPS), mood trouble. A search for predictive factors was carried out using the clinical, paraclinical, dosimetric data.

**Results:** A neurocognitive deficit in at least one cognitive domain was present in 23 patients, this deficit was moderate to severe in 14 patients. It was present in the global efficiency in 15 patients, an IQ <85 was found in 5 patients, STM (17 patients), LTM (11 patients), attention (17 patients), Mental flexibility (18 patients), PSI (14 patients), signs of depression were found in 14 patients. We reported a statistically significant follow-up interval linked to a risk of occurrence of neurocognitive deficit; this interval was 6.78 years [5.76 y-7.81 ] p=0.041. We have found as significant predictive factors of neurocognitive deficit, the average dose to the right hippocampus (48.5 Gy vs 38.9), a low socio-economic level, the presence of psychiatric history, the presence of a mood disorder at our evaluation and grade repetition.

**Conclusions:** The pediatric population treated for a tumor of the central nervous system is subject to developing long-term neurocognitive, we have not objectified neither obvious clinical nor therapeutic predictive factors of these sequelae except a psychiatric history and school dropout.

EP761/#1826 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

LONG-TERM RADIOLOGICAL SEQUELAE OF CHILDREN TREATED FOR A BRAIN TUMOR: ABOUT 16 PATIENTS

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**Background and Aims:** Radiotherapy is a main therapeutic arm for the treatment of children with brain tumors, but, at the expense of developing neurologic and neurocognitive long-term sequelae. The objective of our work was to study the radiological sequelae of a series of children treated by radiation at the Salah Azaiz Institute in Tunisia, and to identify the various predictive factors.

**Methods:** We conducted an analytical cross-sectional study, involving 16 patients treated for a CNS tumor at an age of less than 18 years between 2003 and 2018 with a minimum follow-up of 3 years. we have evaluated 16 MRIs before radiation and 45 MRIs after treatment, we looked for white matter lesions and microvascular lesions.

**Results:** 6 patients (40%) presented at least one focal white matter lesion and 7 patients (43%) presented at least one microvascular lesion. No patient showed cerebral atrophy or radionecrosis lesion. The median occurrence of focal substance lesions was 20 months, and 46 months for microvascular lesions. Complete surgical excision associated with a higher risk of developing focal white matter lesions (p=0.048). An age at diagnosis between 5 and 9 years was at greater risk of occurrence of focal microvascular lesions (p=0.044). Focal white matter lesions were associated with a higher grade repetition rate with a p=0.049. Finally, we did not find any significant correlation between the neurocognitive deficit and the presence of the radiological lesions studied.

**Conclusions:** The pediatric population treated for a tumor of the central nervous system is subject to developing long-term radiological lesions, especially white matter and microvascular lesions, the impact of these lesions was remarkable in the schooling of our patients.

EP762/#1689 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

SECOND NEOPLASMS IN CHILDHOOD CANCER SURVIVORS: EXPERIENCE OF NATIONAL CANCER INSTITUTE - BRAZIL

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**Background and Aims:** With the advances in childhood cancer treatment there was an in survival improvement but the risk of second

neoplasms (SN) is still a challenge in long-term follow-up. SN are tumors histologically distinct from the primary tumor that appear at the end of treatment and can be malignant or benign. In addition to being difficult to manage, they are the second leading cause of late death in survivors. Since 2011, Long-Term Follow-up Group (GSLP) at National Cancer Institute-Brazil offers multidisciplinary follow-up to survivors. Aim: To describe the characteristics of patients with childhood and adolescent cancer who developed NS and their outcomes.

**Methods:** Retrospective analysis of NS cases among survivors who were followed up by Long-Term Follow-up Outpatient Clinic from 2010 to 2022. Medical records were analyzed regarding clinical and histopathological data and outcome.

**Results:** Among 1230 survivors, 56 patients (4.5%) had at least one NS and 4 (0.3%) with 2 or more neoplasms. Median age at initial diagnosis was 3 years (0-16 years) and at second neoplasm diagnosis was 20 years (range 0 to 41 years). Most frequent primary tumors were: retinoblastoma (n=16; 28.5%), rhabdomyosarcoma (n=10; 17.8%) and medulloblastoma (n=7; 12.5%). Median time from first and NS diagnosis was 14 years (range 0 to 39). Most frequent NS: acute leukemias/myelodysplastic syndromes (n=10; 17.8%), thyroid carcinoma (n=7; 12.5%), skin tumors (n=5; 8.9% - 1/5 melanoma; 4/5 basal cell carcinoma) and leiomyosarcoma (n=5; 8.9%). Genetic predisposition to cancer in 20 cases: hereditary RB (n=11), Li Fraumeni (n=6), FAP (n=2), DICER (n=1), NF1 (n=1) and Gorlin-Goltz (n=1). Patients with papillary carcinoma and cutaneous tumors had better prognosis and are alive without evidence of disease (n=12, 21.4%). Mortality was 46.4% (26 deaths) corresponding to 2% of survivors and it was due to disease progression, predominantly acute leukemias, leiomyosarcoma and osteosarcoma.

**Conclusions:** This data confirms that NS incidence in childhood cancer survivors between 3-10% and, in general, associated with an unfavorable outcome. Long-Term Follow-up Group in Cancer Center may favor early diagnosis and access to adequate treatment to improve survival and quality of life.

EP763/#1435 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

#### DETERMINANTS OF SYMPTOM SEVERITY IN YOUNG SURVIVORS OF CHILDHOOD CANCER USING THE PEDIATRIC PATIENT-REPORTED OUTCOMES VERSION OF THE COMMON TERMINOLOGY CRITERIA FOR ADVERSE EVENTS (PED-PRO-CTCAE)

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dren's Research Hospital, Division Of Quality Of Life And Palliative Care, Department Of Oncology, Memphis, United States of America

**Background and Aims:** While evaluation of symptoms for patients undergoing cancer therapy is common, symptom evaluation in long-term childhood cancer survivors is underutilized. This cross-sectional study assessed the severity of symptoms self-reported by young childhood cancer survivors using the Ped-PRO-CTCAE and evaluated associations with demographic, family, neighborhood, and cancer-related factors.

**Methods:** Participants included 302 survivors treated at St. Jude Children's Research Hospital, aged <18 years during enrollment, and survived  $\geq 5$  years from their initial cancer diagnosis. Ped-PRO-CTCAE assessed severity of 12 symptoms (stomach pain, constipation, mouth pain, nausea, fatigue, general pain, headache, numbness, worry, sadness, sleep problems, cough). The Family Environment Scale assessed family conflict and cohesion (continuous variables). The County Health Rankings assessed neighborhood adversity (continuous variables). Clinical information was extracted from medical records. For each of the 12 symptoms, the symptom was considered prevalent if the survivor reported at least mild severity (Grade 1). Multivariable logistic regression examined associations between prevalence of each symptom (binary variables) and demographic, family, neighborhood, and cancer-related factors.

**Results:** Survivors' mean  $\pm$  SD age was 14.2  $\pm$  2.8 years; 49.3% were female. Six symptoms were prevalent by >30% of the survivors: stomach pain (31%), general pain (36%), sleep problems (42%), worry (42%), headaches (44%), and fatigue (45%). When compared to females, males were more likely to report stomach pain (OR=3.21, 95%CI:1.85-5.59), worry (OR=2.76, 95%CI:1.63-4.66), and general pain (OR=2.17, 95%CI:1.24-3.81). Survivors with greater family conflict were at increased risk for reporting sleep problems (OR=1.06, 95%CI:1.02-1.09), fatigue (OR=1.04, 95%CI:1.01-1.06), and stomach pain (OR=1.03, 95%CI:1.00-1.06). Increased risk of sleep problems was associated with neighborhood socioeconomic deprivation (OR=1.34, 95%CI:1.09-1.65) and prior treatment with anthracyclines (OR=2.04, 95%CI:1.16-3.61).

**Conclusions:** Severity of pain, fatigue, sleep problems, and symptoms of worry are prevalent among young childhood cancer survivors, and are associated with demographic, family, neighborhood, and treatment factors. Symptom screening in survivors may identify important targets for intervention in this population.

EP764/#806 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

#### ASSOCIATION OF LATE EFFECTS BURDEN AND KNOWLEDGE ON HEALTH RISK BEHAVIORS IN ADOLESCENT AND YOUNG ADULT SURVIVORS OF CHILDHOOD CANCER

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**Background and Aims:** Late effects of childhood cancer can be exacerbated by health risk behaviors among adolescent and young adult (AYA) survivors of childhood cancer, yet the extent to which late effects impact engagement in risk behaviors is unknown. This study investigates this relationship, hypothesizing that an increased number, and greater knowledge, of late effects will be associated with lower engagement in risk behaviors.

**Methods:** AYA [n=589, Mage=19.7 years (SD=2.5), 52.6% female, 61.8% non-Hispanic White (NHW)] participating in a longitudinal study at three pediatric cancer centers completed the Health Knowledge Inventory and reported on health behavior items from established population science surveys. Late effects were determined via electronic health record (EHR) review. Knowledge scores were calculated as the percentage of EHR-confirmed late effects correctly identified by the AYA. Engagement in risk behaviors was dichotomized according to the CDC guidelines. Binary logistic regressions were used to assess the relationship between late effects and odds of risk behaviors.

**Results:** Controlling for demographics and treatment history, a greater number of late effects was associated with lower odds of engaging in risk behaviors (Exp (B)=0.936, p=0.026), particularly vaping (Exp (B)=0.878, p=0.009). Older (Exp (B)=1.133, p=0.047) and male AYA (Exp (B)=1.702, p=0.007) were more likely to engage in any risk behavior, while NHW AYA (Exp (B)=0.636, p=0.049) had lower odds of exhibiting risk behaviors. Greater knowledge of late effects was associated with lower odds of unsafe sun exposure (Exp (B)=0.991, p=0.002) but not associated with substance use.

**Conclusions:** That the absolute number of late effects and not knowledge (apart from sunscreen use), is related to overall risk behavior, may be related to physical impact of late effects hindering desire for or opportunities to engage in risk behaviors. Education about health behavior impact of late effects should target those not currently experiencing late effects and older male AYA.

EP765/#282 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

## HEALTH BEHAVIOR CLUSTERS AND THEIR IMPACT ON NEUROCOGNITION IN ADULT SURVIVORS OF CHILDHOOD CANCER: A REPORT FROM THE ST JUDE LIFETIME COHORT STUDY (SJLIFE)

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**Background and Aims:** Research on childhood cancer survivors has documented harmful effects of risky health behaviors on neurocognition. Often these behaviors are explored individually; however, they often co-occur, and together may have a greater negative effect on neurocognition. This study investigated the impact of patterns of health behaviors on neurocognitive functioning.

**Methods:** Adult survivors of childhood cancer enrolled in SJLIFE (N=3,099; 51% male; median [min-max] 23.6 [6-57] years since diagnosis; 32.2 [18-70] years at evaluation) completed comprehensive standardized neuropsychological testing and behavioral questionnaires. Latent class analysis characterized patterns of health behaviors based on self-reported alcohol consumption, smoking, illicit drug use, marijuana use, physical exercise, and sedentary behavior (e.g., screen time). Separate multinomial logistic regressions examined the associations of primary diagnoses and treatment exposure with behavior clusters, and between behavior clusters and neurocognitive functioning, adjusted for current age, sex, race, age at diagnosis, and cranial radiation exposure.

**Results:** Five clusters were identified: globally unhealthy (30%), heavy/risky drinking (9%), sedentary activity (9%), limited exercise (38%), and healthy (15%). Diagnoses of soft tissue sarcoma (OR [95% CI] 2.6 [1.2-5.5]) and other non-central nervous system solid tumors (OR 2.1 [1.1-3.9]) were associated with higher odds of being in the globally unhealthy cluster. Cranial radiation was associated with lower odds of globally unhealthy behaviors (OR 0.6 [0.5-0.9]) and higher odds of limited exercise (OR 1.4 [1.1-1.9]). The overall globally unhealthy cluster was associated with higher risk of memory impairment (OR 2.6 [1.3-5.2]), whereas the limited exercise cluster was associated with global neurocognitive (OR 4.7 [1.7-13.2]), memory (OR 2.1 [1.1-4.1]), and executive function (OR 1.8 [1.1-2.9]) impairment.

**Conclusions:** Over 60% of survivors engage in multiple unhealthy behaviors or have inadequate levels of exercise, which negatively affect neurocognitive functioning. Interventions targeting lifestyle modification may mitigate neurocognitive problems in this population.

EP766/#434 | Poster Topic: AS05 SIOP Scientific Program/AS05.s  
Survivorship

### LONGITUDINAL CHANGES IN FUNCTIONAL INDEPENDENCE IN SURVIVORS OF PEDIATRIC BRAIN TUMORS: A REPORT FROM THE CHILDHOOD CANCER SURVIVOR STUDY (CCSS)

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**Background and Aims:** Survivors of pediatric brain tumors are at risk for not achieving independence in adulthood. How patterns of independence change as survivors age has not been examined.

**Methods:** 715 adult survivors of pediatric brain tumors (51.6% male, median[*min-max*] 25.7[18.0-44.8] years at baseline assessment, 16.5[7.3-30.2] years since diagnosis), completed CCSS baseline and follow-up questionnaires (median interval 18.2 years [4.1-23.4]). Latent class analysis utilized six variables (ability to attend work/school, marital status, independent living, driver's license, assistance with routine needs, assistance with personal needs) to identify classes of functional independence. Classes of independence were also calculated for 1,929 siblings. Class changes were evaluated using multivariable multinomial logistic regression with survivor characteristics and treatment factors predicting continued dependence or worsening dependence compared to continued or improved independence. Odds ratios (OR) and 95% confidence intervals [95% CIs] are reported.

**Results:** Among survivors, three classes of functional independence were identified: Independent (baseline 33%, follow-up 51%), Moderately Independent – unmarried and living dependently (baseline 47%, follow-up 22%), and non-Independent (baseline 20%, follow-up 27%). Compared to siblings (5%), survivors (18%) were more likely to have worsening independence (Relative Risk=0.53[0.48-0.59]). Relative to survivors with continued or improved independence, Medulloblastoma/PNET survivors were more likely to remain or become non-Independent from baseline to follow-up (OR=1.97[1.3-3.01]) compared to Glioma survivors. Conversely, Ependymoma survivors were less likely to remain or become non-Independent (OR=0.47[0.22-0.99]) than Glioma survivors. Compared to survivors without expo-

sure, >40Gy focal (OR=2.71[1.64-4.49]) and whole brain radiation (OR=4.98[2.82-8.78]) conferred risk of survivors remaining or becoming non-Independent. Younger diagnosis age (OR=0.93[0.88-0.98]) predicted continued or worsened non-Independence.

**Conclusions:** Although 51% of brain tumor survivors achieved independence at follow-up, a significant proportion of survivors experience worsening functional independence as they age. Understanding risk factors for decline in independence over time can inform intervention strategies.

EP767/#1803 | Poster Topic: AS05 SIOP Scientific Program/AS05.s  
Survivorship

### RISK ASSESSMENT OF LATE EFFECTS OF SURVIVORS OF PEDIATRIC CNS-TUMORS AT THE TIME OF TRANSITION TO ADULT FOLLOW-UP CARE

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**Background and Aims:** Survivors of pediatric CNS-tumors have the highest cumulative burden of chronic health condition, with neurological, endocrine, cardiovascular problems at the top of the list (Bhakty et al., 2017). Therefore, existing guidelines clearly indicate the need for monitoring of bio-psycho-social late effects, both in childhood/adolescent and adult follow-up care. The transition to adult care is an extremely critical point here and carries the risk that appropriate and specific care is no longer provided.

**Methods:** To initiate the best possible care in adult follow-up care, a standardized, clinical assessment of burden in 5 dimensions of possible late effects was performed as part of the transition process from follow-up care at the pediatric neuro-oncology unit (Medical University of Vienna) to the continuing adult follow-up care team (IONA). Physical, psychological, social, educational, and family factors, derived from current guidelines, were assessed by an interdisciplinary team. In case of the presence of the defined factors, an increased need for care was identified and handed over to the continuing adult follow-up-care team.

**Results:** One hundred and sixteen survivors were assessed (Medulloblastoma 13%, Low-grade-glioma 41%, Germ-cell tumor 9%, Craniopharyngioma 8%, Ependymoma 8%, High-grade-glioma 7%; mean age at onset: 10.81 years). 93% of them received neurosurgery,

47% chemotherapy, 47% radiation, 7% antiangiogenetic therapy, 10% intraventricular therapy. Transition was performed at an average age of 24.9 years (age range: 18-38 due to new start of the adult follow-up-clinic). Risk assessment of burden revealed that 90%/66%/41%/71%/37% of survivors had increased care needs along the physical/psychological/social/educational/family dimension, with the tumor groups showing different patterns of burden.

**Conclusions:** A substantial proportion of survivors showed increased care needs in all dimensions studied, particularly in the physical, psychological, and educational dimensions. The numbers clearly illustrate the importance of personalized, well-prepared, interdisciplinary transition and the need for targeted, low-threshold bio-psycho-social services in long-term follow-up care.

EP768/#785 | Poster Topic: *AS05 SIOP Scientific Program/AS05.s Survivorship*

#### EFFECT OF AN ONLINE NUTRITION INTERVENTION (REBOOT-KIDS) ON THE DIETARY INTAKE OF YOUNG CHILDHOOD CANCER SURVIVOR'S FRUIT AND VEGETABLE INTAKE: A RANDOMISED-CONTROLLED TRIAL

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**Background and Aims:** Cancer treatment affects a child's food preferences, eating habits and how parents and caregivers respond to these preferences. These dietary changes can continue for childhood cancer survivors (CSS) once treatment is completed, placing them at increased risk for Metabolic Syndrome. We aimed to improve fruit and vegetable intake in CCS using an online parent nutritional intervention with optional telephone support.

**Methods:** This study was a multi-centre wait-list randomised controlled trial assessing change in fruit and vegetable intake from baseline to post-intervention (8 weeks from baseline). Participants (n=50) were parents of CCS aged 2-16 years old who had completed cancer treatment. Participants completed three one online learning module, every 2 weeks, for six weeks, and up to three optional telephone support calls, addressing practical strategies to manage fussy eating and improve fruit and vegetable intake. End of program interviews were conducted via telephone to assess in-depth parental views of their experiences with Reboot-Kids. The interviews focussed on perceived benefits and burdens to participation parent skill acquisition and availability of relevant support services.

**Results:** There was an increase in children's fruit serves (1.9 to 2.8,  $P=0.16$ ), and vegetable serves (1.5 to 2.2,  $P=0.47$ ) from baseline to post program. The intervention group reported higher intakes of both fruit

(2.8 vs 2.2,  $P=0.41$ ) and vegetable serves (2.2 vs 1.7,  $P=0.73$ ) compared to control group, post program. Parent participants reported positive behaviour change following the program, including increased variety in children's diet including fruits and vegetables, increased confidence to introduce and try new foods, and cooking together as a family unit.

**Conclusions:** Reboot-Kids was positively received by parents of CCS and led to promising improvements in children's dietary intake and parent confidence in managing their child's eating habits post treatment.

EP769/#1551 | Poster Topic: *AS05 SIOP Scientific Program/AS05.s Survivorship*

#### GROWTH CHARACTERISTICS AND FINAL HEIGHT IN SURVIVORS OF CHILDHOOD MEDULLOBLASTOMA

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**Background and Aims:** Medulloblastoma is a highly malignant childhood brain tumor, requiring treatment with high-dose craniospinal irradiation and aggressive chemotherapy. Survivors are at high risk for multiple endocrine deficiencies, including growth retardation, which is mainly due to growth hormone (GH) deficiency. Previous studies reported decreased final adult height in survivors of childhood medulloblastoma, with height-SDS (standard deviation score) ranging from -1.9 to -1.5 in patients treated with GH, and from -5 to -3.2 in those not treated with GH. We aimed to describe growth outcomes, response to GH treatment, and final height in survivors of childhood medulloblastoma.

**Methods:** Retrospective analysis of 85 children, adolescents and young adults (males=54) treated for medulloblastoma in a tertiary care center, with a follow-up of at least one year from diagnosis.

**Results:** Fourteen patients (16.4%) completed linear growth before the time of diagnosis. The remaining 71 patients were included in the current analysis. Sixty-two patients (87.3%) exhibited growth retardation over the follow-up period, of whom 36 (58%) were formally diagnosed with GH deficiency, and 23 were treated with GH. Twenty-eight patients achieved final height at the time of analysis, with a mean height-SDS of  $-1.46 \pm 1.4$ . Thirteen of these patients were treated with GH, with a mean final height-SDS of  $-1.29 \pm 1.5$ . One GH treated patient (4.3%) had recurrence of medulloblastoma, and three patients had secondary carcinoma of thyroid. In the group not treated with GH, six patients (12.5%) had recurrence of their disease and two had secondary neoplasms (meningioma and uterine leiomyosarcoma).

**Conclusions:** Growth retardation and GH deficiency are observed in the vast majority of medulloblastoma patients. Final height-SDS in our cohort was higher compared to previously published series. We

suggest that with careful follow-up and early intervention improved adult-height outcome can be achieved. Long term safety is still a concern, and should be discussed with the family prior to initiating treatment.

EP770/#1422 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

### TRAJECTORIES OF PITUITARY HEIGHT AND ENDOCRINE FUNCTION IN SURVIVORS OF CHILDHOOD AND ADOLESCENCE BRAIN TUMORS

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**Background and Aims:** Multiple studies demonstrated hypothalamic-pituitary dysfunction in survivors of pediatric brain tumors, however few studies investigated the trajectories of pituitary height in these patients and their associations with pituitary function. We aimed to evaluate longitudinal changes of pituitary height in children and adolescents with brain tumors, and their association with endocrine deficiencies.

**Methods:** One-hundred and ninety-three patients (males=54.9%) with a diagnosis of brain tumor before age 18 years, with at least two years of radiological follow-up after diagnosis were included in this retrospective study. Patients who had tumors involving the sellar/suprasellar region or the hypothalamus were excluded. Pituitary height was measured on MRI scans performed at the time of diagnosis, and 2, 5, and up to 10 years thereafter. Demographic and clinical data were obtained from the patients' charts.

**Results:** Mean age at the time of diagnosis was  $7.6 \pm 4.5$  years, and mean length of follow-up was  $6.1 \pm 3.4$  years. One-hundred and two patients (52.8%) were treated with radiotherapy; seventy-three patients (37.8%) had dysfunction of at least one pituitary hormone. Regression analysis identified radiation treatment as a predictor of pituitary height at all three post-treatment time points ( $p=0.016$ ,  $p<0.001$ ,  $p=0.008$ , respectively). history of chemotherapy ( $p=0.004$ ) or radiotherapy ( $p=0.022$ ) and pituitary height at the 10-year time point ( $p=0.047$ ) were identified as predictors of endocrine deficiencies. ANOVA for repeated measures showed a significant increase in pituitary height over time ( $p<0.001$ ), as expected in pediatric patients, however there was a significant difference in change in pituitary height between participants with or without a history of radiation treatment

( $p$  for interaction = 0.005) as well as between males and females ( $p$  for interaction=0.025).

**Conclusions:** Cranial irradiation in pediatric patients is associated with impairment of the physiologic increase in pituitary size; in turn, decreased pituitary height is associated with endocrine dysfunction.

EP771/#1328 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

### LATE MORTALITY AMONG 5-YEAR SURVIVORS OF CHILDHOOD CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Background and Aims:** Estimation of the risk of late mortality and number of excess deaths in 5-year childhood cancer survivors (CCS) relative to the general population is useful to measure progress in childhood cancer treatment and long-term adverse health impacts in survivors. We conducted a systematic review and meta-analysis to provide comprehensive estimates of late mortality risk among 5-year CCS.

**Methods:** Multiple databases were searched from inception to March 2023 for cohort studies comprised of 5-year CCS that included multiple malignancies. Eligible studies assessed the risk of all-cause death in survivors relative to the general population using standardized mortality ratios (SMR) and/or absolute excess risks. Cause-specific mortality risk was assessed if reported. Only the most recent publication for each cohort was included. Outcome data was meta-analyzed from studies without overlapping cohorts.

**Results:** Nineteen studies were included comprising a total of 255,788 CCS and 26,856 deaths. Twelve studies (63%) were conducted in Europe. Cohort sample sizes ranged from 314 to 77,423. At 5-9 years from original cancer diagnosis, the pooled SMR for all-cause mortality was 34.0 (95% CI: 16.2-71.1), declining to 9.4 (95% CI: 5.8-15.2) at 10-14 years, 5.7 (95% CI: 4.9-6.5) at 15-19 years, 4.9 (95% CI: 3.9-6.3) at 20-24 years, 4.7 (95% CI: 3.4-6.6) at 25-29 years, and 4.8 (95% CI: 3.9-5.9) at 30-35 years from diagnosis. Despite variation in how deaths were categorized, deaths related to primary cancer and to subsequent malignant neoplasms were the leading and second leading causes of death, respectively, across most studies.

**Conclusions:** Five-year CCS have a statistically significantly increased risk of mortality that declines as time from diagnosis increases but remains elevated throughout survivorship. Pooling individual participant data from these studies may considerably reduce heterogeneity and facilitate further comparison across international cohorts.

EP772/#1343 | Poster Topic: AS05 SIOP Scientific Program/AS05.s  
Survivorship

### PROJECTING THE FUTURE PREVALENCE OF CHILDHOOD CANCER IN ONTARIO USING MICROSIMULATION MODELING

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**Background and Aims:** Although the prevalence of childhood cancer has increased steadily, projections of future incidence and prevalence to anticipate health system demands are limited. To support long-term system planning for acute cancer care and long-term follow-up services, we constructed a population-based, open-cohort microsimulation model to project the incidence and limited-duration prevalence of childhood cancer in Ontario, Canada by cancer type, until 2040.

**Methods:** The simulated population was updated annually between 1970 and 2040 with births, deaths, net migration, and incident cases of childhood cancer. Prevalent individuals were followed until death, emigration, or the end of the simulation. Data sources to inform the model included health administrative databases, provincial population estimates, and external literature. One hundred Monte Carlo simulations were run to vary model inputs and generate median health outcomes with 95% credible intervals (CI).

**Results:** Annual incidence counts in children aged 0-14 are projected to increase by 39% from 2020 to 2040, from 408 (95% CI: 354-478) to 569 (95% CI: 495-650) cases, respectively. Five-year overall survival for all cancers combined is projected to reach 90.3% (95% CI: 87.8%-92.2%) in 2030-2039. In 2040, 24,724 (95% CI: 22,969-26,261) individuals with a prior history of childhood cancer (diagnosed in Ontario or elsewhere) are projected to reside in the province, up 70% from 14,585 (95% CI: 14,265-14,946) in 2020. By 2040, 37% of the overall prevalent population will be  $\geq 40$  years old, and 59% will have survived  $\geq 20$  years from diagnosis. Survivors of lymphoid leukemias will comprise 30% of prevalence in 2040, followed by astrocytomas (11%).

**Conclusions:** Rising childhood cancer incidence will impact caseloads and resource needs in pediatric hospitals. With a projected shift towards an older prevalent population, ensuring capacity for long-term follow-up care into later decades of life will be vital in preventing and managing late-occurring morbidities.

EP773/#1120 | Poster Topic: AS05 SIOP Scientific Program/AS05.s  
Survivorship

### MODELING ANTICANCER RELATED LATE EFFECT ON NEUROCOGNITION (MARLEN STUDY)

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**Background and Aims:** Long-term survivors of pediatric medulloblastoma present significant impairments in specific cognitive functions. Our major objective was to create retrospectively a mathematical model evaluating the contribution of key clinical factors as hydrocephalus, age, and sex at diagnosis and cranial irradiation to impaired neurocognitive performances and their dynamic interactions.

**Methods:** The cohort concerned children treated for a medulloblastoma in Institute Gustave Roussy. We used pivot tables to select significant factors to be incorporated in complex and dynamic models. We evaluated neurocognitive patient' dynamic trajectories in terms of Full-Scale Intellectual Quotient (FSIQ) scores using a discrete-time Markov chains analysis. A simulator integrating a Bayesian approach was created to describe the interactions between significant co-variables.

**Results:** 78 patients were included with a median age of 6 years. Neurocognition outcome has been evaluated at 4 time points with FSIQ score. Analysis by pivot tables revealed a difference in mean loss of FSIQ with a loss of 0.7%/year for children without hydrocephalus against 3.3%/year for children with hydrocephalus. A Markov decision analysis model was developed using four states from 1 (the best score) to 4 (the worst score). For the first time this simulator allowed to reveal the dynamic impact of sexe and hydrocephalus according the age and the craniospinal dose levels for every state. Our results obtained from this model showed that in any case, neurocognitive impact is higher for girls compared to boys whatever age and dose.

**Conclusions:** We elaborated an original mathematical tool to analyse the dynamic process of decline neurocognition according to main clinical factors. We reported the major impact of sexe on neurocognitive outcome after treatment for medulloblastoma. This tool will allow to early assess the potential impact of any corrective medication or rehabilitation programs in hope to mitigate the impaired neurocognition.

EP774/#1691 | Poster Topic: AS05 SIOP Scientific Program/AS05.s  
Survivorship

### GENETIC MARKERS ASSOCIATED WITH OBESITY, DYSLIPIDEMIA AND INSULIN RESISTANCE IN PATIENTS WITH HEMOBLASTOSIS WHO RECEIVED ANTICANCER THERAPY

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**Background and Aims:** Metabolic disorders (dyslipidemia, insulin resistance, obesity) occur in more than 30% of patients treated for childhood malignancies. Pharmacogenetic characteristics of a patient as well as polymorphism of genes involved in lipid and carbohydrate metabolism may contribute to the development of chronic metabolic problems. The aim of the study was to assess the possible role of genetic predisposition in the formation of metabolic syndrome signs in children with hemoblastosis who received anticancer therapy.

**Methods:** In total, 193 children, 87 girls and 106 boys, underwent rehabilitation in Rehabilitation Center "Russkoye Pole" were included in the study. The 137 patients were treated for acute lymphoblastic leukemia and 56 patients for lymphoma. Mean age was  $10.65 \pm 6.45$  years, duration of remission was  $5.8 \pm 0.44$  years. Body mass index (BMI), fasting glucose level, HOMA-IR index, cholesterol level were determined. Genetic testing was performed using next-generation sequencing on the Illumina platform, the analysis included exons of 132 genes involved in lipid and carbohydrate metabolism, and anticancer drug metabolism.

**Results:** Overweight was observed in 44% of patients (including obese children) and obesity ( $+2.0$  SDS BMI depending on age) was reported in 5% of cases. Insulin resistance ( $\text{HOMA-IR} > 3.2$ ) was observed in 27% of children, and a combination of insulin resistance and overweight in 18% of patients. Insulin resistance was more common in overweight patients than in normal weight patients (42% vs. 14%,  $p < 0.0001$ ). Rare pathogenic/probably pathogenic variants in the LPL (c.C592G), LIPC (c.C1214T), CD36 (c.C592G), LRP1 (c.12038+2T>G) genes were found in patients with metabolic disorders, particularly with dyslipidemia and overweight. Also, SNPs in LPL, APOA5, APOE, PPARG genes were analyzed.

**Conclusions:** Detailed clinical and genetic analysis during rehabilitation of children and adolescents with hemoblastosis allows the formation of risk groups for dynamic monitoring and the development of personalized recommendations for controlling the treatment of somatic pathology and correction of lifestyle and diet.

EP775/#927 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

#### EVALUATION OF THE CURRENT CAPACITY AND POTENTIAL RISK FOR DEVELOPING TREATMENT-ASSOCIATED LATE EFFECTS AMONG CHILDHOOD CANCER SURVIVORS IN TANZANIA

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**Background and Aims:** Global advancement in pediatric cancer treatment has significantly increased survival rates for children with cancer, thus emphasizing the importance to extend capacity development to include post-treatment follow-up care. This study evaluates the current capacity and potential risk of developing treatment-associated late effects for childhood cancer survivors in Tanzania.

**Methods:** This was a mixed-method study design. Nine key stakeholders, including medical providers and psychosocial support staff at the three childhood cancer treatment centers in Tanzania participated in in-depth interviews (IDIs) to describe the current capacity to complete off-therapy guideline recommendations. A childhood cancer survivor cohort was established for patients who completed therapy from 2016-2022 at Bugando Medical Centre (BMC). Patient's demographics and off-therapy practice were extracted and late effect risk assessment was determined based on primary diagnosis, treatment site and the type of treatment received.

**Results:** Among recommended treatment, only pulmonary function testing and psychosocial evaluation were not currently available in Tanzania. A total of 173 patients were included in the survivor cohort (47% female, average age = 7). The most common diagnoses were Burkitt lymphoma (26%,  $n=45$ ) and Wilms (30%,  $n=52$ ). Only 42% ( $n=61$ ) of patients presented for any off-therapy appointment during the first year, decreasing to 20% ( $n=30$ ) during the second year. Distribution of British Childhood Cancer Survivorship Study late effect risk assessment included 6% low ( $n=10$ ), 80% moderate ( $n=139$ ) and 14% ( $n=24$ ) high risk. The highest potential late-effect risks were cardiomyopathy (57% of patients,  $n=98$ ), bladder and urinary tract toxicity (50%,  $n=87$ ), and ototoxicity (22%,  $n=38$ ).

**Conclusions:** Despite the high risk of late effects among childhood cancer survivors at BMC, there is still low compliance to follow-up care. Patient and caregiver education on off-therapy risk and importance of continued surveillance may improve compliance, and reduce future treatment-associated morbidity.

EP776/#1732 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

#### HEALTH-RELATED RISK BEHAVIORS AMONG U.S. CHILDHOOD CANCER SURVIVORS: A NATIONWIDE ESTIMATE

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**Background and Aims:** To provide updated information on currently smoking, physical inactivity, binge drinking patterns and associated

factors among childhood cancer survivors (CCS) using a nationwide dataset. Findings from this study supplement existing research utilizing data from participants recruited at medical centers.

**Methods:** We constructed a sample of CCS (cancer diagnosis at ages <21y) and healthy controls (matched on age, sex, residency, race/ethnicity) using 2020 Behavioral Risk Factor Surveillance System. We used standard tests to examine differences in sociodemographics and clinical characteristics between two groups. Logistic, ordinal regression and multivariable models (conditional models for matching) were used to determine factors associated with risk behaviors.

**Results:** The final sample (18-80y) included 372 CCS and 1,107 controls. Compared to controls, CCS had a similar proportion of binge drinking (~18%) but higher prevalence of currently smoking (26.6% vs. 14.4%,  $p<0.001$ ), physical inactivity (23.7% vs. 17.7%,  $p=0.012$ ), and of having 2-or-3 risk behaviors (17.2% vs. 8.1%,  $p<0.001$ ). Younger age, lower educational attainment, and having multiple chronic health conditions were associated with engaging more risk behaviors among CCS. Females, compared to male counterparts, had lower odds of binge drinking (adjusted odds ratio (aOR)=0.30, 95% confidence interval (CI): 0.16-0.57) among CCS but not in all sample. Having multiple health chronic conditions increased odds of both currently smoking (aOR=3.52 95%CI: 1.76-7.02) and binge drinking (aOR=2.13 95%CI: 1.11-4.08) among CCS while it only increased odds of currently smoking in all sample.

**Conclusions:** Our study provided risk behavior information for wide age-range CCS, which is currently lacking. Every one in four CCS was currently smoking. Interventions targeting risk behavior reduction should focus on CCS with multiple chronic health conditions.

EP777/#709 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

### "BEYOND CANCER CURE": UNMET SEXUAL AND REPRODUCTIVE HEALTH NEEDS AND CONCERNS OF ADOLESCENT AND YOUNG ADULT CANCER SURVIVORS IN UGANDA

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**Background and Aims:** Sexual and reproductive health (SRH) issues among cancer survivors remain underreported in developing countries. In these settings, Uganda included, SRH services, including fertility preservation, and data are lacking to address adolescent and young

adult (AYA) survivors' SRH needs. This study aimed to assess the SRH needs of AYA cancer survivors in Uganda.

**Methods:** We surveyed AYA cancer survivors at two facilities on SRH. Data were analyzed and reported using descriptive statistics.

**Results:** A total of 85 AYA cancer survivors, with a median age of 19 years (IQR: 18-22), were interviewed. The median time since cancer diagnosis was 18 months (IQR: 12-31), and the median time since cancer-specific treatment was 16 months (IQR: 10-28.8). One-third (34.2%) were in a sexual relationship, and 78 (91.8%) desired to have children in the future. Only 10 (11.8%) of the AYA cancer survivors received reproductive health (RH) counselling during their cancer treatment; nearly all of those who didn't receive counselling ( $n = 74/75$ ; 98.7%) desired to have had RH counselling. Only 25 (29.4%) of the survivors had ever used contraception, and half of those who had never used contraception ( $n = 30/60$ ) expressed a desire to do so. During their cancer treatment, at least five of the female participants became pregnant; all but one did not receive RH counselling. The AYA cancer survivors were concerned about how their cancer (and treatment) might affect their reproductive potential ( $n = 64$ ; 75.3%) and about not having been counselled on RH.

**Conclusions:** There is an unmet need and concern with AYA cancer survivors in Uganda regarding RH. We recommend standard SRH communication and interventions for AYA cancer patients.

EP778/#60 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

### LIFESTYLE AND SUBSEQUENT MALIGNANT NEOPLASMS IN CHILDHOOD CANCER SURVIVORS: A REPORT FROM THE ST. JUDE LIFETIME COHORT STUDY

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**Background and Aims:** Poor lifestyle increases the risk of cancer in the general population. This study aimed to assess longitudinal

associations between lifestyle and subsequent malignant neoplasms (SMN) in childhood cancer survivors.

**Methods:** Survivors age  $\geq 18$  years with  $\geq 5$  years after diagnosis participating in the St. Jude Lifetime Cohort Study were evaluated. Lifestyle factors included self-reported physical activity, smoking, risk drinking, directly assessed cardiorespiratory fitness (6-minute walk test), body mass index (BMI), and a combined lifestyle score. Time to first SMN, excluding non-malignant neoplasms and non-melanoma skin cancer, was the outcome. Piecewise exponential models starting follow-up 1 year after first assessment included demographic, treatment, diagnostic, and lifestyle variables.

**Results:** The study included 4,043 survivors, 47% female, 29% smokers, 37% risky drinking, 34% obese, 49% physically inactive; mean (SD) age was 8.7 (5.7) years at diagnosis and 30 (8.4) years at baseline SJLIFE evaluation. Subsequent length of follow-up was 6.0 (3.3) years. Any SMN was experienced by 178 (4.4%) survivors, including 38 breast, 41 thyroid, and 28 gastrointestinal SMNs. Being male (hazard ratio (HR) 0.6, 95% confidence interval 0.5-0.9) and having a cancer diagnosis after 1990 (HR 0.3, 0.1-0.7) were associated with a lower SMN risk. Survivors of Hodgkin lymphoma (HR 3.2, 1.8-5.9), neuroblastoma (HR 4.2, 1.6-10.6) and those treated with radiotherapy (HR 2.2, 1.5-3.2) had a higher risk of SMN compared to other survivors. Neither the individual lifestyle factors nor a healthy combined lifestyle score (HR 0.9, 0.6-1.4) were associated with the risk of developing an SMN.

**Conclusions:** We did not identify any association between lifestyle factors and risk of SMN in childhood cancer survivors. This might be explained by too few events after assessment of lifestyle factors to detect small effects. However, it is also possible that the increased risk for SMN from treatment exposures cannot be modified by lifestyle in relatively young survivors.

EP779/#1289 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

DOES THE NUTRITIONAL STATUS AT DIAGNOSIS IMPACT THE LONG TERM NUTRITIONAL OUTCOMES IN CHILDREN WITH CANCER?

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**Background and Aims:** We aimed to identify if undernutrition at diagnosis impacts the nutritional outcomes (obesity and cardiometabolic complications) in survivors of childhood cancer (CCS).

**Methods:** We included CCS (<18 years at diagnosis, >5 years from diagnosis and in remission) who visited our After Completion of Therapy Clinic in 2022. Nutritional status (NS) at diagnosis and last follow-up were assessed using WHO classification for children by weight/BMI-for-age (undernourished <-2SD, overnourished >1SD)

and WHO Asian adult standards by BMI [underweight (<18.5kg/m<sup>2</sup>, overweight (>23kg/m<sup>2</sup>)]. Metabolic syndrome (MS) and components were defined per the International Diabetes Foundation criteria. The odds ratio of developing outcomes (obesity/MS) was calculated using logistic regression analysis.

**Results:** 411 survivors were included in the analysis, current age 21(6-49) years, 73% male. The median age at diagnosis was 6(0-18) years, median follow-up duration was 12(5-36) years. Diagnosis acute lymphoblastic leukaemia-114(27.7%), hodgkin lymphoma-83(20.2%) and wilms tumour-38(9.2%);327(80%) received anthracyclines, 119(29%) received cranial or whole abdominal radiation. At diagnosis, 207(50.4%) were undernourished, 55(13.4%) overnourished and 148(38.1%) well-nourished. At a follow-up of 5,10 and 20-years,123(29.9%), 88(32.5%) and 29(39.7%) were overnourished. At last follow-up, 49(23.5%) children underweight at diagnosis continued to be undernourished, 50(24%) were overnourished and 109 (52%) well-nourished. Overall, metabolic syndrome was seen in 30(7.3%), dyslipidemia in 100(24.3%), hypertension in 17(4.1%) and diabetes mellitus in 6(1.5%). Underweight at diagnosis were less likely to develop metabolic syndrome (OR 0.4; 95% CI 0.2-0.4, p=0.036), and dyslipidemia (OR 0.6; 95%CI 0.4-1.04, p=0.07). Surprisingly, overweight at diagnosis did not have an increased risk of developing metabolic syndrome (OR1.1; 95%CI 0.4-2.9, P 0.87) or dyslipidemia (OR1.0; 95% CI 0.5-1.9), p=0.92)

**Conclusions:** Overweight, metabolic syndrome and its components are highly prevalent in CCS in India, including in those who were undernourished at diagnosis. There is an urgent need for further research, including body composition analysis and identification of individuals who have normal weight but are metabolically obese, in order that appropriate interventions are instituted.

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A MULTISITE LONGITUDINAL STUDY OF ENGAGEMENT IN CARE OF ADOLESCENT AND YOUNG ADULT SURVIVORS OF CHILDHOOD CANCER: PREDICTORS OF ENGAGEMENT AFTER ONE YEAR

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**Background and Aims:** Despite recommendations for annual follow-up care, adolescent and young adult survivors of childhood cancer (AYA) are increasingly disengaged from follow-up care as they age into adulthood. Understanding patterns and predictors of health care utilization is key to optimizing long-term engagement in care. As such, we recruited a large multisite cohort of AYA to study longitudinal patterns of engagement in follow-up care and related demographic, disease-related, and self-management predictors.

**Methods:** AYA survivors (16-25 years, > two years off treatment, > 5 years since diagnosis) were recruited from pediatric cancer centers in Philadelphia, Cincinnati, and Los Angeles. They completed measures at baseline and one year later. Engagement in follow-up care and demographic and disease variables were ascertained via electronic health record and self-report (if needed). Univariate (*r* and *t*-tests) and multivariate (logistic regression) were used to test associates of engagement at T2.

**Results:** AYA (N=589) completed measures at T1 (48% male, 62% non Hispanic white). Currently, 435 are eligible (in study 12+ months) for T2. Of these, 174 (40.0%) did not attend or have an appointment scheduled 1 year after enrollment. Univariate analyses revealed the following to be associated with T2 engagement in care (*p* < .05): less years off treatment, lower age, higher number of late effects, less self-management skills at T1, and increase (change) in self-management skills from T1 to T2. Other socio-demographics were not related. Multivariate analysis (logistic regression) revealed only change in self-management skills to be significantly associated with T2 engagement.

**Conclusions:** Despite being connected with cancer centers and guidelines for care, 40% are not returning for care after one year. Results confirm the vulnerability of those transitioning to adulthood and adult care, and who are further from treatment, especially those who may be asymptomatic. Results also indicate need to enhance self-management skills for engagement in follow-up care, regardless of socio-demographics.

EP781/#1727 | Poster Topic: AS05 SIOP Scientific Program/AS05.5 Survivorship

#### TREATMENT EXPOSURES IN THE LARGEST SURVIVOR COHORT FROM THE INDIAN CHILDHOOD CANCER SURVIVORSHIP STUDY (C2S STUDY)

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**Background and Aims:** A priority area for the pediatric oncology community is care of childhood cancer survivors and monitoring of late effects. With improved survival the population of childhood cancer survivors has increased. This has been a neglected area and no registry for childhood cancer survivors existed in India in the past. We proposed to establish the first ever registry and systematically compile clinical, demographic and treatment exposure details of children completing cancer treatment.

**Methods:** Centres across India were invited to participate in the C2S study. All children completing treatment were enrolled within six months of treatment completion. Demographic and treatment details with cumulative doses of chemotherapy/radiation were recorded. Follow up done by teleconsultation/physical visit to hospital.

**Results:** 2390 survivors were enrolled from participating centres. Age distribution is as follows: less than 5 years (43%), 5-10 years (29%) and 10-18 years (28%). Majority are males (70%). Commonest malignancy was acute leukemia (42%) followed by lymphoma (21%), retinoblastoma (10%) and bone sarcoma (9%). Period of follow up of more than 5 years was seen in (11%), 2-5 years was seen in (34%) and less than 2 years was seen in (55%) patients. Chemotherapy was the commonest treatment exposure (96%) followed by radiation (71%), surgery (67%), blood products (67%) and HSCT (2%). Amongst chemotherapy anthracyclines were the commonest exposure followed by methotrexate. Median cumulative doses of chemotherapy are: bleomycin 120 IU/m<sup>2</sup>, carboplatin 1680 mg/m<sup>2</sup>, cisplatin 450 mg/m<sup>2</sup>, cyclophosphamide 3000 mg/m<sup>2</sup>, dacarbazine 4500 mg/m<sup>2</sup>, daunorubicin 210 mg/m<sup>2</sup>, doxorubicin 160 mg/m<sup>2</sup>, etoposide 1200 mg/m<sup>2</sup>, ifosfamide 24000 mg/m<sup>2</sup>. Majority (94%) are alive and under follow up. 6.3% of the cohort has died. The online database is in place for the C2s study.

**Conclusions:** The C2S Study is the first childhood cancer survivor study/ registry from India. The study cohort will serve as a platform for further studies based on disease/treatment exposure related late effect.

EP782/#365 | Poster Topic: AS05 SIOP Scientific Program/AS05.s  
Survivorship

### PANCREATIC LATE EFFECTS IN ACUTE LYMPHOBLASTIC LEUKEMIA SURVIVORS WITH ASPARAGINASE ASSOCIATED PANCREATITIS, A PART OF THE ALL-STAR STUDY

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**Background and Aims:** Asparaginase-associated pancreatitis (AAP) is a severe toxicity occurring during acute lymphoblastic leukemia (ALL) treatment. With increasing survival, focus on late effects is paramount. The aim of our study was to explore pancreatic late effects in ALL survivors with a history of AAP (AAP) compared to both ALL survivors without AAP (non-AAP) and community controls (controls).

**Methods:** We conducted a cross-sectional, Danish, national cohort study of ALL survivors treated according to the NOPHO ALL2008 protocol and at least 1 year off treatment. Community controls were matched on sex and age. All participants underwent evaluation of the pancreatic function. Blood samples were fasting, morning-samples. Linear and logistic regression were applied.

**Results:** We included 370 ALL survivors (medians: 6.8yrs (IQR 4.7–9.0) from ALL diagnosis and 4.5yrs off treatment (IQR 2.5–6.5)), including 46 AAP survivors, and 320 controls. Median age (IQR) was 14yrs (10.8–21.8) and 14.7yrs (11.4–23.2) in ALL survivors and controls, respectively ( $p=0.4$ ). Median lipase levels (U/L, IQR) were 22.5 (14–32), 29 (24–35), and 28 (22–33) in AAP compared to both non-AAP and controls, respectively ( $p<0.001$ ). Median pancreas-type amylase (U/L, IQR) was 18 (10–25), 22 (17–28), and 21 (17–26), ( $p=0.001$ ). Median fecal elastase (unit, IQR) was 526 (351–678) and 573 (469–683) in AAP and non-AAP, respectively ( $p=0.03$ ). A higher proportion of AAP had lipase, pancreas-type amylase and fecal-elastase levels below the lower normal limits (12.8%, 18%, 16.7%) compared with both non-AAP (0.4%, 2.6% and 2.9%) and controls (1.1%, 1.8% and NA\*) (all  $p<0.05$ ). Median Hemoglobin A1c (HbA<sub>1c</sub>) levels (mmol/mol, IQR) were 33 (30–36), 33

(31–36), 33 (32–35) for AAP, non-AAP, and controls, respectively. Two, three and zero subjects had HbA<sub>1c</sub> above 42 mmol/mol in the three groups.

**Conclusions:** In conclusion, we found a significantly reduced exocrine pancreatic function in ALL survivors with AAP. Evaluated by HbA<sub>1c</sub> the endocrine pancreas function was normal. \*Not performed in controls.

EP783/#439 | Poster Topic: AS05 SIOP Scientific Program/AS05.s  
Survivorship

### MENTAL WELLNESS OF ADULT CHILDHOOD CANCER SURVIVORS AND THEIR SIBLINGS IN A TERTIARY CENTER IN SINGAPORE

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**Background and Aims:** Childhood cancer survivors (CCS) may develop health complications including psychological distress years after completion of their therapy. These late effects present a pertinent health issue as the number of CCS has significantly increased over the past decades. A few studies have addressed adverse mental health late effects of CCS in Asia. Our study seeks to evaluate the prevalence and associated risk factors of psychological distress among CCS and their siblings in Singapore.

**Methods:** Adult CCS ( $n=143$ )  $\geq 18$  years old attending survivorship clinics in KK Women's and Children's Hospital, who were in remission for  $\geq 5$  years and treatment free for  $\geq 2$  years, and their siblings ( $n=57$ ) were recruited to complete the Brief Symptom Inventory (BSI-18) questionnaires from September 2021 - July 2022.

**Results:** There were 19 (13.3%) CCS and 8 (14.0%) siblings who reported mental distress in BSI-18 somatization subscale, 32 (22.4%) CCS and 11 (19.3%) siblings in the depression subscale, 23 (16.1%) and 7 (12.3%) siblings in the anxiety subscale and 35 (24.5%) CCS and 10 (17.5%) siblings in the Global Severity Index (GSI). The differences in their scores were not statistically significant across all subscales and GSI of BSI-18. Associated risk factors of significant psychological distress in CCS were history of psychiatric illness [OR 23.1, 95% CI 4.4 – 122.0;  $p<0.01$ ], mood affected by COVID pandemic [OR 3.1, 95% CI 1.3 – 7.3;  $p=0.01$ ] and being overweight [OR 2.8, 95% CI 1.1 – 7.0;  $p=0.03$ ].

**Conclusions:** CCS in this cohort reported a significant level of mental distress, although it did not differ from their siblings. We recommend a holistic and risk factor-centric follow-up program for early detection and mitigation of mental distress for CCS and their families.

EP784/#711 | Poster Topic: *AS05 SIOP Scientific Program/AS05.s Survivorship*

### FRONTO-PARIETAL FUNCTIONAL CONNECTIVITY IN SURVIVORS OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA WITH WORKING MEMORY IMPAIRMENT

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**Background and Aims:** Despite high survival rates of acute lymphoblastic leukemia (ALL), long-term survivors are at increased risk for atypical brain function and neurocognitive impairment which adversely affects quality of life. This study aimed to examine functional connectivity patterns during working memory in 5-year survivors of pediatric ALL maintaining remission after treatment with chemotherapy only for 2.5 years.

**Methods:** Neurocognitive assessments and functional magnetic resonance imaging (fMRI) were obtained in 111 survivors treated on St. Jude Total XV therapy protocol (48% male; median[*min-max*] age 15.1[8.3-26.5] years; time since diagnosis 7.9[5.1-12.5] years). Neurocognitive impairment was defined as age-adjusted normative scores below the 10th percentile. fMRI images were obtained during a N-back working memory task on a 3T scanner. Images were preprocessed and analyzed using the CONN toolbox. Seed regions of interest (ROIs) were chosen based on previously detected sex-based differences in brain activation. Task-modulated ROI-ROI functional connectivity matrices were estimated for each survivor using a generalized psychophysiological (gPPI) multiple regression model. A general linear model was used to investigate group-level effects of sex and working memory impairment status adjusted for age at evaluation, plasma concentration of methotrexate for 42 hours following high-dose intravenous injections, and number of intrathecal injections of methotrexate, hydrocortisone, and cytarabine.

**Results:** Survivors with working memory impairment exhibited reduced connectivity (FDR-corrected  $p < 0.05$ ) in frontoparietal areas, including connections between the right anterior supramarginal gyrus and right middle frontal gyrus (MidFG), bilateral superior frontal gyrus, and right posterior supramarginal gyrus, and between right MidFG and right parietal operculum. Group comparisons revealed no sex-based differences in functional connectivity.

**Conclusions:** Survivors with working memory impairment demonstrated reduced functional connectivity in frontal and parietal regions, which is consistent with findings in general populations without cancer.

These brain regions may be particularly susceptible to the neurotoxic effects of chemotherapy treatment.

EP785/#1420 | Poster Topic: *AS05 SIOP Scientific Program/AS05.s Survivorship*

### BODY COMPOSITION PHENOTYPES AMONG SURVIVORS OF PEDIATRIC CANCER

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**Background and Aims:** We aimed to determine the prevalence of and risk factors for body composition phenotypes high adiposity/high muscle mass (HA-HM; "obese"), low adiposity/low muscle mass (LA-LM; "sarcopenic"), high adiposity/low muscle mass (HA-LM; "sarcopenic obese") and low adiposity/high muscle mass (LA-HM; "normal"), among childhood cancer survivors participating in the St. Jude Lifetime Cohort. Additionally, we examined associations between body composition and risk of subsequent malignancies and mortality.

**Methods:** Among 4,097 survivors (median age=29 (range: 18-70) years), whole-body dual X-ray absorptiometry was used to assess fat and lean mass. Survivors were assigned to a body composition phenotype using sex- and BMI-specific cut-points (50th percentile) for appendicular skeletal muscle index ( $\text{kg}/\text{m}^2$ ) and fat mass index ( $\text{kg}/\text{m}^2$ ). Poisson regression was used to evaluate associations between treatment and lifestyle factors with body composition phenotypes. Cox regression was used to evaluate associations between body composition and risk of subsequent malignancies and mortality.

**Results:** Twenty-seven percent, 21% and 19% of survivors had LA-LM, HA-HM and HA-LM respectively. The HA-LM phenotype was most prevalent among brain tumor survivors (36%). Cranial irradiation (LA-LM,  $\text{RR}=1.1$ ,  $95\% \text{CI}=1.0-1.2$ ; HA-HM,  $\text{RR}=1.1$ ,  $95\% \text{CI}=1.1-1.2$ ; HA-LM,  $\text{RR}=1.3$ ,  $95\% \text{CI}=1.3-1.5$ ) and being physically inactive (LA-LM,  $\text{RR}=1.1$ ,  $95\% \text{CI}=1.1-1.2$ ; HA-HM,  $\text{RR}=1.1$ ,  $95\% \text{CI}=1.0-1.2$ ; HA-LM,  $\text{RR}=1.4$ ,  $95\% \text{CI}=1.3-1.5$ ) were associated with all three abnormal phenotypes. Compared to survivors with LA-HM, survivors with LA-LM ( $\text{HR}=2.0$ ,  $95\% \text{CI}=1.2-3.3$ ), HA-HM ( $\text{HR}=2.0$ ,  $95\% \text{CI}=1.2-3.5$ ), and HA-LM ( $\text{HR}=3.1$ ,  $95\% \text{CI}=1.8-5.2$ ) had an increased risk of all-cause mortality, while survivors with HA-LM also had an increased risk of death from cardiovascular ( $\text{HR}=10.8$ ,  $95\% \text{CI}=1.2-96.0$ ), neoplasm ( $\text{HR}=3.4$ ,  $95\% \text{CI}=1.2-9.7$ ) and other health-related ( $\text{HR}=6.8$ ,

95%CI=1.8-25.4) causes. HA-HM was associated with increased risk of subsequent malignancies (HR=1.6, 9%CI=1.1-3.0).

**Conclusions:** HA or LM, frequent among childhood cancer survivors, are associated with increased mortality among survivors. Further research is warranted to determine if prevention and/or remediation of HA or LA can improve health outcomes among survivors.

EP786/#177 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

### OUTCOMES AMONG SURVIVORS OF CHILDHOOD CANCER IN LOW- AND MIDDLE-INCOME COUNTRIES: A SYSTEMATIC REVIEW

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**Background and Aims:** Low- and middle-income countries (LMICs) account for most of the global childhood cancer burden. Late effects of cancer or cancer therapy are well-documented among childhood cancer survivors (CCS) in high-income countries, but whether prevalence and risk factors of late effects are comparable in LMICs is unclear. We thus conducted a systematic review to assess LMIC CCS outcomes.

**Methods:** Five major health sciences databases were searched from inception to November 2022 in all languages. We included observational studies conducted in LMICs that evaluated outcomes in CCSs. Mean or median length of cohort follow-up must have been  $\geq 5$  years from original cancer diagnosis. Meta-analyses were precluded by cohort and outcome heterogeneity.

**Results:** We included 16 full articles and 5 conference abstracts. Studies were conducted in lower-middle income (N=12, 57%) or upper-middle income (N=9, 43%) countries. Nearly half (N=9, 43%) of studies were conducted in India; only one African study from Cameroon was identified. Only five (24%) cohorts were comprised entirely of 5-year survivors. CCS of all cancer types were evaluated in 12 (57%) cohorts, and 9 (43%) were specific to one cancer type. Second cancers were reported in 1%-11% of CCS cohorts (N=10 studies). Among endocrine outcomes, hypothyroidism and metabolic syndrome prevalence ranged from 2%-49% (N=6 studies) and 4%-17% (N=5 studies), respectively. Gonadal dysfunction was defined and reported heterogeneously, ranging from 2%-82% (N=6 studies). Cardiac dysfunction ranged from 1%-16% (N=3 studies). Late effects of the musculoskeletal (N=4 studies) and urinary (N=4 studies) systems were least investigated.

**Conclusions:** Substantial knowledge gaps exist in LMIC childhood cancer survivorship. No low-income country data were found. In middle-income countries, variability existed in how late effects were defined and assessed; data was also limited by selection bias and small

sample sizes. Additional systematically collected data on LMIC CCS cohorts are urgently needed.

EP787/#184 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

### PEDIATRIC CANCER SURVIVORSHIP CARE IN AFRICA: A SCOPING REVIEW

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**Background and Aims:** Over the last few decades, improved treatments and better supportive care have helped many children survive cancer around the world, with a growing body of literature focusing on survivorship care and survivors' experiences. It is expected that by 2050, ~50% of the global pediatric cancer burden will be in Africa. Learning about existing survivorship care models and understanding experiences of patients and families can help researchers ask questions that are context relevant and test strategies that might be locally sustainable. The current review aimed to explore the scope of pediatric survivorship care in African countries.

**Methods:** We conducted a scoping review of peer-reviewed journal articles, technical reports, and conference abstracts published from 2011 to 2022. Included articles focused on post-treatment, long-term follow-up care of adult or pediatric patients diagnosed with cancer in African countries. Databases searched include PubMed, Embase, Web of Science Core, and CINAHL Plus. We used Covidence® for title/abstract, full text screening and data extraction, and Excel for descriptive analysis.

**Results:** Of 7878 studies screened, 122 studies met inclusion criteria (addressing survivorship in both adults and pediatric age groups). Of these, just 27 (22%) focused on survivors of pediatric cancers, including 14 (52%) focused on hematologic malignancies and 6 (22%) focused on solid malignancies. 12 (44%) Addressed physical effects of cancer therapy, and 11 (40%) addressed psychological effects.

**Conclusions:** Our study shows that, though limited and mostly descriptive, there are examples of post-treatment follow-up care happening in African countries for pediatric cancer survivors. Policymakers, clinicians, and community leaders should work with people affected by cancer to use these findings as a baseline to work strategically to design care models that are context-relevant, feasible and sustainable.

EP788/#1010 | Poster Topic: AS05 SIOP Scientific Program/AS05.s Survivorship

### MATRIX METALLOPROTEINASES CONTRIBUTE TO CISPLATIN-INDUCED HEARING LOSS

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**Background and Aims:** Cisplatin is a highly potent chemotherapeutic agent used for treating solid tumors in children; however, the toxicity and adverse effects have limited its application. Cisplatin-induced ototoxicity (CIO) is a progressive, irreversible bilateral hearing loss that affects up to 70 % of patients treated with cisplatin, and age, is a significant risk factor in CIO as the incidence is higher among children. CIO is especially detrimental to children because it impairs their neurocognitive abilities and psychosocial development. Therefore, investigating the underlying mechanisms of CIO and developing new strategies to prevent or mitigate CIO seems vital. Since the production of reactive oxygen and nitrogen species (RONS) elicited by cisplatin is critical to cochlear cell death and hearing loss and the fact overexpression of matrix metalloproteinases (MMPs) are key mediators downstream of RONS, we hypothesized that MMPs and their catalytic activities might play a role in CIO.

**Methods:** We used mouse outer hair cells (HEI-OC1) and treated them with cisplatin for different time points and evaluated gene expression of MMP2 and MMP9 using qPCR. The MMPs activities were measured using gelatin zymography. We also used two MMP2-preferring small molecule inhibitors (ONO-4817 and ARP-100) in combination with cisplatin and measured Interleukin-6 (IL-6) secretion using ELISA.

**Results:** Our data shows that MMP2 and MMP9 gene expressions are upregulated quickly after treatment of HEI-OC1 with cisplatin. Gelatin zymography also reveals that MMP2 and MMP9 proteolytic activities are elevated upon cisplatin treatment. Moreover, inhibition of MMP2 mitigates the IL-6 secretion induced by cisplatin. Currently, we are analyzing the result of the N-degradomic assay to find specific MMP2 substrates in the CIO condition.

**Conclusions:** The result of this study indicates that MMPs may play a role in CIO and that inhibition of MMPs could render a therapeutic opportunity for CIO treatment.

## PUBLICATION ONLY ABSTRACTS

PO001 / #1822 | Publication Topic: AS01 Surgery - IP SO

### MYOEPIHELIAL CARCINOMA OF THE PELVIC LIMB, A RARE SARCOMA. CASE REPORT

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**Background and Aims:** Myopellial neoplasms were initially recognized in the salivary glands. Myoepithelial carcinoma (CM) is a rare, aggressive, and recurrent tumor in children. Kilpatrick reported the first soft tissue case in 1997<sup>(1)</sup>. The highest incidence is between the third and fifth decade of life, a fifth of them occurs in pediatric ages, located in limbs<sup>(2)</sup>. The Staging system is performed according to TNM and IRS (Intergroup Rhabdomyosarcoma Study). There is no standardized treatment. Surgery is the mainstay for treatment,<sup>(3)</sup> combining chemotherapy and radiotherapy.

**Methods:** Females 12-yo, no relevant medical history. Started in December 2021 with volume increase in the proximal third of the right thigh, it presents slow and painless growth progression, performing US and MRI with suspicion of lipoma. An incisional biopsy was performed, reporting a mixed soft tissue tumor. She was admitted to HITO in July 2022, extension studies were performed: CT, MRI, and PET CT, which reported a soft tissue tumor of 20 × 13 × 10cm with inguinal lymph node activity. Extended local resection and inguinal exploration were performed. *Pathology report:* Myoepithelial carcinoma metastatic to inguinal lymph nodes, microscopic positive border, FISH EWSR1 (22q12) positive. *Staging:* group III, TNM T2B N1 M0. The following were analyzed according to the recommendations of the TREP project (Tumori Rari in Etá Pediatrica): 4 cycles with Ifosfamide, Cisplatin, and Etoposide + 60Gy radiotherapy + 3 cycles with Ifosfamide, Vincristine, and Etoposide. The patient is in remission.

**Results:** Great results was obtained using TREP recommendation, since the diameter of the tumor was greater than 5cm. The experi-

ence treatment of this pathology is limited in pediatric ages, in addition to the fact that in developing countries it may be underdiagnosed, it is important to share the results with international groups that allow knowing the best treatment to improve patient survival.

**Conclusions:** is rare tumor and don have results

PO002 / #892 | Publication Topic: AS01 Surgery - IPSO

### GASTRIC BURKITT'S LYMPHOMA WITH MASSIVE GASTRIC ULCER - AN UNUSUAL DIAGNOSIS IN CHILDREN

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**Background and Aims:** Burkitt's lymphoma (BL) is a high grade non-Hodgkin's lymphoma most commonly occurring in the terminal ileum/caecum in children. It may however arise in other locations of the gastrointestinal tract. We present the case of a 4-year-old boy with gastric BL.

**Methods:** Case report.

**Results:** A 4-year-old boy presented with fever, coryzal symptoms, and increasing fatigue over the preceding months. He had no significant past medical or family history. Abdominal examination revealed a large, firm mass in the epigastrium. His blood film showed iron deficiency anaemia. Abdominopelvic Computed Tomography (CT) showed a large irregular infiltrative mass arising from the posterior wall and greater curve of the stomach with only small volume locoregional lymphadenopathy. Biochemistry: LDH 482 IU/l (twice upper limit of normal), normal AFP/HCG and calcium. Endoscopy showed a large friable gastric ulcer in the greater curvature. Biopsies revealed features consistent with Burkitt lymphoma, with a Ki67 index of almost 100%, as well as IGH:MYC gene arrangement; no evidence of BCL2 or BCL6 rearrangement. Serology was negative for EBV. CSF/bone marrow were clear. Resection was not deemed appropriate and he was commenced on chemotherapy treatment as per CCLG 2020 Interim Guidelines for High risk Group B non-Hodgkin's lymphoma (COP\*2/R-COPADM\*2/R-CyM\*2regime). Given the significant gastric ulcer with risk of perforation and bleeding, stomach protection was instigated with high dose proton pump inhibitors and a soft diet, but he tolerated chemotherapy well. Upper GI endoscopy was repeated 2 months following start of chemotherapy which found complete resolution of the gastric ulcer with only minimal residual scarring around antrum and pylorus. Endoscopic biopsies showed no evidence of malignant cells.

**Conclusions:** Our case demonstrates that despite significant gastric wall involvement, chemotherapy can be well tolerated and a timely remission of disease is possible. Endoscopy should form part of the initial assessment of gastric BL to ensure large gastric ulcers can be managed appropriately to avoid complications.

PO003 / #132 | Publication Topic: AS05 SIOP Scientific Program / AS05.a Acute Lymphoblastic Leukaemia

### IMPACTS OF POOR ACCESS TO ANTINEOPLASTIC AND SUPPORTIVE CARE MEDICINES IN THE MANAGEMENT OF ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN AT MBINGO BAPTIST HOSPITAL, CAMEROON

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**Background and Aims:** Medications constitute the live wire of every healthcare delivery system and access to medicines is a fundamental human right. Poor access to medications remains one of the most frequently encountered challenges in healthcare systems and affects the clinical, economic and human aspect of care of patients living with cancer. Poor access to frontline medications for paediatric acute lymphoblastic leukemia (ALL) compromises proper patient care and potentially impacts outcomes. AIM: To assess the impact of poor access to antineoplastic and supportive care treatment to pediatric patients with ALL.

**Methods:** Data collection forms were designed to capture retrospective clinical and outcome data from patient's records among paediatric patients diagnosed with acute lymphoblastic leukemia from January 2022 to January 2023. Stock management data highlighting stock out days and durations of stock out per treatment cycle interval, when the cancer therapy was intended to be administered to paediatric patients with ALL were also collected. Primary exposure was duration of stock out and primary outcome, suboptimal therapy delivery. Comparative analysis done with  $p < 0.05$  considered statistically significant.

**Results:** Twenty eligible patient records were retrieved during the study period. The median and mean durations of stock out per treatment cycle interval were 11 and 15 days respectively (standard deviation, 13 days), with a range of 1 to 33 days. There was a positive correlation with statistical significance between mean duration of stock outs with sub-therapy delivery events leading to poor clinical response, increase patient morbidity and mortality, increase admission days, and overall quality of life and healthcare associated cost.

**Conclusions:** Poor access to some essential cancer medicines remains a major health care delivery problem. Improved drug access is a good prognostic factors for Patients with ALL. A concerted efforts between policy makers and cancer specialists is needed to design implementation strategies to build sustainable systems promoting reliable supply of cancer medicines.

PO004 / #22 | Publication Topic: AS05 SIOP Scientific Program / AS05.a Acute Lymphoblastic Leukaemia

### PEDIATRIC ACUTE LEUKEMIA IN OMAN: SINGLE CENTER EXPERIENCE

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**Background and Aims:** Leukemia is the most common cancer in children and teens, accounting for almost one out of three cancers. To date, there are limited research about childhood leukemia in Oman and the middle east in general. This study aims to provide new information regarding epidemiology, patient characteristic, and management outcomes of children with acute leukemia in Oman, comparing it to international and other local data.

**Methods:** retrospective cohort study Continuous variables were presented as mean, median and standard deviation whereas categorical variables were presented as frequencies and percentages. Kaplan Meier curve survival analysis was applied to estimate overall survival (OSA) and event-free survival (EFS). A Chi-square log-rank test was also applied to find the statistical significance difference between both OSA and EFS between different levels of phenotypes, a p-value <0.05 was considered statistically significant

**Results:** A total 126 patients were included in the study. The median age was fourty Months. Males were 60%. Geographically, the majority of patients were from Muscat region (22.2%). Majority of patients (75%) were diagnosed with B-cell ALL, followed by AML (13%) and T-cell ALL (10%). CNS involvement was present in only 2% of patients. The majority of cases (62%) were standard/low risk, 26% were high risk and 12% of the cases were intermediate risk. Ten-year overall survival (OS), and relapse-free survival (RFS) were 85.4%, and 64.5%, respectively. The OS for patients with B-cell ALL was significantly higher than for T-cell ALL and AML (93.2% vs. 46.9% vs. 71.8% P-value <0.01). The RFS for patients with B-cell ALL was significantly higher than for T-cell ALL and AML (85.2% vs. 62.5% vs. 27.8%; P-value <0.01).

**Conclusions:** This study showed that overall survival in Omani children with Acute leukemia is similar to international results. Further studies are needed to confirm these studies prospectively.

PO005 / #1637 | Publication Topic: AS05 SIOP Scientific Program / AS05.a Acute Lymphoblastic Leukaemia

### NEUROLOGICAL COMPLICATIONS DURING TREATMENT OF CHILDHOOD ACUTE LYMPHOBLASTIC LEUKAEMIA –A COMPELLING ISSUE FOR LOW AND MIDDLE INCOME COUNTRIES (LMIC): A MULTICENTRIC STUDY IN BANGLADESH

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**Background and Aims:** Acute lymphoblastic leukemia (ALL) is the commonest childhood malignancy with high cure rates. But CNS related complications remain as a major issue yet to be resolved. The objective of this study was to analyze the pattern of neurological complications along with related risk factors during induction phase of chemotherapy.

**Methods:** This observational study was conducted in the Pediatric Oncology unit of Bangabandhu Sheikh Mujib Medical University and Dhaka Medical College from July 2014 to June 2020. Children (diagnosed as ALL) selected at dx were classified according to age range, sex, ALL type and neurological manifestations (NM).

**Results:** We analyzed 564 patients. 59.21% boys and 40.79% girls, with a mean age of  $6.63 \pm 4.39$  years. Patient with NM (173 pts, 30.6%) was significantly older ( $p = 0.03$ ), and the highest prevalence was between 9 to 13 yrs. High risk group specially T cell ALL was predominant over the other lineages ( $p \leq 0.03$ ) with more positive MRD at D29 ( $p \leq 0.001$ ) in NM group. The most frequent NM was CNS infiltration, seizures, headache and neuropathy, cerebral infection. Important risk factor or co-morbid conditions like thrombocytopenia with coagulation disorder (75%), severe febrile neutropenia (66.6%), traumatic IT (23.2%) dyselectrolytaemia with hypocalcemia (16.6%), H/O of ear infection (10%), L-asparaginase related complication (12%) and metabolic abnormalities (8.3%) were observed. Higher mortality in pts with NM group (58.3%) in compare to non-NM 6%. Lack of emergency care (53%), blood product availability (41%), lab facilities (39%) parents awareness and economic burden (33%) etc were noticed.

**Conclusions:** The wide spectrum of neurological manifestations occur during early phase of chemotherapy. Some important risk factors like disease itself, chemotherapy induced neurotoxicity economic burden etc are related to mortality and morbidity. As these are treatable, early diagnosis and prompt treatment is essential to limit permanent damage.

PO006 / #626 | Publication Topic: AS05 SIOP Scientific Program / AS05.a Acute Lymphoblastic Leukaemia

### IMMUNOPHENOTYPIC PATTERNS OF CHILDHOOD ACUTE LEUKEMIAS BY FLOW CYTOMETRIC ANALYSIS

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**Background and Aims:** Immunophenotype is a most popular and powerful technology around the Globe. Immunophenotype plays a vital role in the diagnosis, classification, prognosis and treatment of the acute leukemia in children. Therefore, we aimed to determine the proportion of the Immunophenotypic subtypes of acute leukemia in children.

**Methods:** Samples were obtained from children (2-18 years of age) in pediatric Hematology and Oncology Department, of a tertiary care hospital. We analyzed 542 clinically suspected leukemia samples from Jan 2021 - Dec 2021) by ten-color flow Cytometry. Immunophenotyping allowed classification into Acute lymphoblastic leukemia (ALL) (B-lineage and T-lineage ALL) and acute myeloid leukemia (AML). We use 12 CD markers for evaluation of acute leukemia. Among them most specific are CD3, CD5, CD19, cCD79a, CD13, CD33, HLADR, CD34, cMPO.

**Results:** Among 542 samples, ALL was 299 (55.1%), AML 70(12.91%), AMLL (Acute mixed lineage leukemia) 12(2.21%). Of the ALL samples 262(48.33%) were B-lineage ALL and 37(6.82%) T-lineage ALL. ALL with aberrant expression were 57(10.51%), AML With aberrant expression 65(11.99%). Our data showed the CD markers expression for ALL were CD19+and cCD79a+ (100%), CD10+ (54%), HLA-DR+ (80%), and CD34+ (90%). CD markers expression for B-ALL were CD19+ (100%), CD10+ (37.3%), cCD79a+ (80%), and HLA-DR+ (78%). CD markers expression for T-ALL were CD3+ (100%), CD5+ (40%), CD7+ (68%). CD markers expression for AML were CD13+ (78%), CD33+ (80%) and MPO (100%). Most common aberrant expression of B-ALL with CD13 was 17(3.13%) and AML With aberrant expression of CD7 was most common 26(4.79%).

**Conclusions:** Immunophenotyping is a very useful high-tech investigation, particularly important for diagnosis, classifications, risk stratification, prognosis and to make plan for chemotherapy of childhood acute leukemia in low and middle income countries.

PO007 / #14 | Publication Topic: *AS05 SIOP Scientific Program / AS05.a Acute Lymphoblastic Leukaemia*

#### MANAGEMENT OF ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN IN ALGERIA: A CHALLENGE FOR A PEDIATRICIAN FACE TO A SUFFERING CHILD

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**Background and Aims:** Acute lymphoblastic leukemia ALL is the most common malignant disease in children. Imminent progress has been achieved in management with survival results improvement. However, resources are still limited in Algeria since molecular studies are inaccessible. The aim of this study is to evaluate outcome of children regarding our working conditions.

**Methods:** This is a retrospective study carried out at the pediatric department of CHU Béni Messous, Algiers, including children aged less 16 years with ALL and treated between January 2005 and December 2022. Data were collected from patients' files. Diagnosis was established on cytological and/or immuno-histochemical studies, management was performed according to EORTC protocols.

**Results:** Out of 193 patients registered for acute leukemia, ALL is reported in 150 (77.7%), with a sex ratio of 1.3 and a median age at

diagnosis of 67 months (26 days- 12 years). Median time to diagnosis was 44 days (3 days to 12 months). Fourth patients had CNS involvement at diagnosis (2.6 %) while 13 had mediastinal enlargement (8.6 %). Thirty two patients presented with major hyperleukocytosis (21.3%). Flow cytometry was performed into 106 patients (70.6 %) revealing a large predominance of B- cell ALL in 79 patients (52.6 %), T- cell in 10 (6.6%). Diagnosis was cytological in the remaining patients with identification of Burkitt leukemia in 8 (5.3%). Corticosenibility was noted in 77.3 % with complete remission at induction course in 81.3 %. Thirty eight patients exhibited relapse 25.3 % and 13 had progressive disease 8.6 %, overall survival rate is 61.7%.

**Conclusions:** Management of children with ALL in Algeria still suffers from diagnosis delay with significant consequences. Without cytogenetic studies, identifying patients at high risk of relapse requiring therapeutic intensification or stem cell transplantation seems hard. Pediatricians must still fight to improve management of such patients in Algeria.

PO008 / #195 | Publication Topic: *AS05 SIOP Scientific Program / AS05.a Acute Lymphoblastic Leukaemia*

#### RAPID DEPLETION OF ASPARAGINE, AS A POSSIBLE RISK MARKER FOR PANCREATITIS IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA UNDER TREATMENT WITH L-ASPARAGINASE

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**Background and Aims:** We describe our experience with 5 patients with acute lymphoblastic leukemia (ALL) who developed L-Asparaginase (L-Asp)-induced pancreatitis during their remission induction stage.

**Methods:** The patients were cared for at the Durango Mexico State Cancer Center since December 2021 along with 31 patients who did not develop pancreatitis. In the 5 patients who developed pancreatitis and 31 children who did not develop it, 3 levels per patient for L-Asp enzyme activity and 3 asparagine (Asp) concentrations were routinely measured. A previously assembled and validated population pharmacokinetic/pharmacodynamic (PK/PD) model (by Monolix from Lixsoft Software) was used to determine their PK/PD parameters.

**Results:** Four of the patients after the ninth administration and one after the sixth administration of L-Asp revealed an increase in amylase and lipase enzymes even when the patients were asymptomatic. In three of the patients the abdomen was slightly distended and diffusely painful. A computed tomography (CT) scan was performed to confirm the diagnosis of pancreatitis due to the use of L-Asp, which was immediately discontinued. According to the data obtained from Asp levels, it was observed that the five patients reached complete depletion close



to the first 24 hours, while the 31 patients without pancreatitis did so close to day 9. When obtaining the Asp decay slope we found that this could be a risk marker for developing pancreatitis as was evident in 5 patients who had been given L-Asp.

**Conclusions:** The pharmacodynamic profiles of patients who developed pancreatitis show much shorter Asp fall time and slope than patients who did not develop pancreatitis. In such a way that these results, together with the doses administered, could be a marker of risk of pancreatitis due to L-Asp in children with ALL under treatment.

PO009 / #1430 | Publication Topic: AS05 SIOP Scientific Program / AS05.a Acute Lymphoblastic Leukaemia

#### CYTOGENETIC AND IMMUNOPHENOTYPIC PROFILE OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA: A RETROSPECTIVE OBSERVATIONAL STUDY

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**Background and Aims:** Acute lymphoblastic leukemia (ALL) is the most common pediatric malignancy with 5-year overall survival (OS) over 90%. OS in India ranged from 45–81% and there are differences in prevalence of cytogenetic abnormalities between different ethnic groups, which may have significant impact on survival outcomes. Collect data regarding immunophenotyping and cytogenetics in addition to conventional prognostic indicators.

**Methods:** ALL patients 1 and 18 years of age and underwent treatment between 1-1-2015 to 29-02-2022. Immunophenotypic and cytogenetics data were collected

**Results:** 147 children showed Males were 78(53.1%) and females were 69 (46.9%). Male to female ratio 1.13:1. Peak age of presentation was between 1 to 7 years. Hyperleukocytosis was seen in 10(7%) patients. CNS3 disease was present in 9 (6.4%). Out of 114 children with risk stratifications available 28 (24.6%) were standard risk, 62(54.4%) were moderate risk and 24 (21.1%) were high risk. Majority was Pre-B cell phenotype 109(79.6%), 27(19.7%) patients were T cell ALL and 1 patient had TLBL. Hyper diploidy was the most common karyotypic abnormality 16 (21.9%) followed by hypodiploidy 3(4.1%). Most common chromosomal translocation was ETV-RUNX1 15 patients (13.2%). BCR -ABL was positive in 7(6.3%) patients and TCF3 -PBX1 3(2.8%) of patients. Day 8 prednisolone response, 131(94.9%) had prednisolone good response and 7 (5.1%) had poor response. On day 33 BM, 122(93.1%) had M1 (<5%) status and 9(6.9%) patients had either M2 or M3 status. MRD was negative in 105 (80.8%) patients and positive in 25(19.2%) children at the end of induction (day33). At a median follow up of 28 months, OS of standard risk, moderate risk and high risk was 81.25%, 85%, and 56% respectively and estimated 5year OS was 57.85%, 65.7% and 43% respectively.

**Conclusions:** We observed that good risk cytogenetics were more prevalent, whereas T cell phenotype is less frequent in our cohort as compared with other Indian studies.

PO010 / #1233 | Publication Topic: AS05 SIOP Scientific Program / AS05.a Acute Lymphoblastic Leukaemia

#### BLOOD FRACTIONAL PROTOCOL FOR IMPROVING RNA QUALITY & YIELD IN LOW TLC SAMPLES

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**Background and Aims:** Sample adequacy in quality and quantity is a challenge in all molecular diagnostic laboratories. The problem of low TLC counts and sub-optimum sample submissions are commonly encountered in hemato-proliferative disorders owing to pancytopenia and BM suppression in the majority of conditions. Sample rejection is often not possible owing to various reasons- precious samples, patient unavailability, and inaccessible clinical reasons for repeat sampling. PBMC separation and blood fractionation are alternate solutions to this problem. There are numerous techniques for isolating leukocytes prior to RNA extraction. The buffy coat (BC) extraction mostly contains leukocytes and platelets, but some red blood cells are unavoidably present. We propose a new protocol developed in our laboratory to increase the yield and quality of RNA extracted for molecular diagnostic services.

**Methods:** The samples were isolated with whole blood and buffy coat fractionation protocol developed by us and the yield was compared in both two groups A and B in the table For the isolation assessment, fresh peripheral blood samples from 547 (197 RBC lysis buffer only, 350 BC+ lysis buffer) leukemic cases were collected using EDTA tubes and processed immediately. RBC lysis eliminates red blood cells while leaving leukocytes and platelets. After plasma isolation, the addition of RBC lysis buffer (*Cat 52304, Qiagen RNA Blood Mini Kit*) eliminates all red blood cells, leaving only leukocytes which improves RNA yield and quality. The purity and integrity of the nucleic acids obtained were assessed by spectrophotometry and validation of housekeeping genes ABL copy number was tested in both groups and validated.

**Results:** Table: Summary of leukocyte isolation from two methods  
**Conclusions:** RNA yield and quality were significantly improved in BC + RBC lysis buffer, with a mean RNA yield of 417 ng/ $\mu$ l and whole blood was 256 ng/ $\mu$ l and a p-value of P<0.0001.

PO011 / #932 | Publication Topic: AS05 SIOP Scientific Program / AS05.a Acute Lymphoblastic Leukaemia

#### BACTERIAL PROFILE AND ANTIBIOTIC-RESISTANCE IN BLOOD CULTURE FROM CHILDREN WITH ACUTE LEUKEMIA IN MOZAMBIQUE: PRELIMINARY RESULTS

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**Background and Aims:** A high prevalence of antimicrobial-resistant bacterial strains has been noticed globally. Patients undergoing intensive immunosuppressive treatment are at high risk of severe life-threatening bacterial infections. We aimed to determine the predominant bacterial species associated with bacteremia and their antibiotic resistance pattern, among febrile pediatric patients diagnosed with acute leukemia (AL) at Maputo Central Hospital in Mozambique.

**Methods:** From January 2021 to October 2022, retrospective evaluation of data from 34 children with acute leukemia under chemotherapy diagnosed at the Hematology-Oncology Service of the Maputo Central Hospital, with clinical sign and symptoms of bacteremia was done. Samples were collected at different time points and inoculated directly into BacT/ALERT PF Plus bottles. Isolates were identified by culture and antibiotic susceptibility testing done using a Kirby-Bauer disk diffusion.

**Results:** Fifty-four blood culture tests from children diagnosed with B-cell acute lymphoblastic leukemia (n = 14), T-cell acute lymphoblastic leukemia (n = 9) and acute myeloid leukemia (n = 11) were collected. Pathogenic strains were isolated in 44.4% (24/54) of cultures. Gram-positive bacteria were the most common isolate, 25.9% (14/54), with predominance of the coagulase negative Staphylococci (CoNS) 16.7% (9/54), followed by *S.aureus* 7.4% (4/54). Gram-negative bacteria were observed in 14.8% (8/54) of cultures, and the *Klebsiella pneumoniae* was the most frequent isolate 7.4% (4/54). Multidrug resistance (MDR) was high in both Gram-negative and Gram-positive bacteria for common antibiotics, with high levels of resistance to Penicillin (86%; 6/7) and Cefoxitin (67%; 4/6) in CoNS strains. Ampicilin and cotrimoxazole resistance was in 100% *Klebsiella spp* (n = 5).

**Conclusions:** Coagulase negative Staphylococci was the dominant bacterial isolate associated with bacteremia in children with AL at Maputo Central Hospital. The proportion of MDR rate was high in children with AL at the hospital.

PO012 / #1218 | **Publication Topic:** AS05 SIOP Scientific Program / AS05.a Acute Lymphoblastic Leukaemia

#### 6-MP INDUCED ANOREXIA : A DIAGNOSTIC DILEMMA

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**Background and Aims:** 6-Mercaptopurine (6-MP) is a cornerstone drug in treatment of Acute Lymphoblastic Leukemia (ALL) which in general, it is a well-tolerated by children. We report a case of 6-MP induced anorexia which is an unusual and debilitating side effect that calls for early diagnosis and intervention.

**Methods:** A 5 year old boy, case of B-cell ALL on maintenance therapy for 1 year, presented with chronic diarrhoea with multiple episodes of vomiting. Child had presented with similar complaints previously and was diagnosed with cryptosporidium infection which was treated with oral Nitazoxanide, with transient clinical improvement. As symptoms relapsed, child was evaluated extensively. Intravenous antibiotics and parenteral nutrition was started in view of neutropenia and cachexia. Stool work-up was negative. Chronic infections like tuberculosis, cytomegalovirus, HIV and Hepatitis B were ruled out. Imaging showed features of enteritis. Endoscopy findings were inconclusive. Suspecting a co-existing primary immunodeficiency with ALL, lymphocyte subset analysis, immunoglobulin profile and nitroblue tetrazolium test was done which was normal.

**Results:** As symptoms worsened with no diagnosis, we started looking at drug induced toxicities and literature review suggested 6-MP could be causative for gastrointestinal complaints and anorexia. We took a drug holiday and with gradual introduction of the drug at tolerable doses we completed therapy. He is currently 1 year post end of treatment, in remission and clinically well.

**Conclusions:** 6-MP is metabolized to active 6-thioguanine nucleotide (6-TGN) for antineoplastic activity. An alternative pathway involves methylation of 6-MP to 6-methylmercaptopurine (6-MMP) which causes intractable nausea, pancreatitis, hepatotoxicity and hypoglycemia at higher levels. It leads to pauses in chemotherapy potentiating increased risk of relapse. A balance to maximize anti-leukemia effect and minimize gastrointestinal and myelosuppressive toxicity is a challenge. This skewed metabolism causes inadequate myelosuppression which leads to dose escalation causing more GI toxicity. Studies suggest a possible role of allopurinol leading to decreased required doses of 6 MP as an aid for pediatric cases with such toxicities.

PO013 / #949 | **Publication Topic:** AS05 SIOP Scientific Program / AS05.a Acute Lymphoblastic Leukaemia

#### IMPACT OF PREMEDICATION USE BEFORE PEG-ASPARAGINASE IN CHILDREN WITH ALL IN BRAZIL: INTERIM ANALYSIS OF A MULTICENTER RANDOMIZED TRIAL

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**Background and Aims:** PEG asparaginase (PEG-ASNase) is a key drug in the treatment of acute lymphoblastic leukemia (ALL). However, PEG-ASNase has a particular toxicity profile and little data exists on these effects in children treated with low middle income countries (LMIC). Objectives: To describe the adverse effects related to PEG-ASNase, compare with what was previously described in high income countries (HIC) and evaluate the influence of the use of premedication in Brazilian pediatric patients treated within a prospective randomized trial.

**Methods:** Patients younger than 18 years with ALL were randomized in two groups: group 1 received premedication (corticosteroid and antihistamine) before each PEG-ASP infusion and group 2 received PEG-ASNase alone (control group). This interim analysis was performed with 30% of the estimated total sample. Adverse effects after each infusion as well as asparaginase activity were systematically monitored.

**Results:** One hundred and thirty four patients were included: 65 (48.5%) in the premedication group and 69 (51.5%) in the control group. The groups are comparable in terms of age, gender, risk group and ALL subtype ( $p > 0.01$ ). Twenty-eight adverse reactions were observed in 25 patients (18.7%): 4 acute pancreatitis (3%), 2 (1.5%) allergic reaction, 3 deep venous thrombosis (2.2%) and 19 hypofibrinogenemia (14.2%). There was no significant difference in the frequency of adverse effects or in their distribution between groups (18.5% with premedication x 18.8% control group) ( $p > 0.01$ ). Silent inactivation rates were also similar.

**Conclusions:** According to this partial analysis, the use of premedication in our population has not changed the profile of undesirable effects associated with PEG-ANSase. Events such as pancreatitis, clinical allergic reactions and silent inactivation were equivalent in both groups. With the continuation of the present study, we intended to better understand whether there is a real benefit from the use of premedication in the treatment of children with ALL in LMIC.

PO014 / #988 | Publication Topic: AS05 SIOP Scientific Program / AS05.a Acute Lymphoblastic Leukaemia

#### CHARACTERIZATION OF GENETIC POLYMORPHISMS RELATED TO ASPARAGINASE METABOLISM IN THE BRAZILIAN PEDIATRIC POPULATION

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**Background and Aims:** Asparaginase (ASNase) is a critical element in treating pediatric acute lymphoblastic leukemia (ALL). However, hypersensitivity reactions to ASNase are major challenges. Detection of single nucleotide polymorphisms (SNPs) that may recognize in advance patients who will be more likely to develop hypersensitivity to ASNase can help optimize treatment. We aim to describe the main pharmacogenetic variations, which influence hypersensitivity correlated to ASNase in the literature, in Brazilian children with ALL.

**Methods:** Patients <18 years old with a diagnosis of ALL between 2021 and 2023 were included. Eight SNPs were genotyped: rs4958351, rs6021191, rs3809849, rs3807342, rs17179470, rs281366, rs73062673, rs6890057. Custom TaqMan® SNP genotyping assays were used for the determination of genotypes.

**Results:** A total of 115 patients were included. We observed the following genotypic distribution of studied SNPs and Hardy-Weinberg equilibrium (HWE): for GRIA1 rs4958351: GG 34.4%, GA 56.3%, and AA 9.2%, HWE = 0.37; for NFACT2 rs6021191: AA 89.1% and AT 10.9%, HWE = 0.05; for MYBBP1A rs3809849 GG 57.1%, GC 36.9% and CC 5.9%; HWE = 0.24; for CPA2 rs3807342 CC 56.3%, CT 39.4% and TT 4.2%; HWE = 0.24; for RGS6 rs17179470: GG 89.1%, GT:10.1% and TT: 0.8%; HWE = 0,06; for ULK2 rs281366: CC:91.6% and CT:8.4%; HWE = 0,04; for CNOT3 rs73062673: TT:75.6%, TC:21.8% and CC:2.5%; HWE:0.13; for GR1A1 rs6890057: CC:63.7%, CT:30.9% and TT:5.3%; HWE = 0.21. There is agreement between the frequencies of polymorphisms in our population and the international one, which was evaluated by ICC = 0.992 (0.984-0.996) from two-way Mixed-effects model. **Conclusions:** Through this analysis, we were able to pre-characterize the polymorphisms of 8 SNPs in our population. Despite the high degree of miscegenation observed in our country, this data was concordant with what was previously described in high income countries (HIC). With the continuity of this study, we will look for new markers capable of anticipating adverse effects associated with the use of asparaginase.

PO015 / #1619 | Publication Topic: AS05 SIOP Scientific Program / AS05.a Acute Lymphoblastic Leukaemia

#### INFLUENCE OF L-ASARAGINASE AND PEGASPARGASE ON COAGULATION SYSTEM AMONG PEDIATRIC PATIENTS WITH A DIAGNOSIS OF ACUTE LYMPHOBLASTIC LEUKEMIA

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**Background and Aims:** Asparaginase (ASP) is one of the important chemotherapeutic agents playing a key role in pediatric acute lymphoblastic leukemia (ALL) treatment schemes, which can be associated with hemorrhagic and thrombotic complications. ASP can potentially disrupt normal blood clotting and bring coagulopathies. As a consequence of ASP decrease in the number of several blood clotting factors can be observed, which can contribute to the development of thrombotic complications with abnormal blood clotting tests. The aim of this study was to compare the effects of two different subtypes of ASP, pegylated asparaginase (PEG-ASP) and L-asparaginase (L-ASP) on coagulation system among 62 children in the Pediatric Cancer and Blood Disorders Center of Armenia.

**Methods:** The clinical features of 62 patients with ALL who received L-ASP or PEG-ASP in the Armenian center were analyzed retrospectively through descriptive statistical methods. The change in coagulation function and the incidence of complications of the 2 treated groups were compared. Blood clotting markers included prothrombin time (PT), activated partial thrombin time (APTT), fibrinogen (FB), and INR (international normalized ratio) and were evaluated after induction chemotherapy.

**Results:** Among 62 patients, 24 patients received treatment with L-ASP and 38 with PEG-ASP. Differences in coagulation abnormalities depending on the distribution of age and sex, white blood cell count at diagnosis, and risk factors of the disease were not observed. The blood clotting profile before therapy, including PT, APTT, INR and FB between the two groups did not differ. In the group treated by L-ASP, PT, INR, and APTT were prolonged, while in the second group hypofibrinogenemia and increased D-dimer levels, ranging from 3–10 ng/ml were reported more frequently.

**Conclusions:** During the ALL treatment, the vast majority of patients with ALL did not develop clinically significant coagulopathies. The sample size limits the validity of the data and the topic requires further research.

PO016 / #1471 | Publication Topic: AS05 SIOP Scientific Program / AS05.a Acute Lymphoblastic Leukaemia

#### IMMUNOPHENOTYPIC PROFILE OF PEDIATRIC ACUTE LEUKEMIAS DIAGNOSED IN MAPUTO, MOZAMBIQUE

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**Background and Aims:** Acute leukemias (AL) are the most prevalent childhood cancer worldwide, with a predominance of acute lymphoblastic leukemias (ALL). Survival rates of LLA in high income countries are more than 80%, however, in Africa, the outcomes of AL remain disappointing. Timely and accurate diagnosis significantly improves the survival rate. Immunophenotyping the leukemic clone is fundamental for appropriate definitive risk group allocation, thus optimization of the treatment protocol. We aimed to describe the profile of AL, since the implementation of immunophenotyping in Mozambique.

**Methods:** From January 2020 to March 2023, 171 children aged less than 14 years, with clinical and laboratorial suspicion of AL were admitted to pediatric Hematology Oncology Pediatric Service at Hospital Central de Maputo. The diagnosis was confirmed by cellular morphology and immunophenotype of the bone marrow aspirate, by four or eight color flow cytometry.

**Results:** Eighty-five cases were diagnosed with AL. At diagnosis, patients with AL showed lower platelet mass and neutrophile absolute counts compared to those without leukemia ( $p = 0.0008$  and  $p = 0.0419$ , respectively). Among patients with AL, 31.76% (27/85) were acute myeloblastic leukemia and 67.05% (57/85) were ALL. Among ALL, 70.18% (40/57) were B-cell ALL and 29.82% (17/57) were T-cell ALL. Furthermore, 35.09% (20/57), 40.35% (23/57) and 17.54% (10/57) of ALL cases were aged between 2 to 5 years, 5 to 10 years and older than 10 years, respectively. Seventeen percent of ALL had white blood cells count above  $50 \times 10^9/l$ . Overall, at diagnosis, 26 (30.59%) cases were classified as provisional standard risk and 59 (69.41%) as high risk.

**Conclusions:** Here, we observed a high occurrence of pediatric B-ALL, as reported in other countries. The elevated frequency of high-risk cases at diagnosis, reinforce the need to strengthen national efforts for early diagnosis of acute leukemia. The use of immunophenotype for leukemia diagnosis is feasible in Mozambique.

PO017 / #1642 | Publication Topic: AS05 SIOP Scientific Program / AS05.a Acute Lymphoblastic Leukaemia

#### CLINICAL AND LABORATORY FEATURES OF CHILDREN WITH ACUTE LEUKEMIA WITH FEBRILE NEUTROPENIA IN MAPUTO CENTRAL HOSPITAL, MOZAMBIQUE

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**Background and Aims:** Febrile neutropenia is a frequent oncological emergency in children with malignancies, occurring in patients with acute leukemia (AL). It is an important cause of morbidity and mortality. A third of children with cancer in treatment experience febrile neutropenia and it is a challenge to identify the cause of infection. We aimed to describe the clinical and laboratory features of children with AL who presented with febrile neutropenia at Maputo Central Hospital, Mozambique.

**Methods:** Retrospective clinical and laboratory data from children aged less than 15 years with AL with episodes of febrile neutropenia from January 2022 to December 2022 was collected from patients' files at the Hematology-Oncology Service at Maputo Central Hospital. Febrile neutropenia was defined as the presence of fever (body temperature higher than 38.3°C) and absolute neutrophil count lower than 1500 cells/ $\mu$ L.

**Results:** A total of 44 children with AL were attended to in 2022, and 218 admissions were registered of which 33% (72/218) were related to febrile neutropenia. Blood culture was performed on 50 episodes of admissions. The most frequent clinical presentation was mucositis (58.33%; 42/72) followed by respiratory infection (26%; 18/72). Sixty-six (66/218) 30.28% of the cases presented with severe neutropenia (less than 500 cells/ $\mu$ L). Gram-positive bacteria, coagulase-negative *Staphylococci* (16.7% 9/72) was the most common isolate, followed by *Klebsiella Pneumoniae* (7.4%; 5/72).

**Conclusions:** Severe febrile neutropenia was associated with hospital admissions and severe illness in children with acute leukemia diagnosed in Maputo. Coagulase-negative *Staphylococci* is the most frequent cause of bacteremia in children with neutropenia and acute leukemia in this study.

PO018 / #1748 | Publication Topic: AS05 SIOP Scientific Program / AS05.a Acute Lymphoblastic Leukaemia

## BLOODSTREAM INFECTIONS IN PEDIATRIC HEMATOLOGY AND ONCOLOGY PATIENTS IN A UNIVERSITY HOSPITAL IN BANGLADESH

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**Background and Aims:** Bloodstream infections (BSIs) is a frequent complication in immunosuppressed and neutropenic cancer patients. Antibiotic-resistance is a problem which is more pronounced in developing countries. Inappropriate use may lead to increased adverse effects, secondary infections, drug interactions, additional costs, prolonged lengths of stay. This study was planned to isolate and identify various bacterial causes of BSIs and susceptibility pattern in pediatric hematological and oncological patients to decide the best empirical treatment

**Methods:** This was a cross-sectional study, carried out on blood culture samples from cases of BSI at Department of Pediatric Hematology and Oncology, Bangabandhu Sheikh Mujib Medical University, Dhaka from November 2020 to December 2022. Patients of 2–15 years were included in this study. Blood was drawn via venipuncture and was inoculated into the designated blood culture bottles and final report were obtained after 72 hours. Patients' records were reviewed regarding type of disease chemotherapy and neutropenia.

**Results:** Febrile neutropenia - 330 episodes of 165 patients were evaluated. Among those 180 episodes of ALL, 115 of AML, 15 of neuroblastoma, langerhans cell histiocytosis 10 and 10 aplastic anemia patients were recorded. Severe neutropenia was observed in case of patients with ALL, AML and langerhans cell histiocytosis (LCH). Blood culture positive were found in 65 reports (19.69%), among them *Klebsiella* 21 (32.3%) were mostly sensitive to colistin, amikacin, meropenam, *Pseudomonas* 18 (27.65%) were mainly sensitive to ceftazidim, tazobactam+piperacillin, netilmycin, MRSA – 1 (1.53%) sensitive to vancomycin, *Serratia* sp. 2 (3.07%), *Enterococci* sp. 1 (1.53%) were sensitive to vancomycin, *Enterobacter cloacae* sp. 1 (1.5%) was sensitive to cotrimoxazole, vancomycin, linezolid, nitrofurantoin and amoxicillin.

**Conclusions:** In this study *Klebsiella* and *pseudomonas* were predominating bacteria isolated in blood culture. Regular surveillance of sensitivity patterns of isolated bacteria, change of hospital antibiotic policies based on existing data will guide and promote rational antibiotic.

PO019 / #640 | Publication Topic: AS05 SIOP Scientific Program / AS05.a Acute Lymphoblastic Leukaemia

## COST-EFFECTIVE UTILIZATION OF PEGYLATED L-ASPARAGINASE IN A UNIVERSITY HOSPITAL IN A LOW MIDDLE INCOME COUNTRY

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**Background and Aims:** Pegylated L-Asparaginase (P-LA) has a longer half life and lower hypersensitivity reactions. Unfortunately it is largely a rich man's domain. P-LA (3750 units) costs USD 525 in India versus conventional L-Asparaginase (C-LA) costing USD 20 (10,000 units),

precluding routine use of P-LA. This study aimed to evaluate the cost of using P-LA by sharing a vial versus using C-LA alone

**Methods:** P-LA was shared among patients with Acute Lymphoblastic Leukemia/Lymphoma. An opened vial was kept for 24 hours and discarded thereafter. The vial was split amongst children who were due to receive L-Asparaginase in this time period. The date of L-asparaginase was adjusted by a maximum of 24 hours to facilitate sharing. One dose of P-LA was considered equivalent to 4 doses of C-LA.

**Results:** Two hundred and ninety five doses were administered to 157 children (age:  $6 \pm 2.66$  [2-13]) years between June 2021 to January 2022. The prescribed dose of P-LA was  $810.34 \pm 264.14$  units ( $400 - 1700$ ) [dose -  $1000$  units/m<sup>2</sup>]. The number of patients who shared a vial of P-LA was  $3.78 \pm 8$  (1-5). The average dose discarded per vial was  $1050 \pm 668$  units. With sharing, average cost of P-LA/dose was USD 112. Cost of 4 doses of C-LA was USD 80. The value of discarded P-LA per vial was 145 USD.

**Conclusions:** Dividing a vial of P-LA amongst patients is feasible and cost-efficient, despite discarding around 1000u/ vial, in centers treating a large number of patients. The difference in cost between an equivalent dose of P-LA and C-LA was reduced to just USD 32 as compared to USD 445 if a vial is not dispersed among patients. A smaller-sized vial of P-LA is the need of the hour, which would enable all patients to receive P-LA, avoid wastage of precious drug & ensure receipt of a superior medication.

PO020 / #1372 | Publication Topic: AS05 SIOP Scientific Program / AS05.a Acute Lymphoblastic Leukaemia

#### HYPERGLYCEMIA AMONG CHILDREN BELOW 18 YEARS WITH ACUTE LYMPHOBLASTIC LEUKEMIA/LYMPHOMA ON CHEMOTHERAPY IN UGANDA: INCIDENCE, RISK FACTORS, AND IMMEDIATE OUTCOMES

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**Background and Aims:** Acute leukemia is the most common childhood malignancy worldwide, accounting for 30% of childhood cancer cases with Acute Lymphoblastic (ALL) constituting 75–80% of paediatric leukemias. Chemotherapy treatment of Acute Lymphoblastic Leukemia/Lymphoma (ALL/LBL) involves the use of Steroids and L-asparaginase among others, both of which are known to induce hyperglycemia in patients with ALL and LBL resulting in increased morbidity and mortality. The aim of the study was to determine the incidence, risk factors, and immediate outcomes of hyperglycemia among children below 18 years with Acute Lymphoblastic Leukemia/Lymphoma on chemotherapy.

**Methods:** This was a hospital-based prospective cohort study carried out at the 2 main pediatric cancer treatment sites in Uganda (Mulago

National Referral Hospital and Uganda Cancer Institute) during the study period from March to August 2022. A total of 84 participants with a confirmed diagnosis of ALL and LBL on either induction or re-induction chemotherapy were recruited into the study and each was followed up for one month. A random blood glucose (RBG) level was recorded at the following intervals: pre-induction, on days 7, 14, 21, and 28 of induction and re-induction chemotherapy. Hyperglycemia was defined as a random blood glucose concentration of  $\geq 200$  mg/dl ( $11.1$  mmol/l) in two or more determinations. The data was analyzed using STATA 16 and reported as frequencies, means and proportions. Cox regression was used for factors associated with hyperglycemia.

**Results:** A total of 84 participants were recruited with a mean age of  $9.2 (\pm 4.2)$  years. Majority were males (65.5%) and below 10 years of age (56.0%). Eight (9.5%) children developed hyperglycemia. Majority 7/8 (87.5%) of patients developed transient hyperglycemia.

**Conclusions:** The cumulative incidence of hyperglycemia was high at 95 per 1000 children with ALL/LBL on chemotherapy. Majority of patients developed transient hyperglycemia which can be fatal thus the need for vigilant screening among these patients.

PO021 / #1654 | Publication Topic: AS05 SIOP Scientific Program / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes

#### PEDIATRIC ACUTE PROMYELOCYTIC LEUKEMIA AND FANCONI ANEMIA: CASE REPORT AND LITERATURE REVIEW

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**Background and Aims:** Acute promyelocytic leukemia (APL) represents 5–10% of childhood acute myeloid leukemia (AML) and, with the advent of Tretinoin and Arsenic trioxide, became the most curable type of AML. Fanconi anemia (FA) is one of the most common inherited bone marrow failure syndrome caused by biallelic pathogenic variants (PVs) in certain DNA-repair genes. Biallelic PVs in BRCA2 (FA-D1) account for  $\approx 3\%$  of all known cases of FA and are associated with early-onset leukemia and a high risk of solid tumors.

**Methods:** Case report and literature review.

**Results:** A four-year old boy from non-consanguineous healthy parents from India was diagnosed with (PML-RARA rearranged) standard risk APL. This child had café-au-lait spots and an extra thumb remnant removed surgically. He tolerated well the induction therapy with Tretinoin and Arsenic trioxide. Morphological remission was achieved after the first month of treatment. He continues on consolidation therapy. Paired tumor/normal DNA sequencing was offered through

the Quebec pediatric cancer research sequencing initiative (Signature study). Germline analysis identified two PVs in BRCA2 confirming a diagnosis of FA. Chromosomal breakage studies were compatible with FA. Each parent carried one variant and had no history of cancer.

**Conclusions:** While the association of AML and FA is well known, PubMed search did not reveal a particular association with APL. Alternative sources revealed one individual with APL/FA-D1 who successfully underwent stem cell transplant (SCT), another individual with APL/FA who died of APL progression without SCT, and a third patient with APL and FA (without treatment or follow-up information). With our patient, four cases with APL/FA (FA-D1, n = 2) have been reported, raising the possibility of an association between such rare disorders. Clinicians should have a low threshold to consider FA among children with APL. Communicating similar cases and collecting APL treatment and follow-up information may lead clinicians to consider APL differently in the setting of FA.

PO022 / #1373 | Publication Topic: AS05 SIOP Scientific Program / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes

#### PROFILE AND OUTCOME OF INFECTIONS DURING PAEDIATRIC ACUTE MYELOID LEUKEMIA THERAPY IN A TERTIARY CANCER CENTRE IN INDIA

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**Background and Aims:** **Background/Aim:** Children with Acute Myeloid leukemia (AML) are at a high risk of infections due to immunosuppression caused by high intensity chemotherapy. They are associated with a mortality rate of 1.5% in developed countries. The aim was to study the incidence, characteristics and the outcome of infectious episodes during paediatric AML therapy.

**Methods:** **Methods** Twenty seven newly diagnosed AML children aged 0–14 years were prospectively analyzed between 1st May 2021 and February 2023. AML treatment consisted of 2 induction courses (“3+7” regimen) with Cytosine arabinoside (ARA-C) and Daunorubicin and 3 consolidation courses with high dose ARA-C. Infectious episodes were categorized as fever of unknown origin (FUO) – (without clear clinical or microbiological evidence), microbiologically documented infection (MDI) – isolation of a pathogen and clinically documented infection (CDI) – (fever with signs of localized infection without microbiological proof).

**Results:** **Results** Among 75 chemotherapy cycles (induction-41, consolidation-34) administered in 27 children, there were 53 (70.6%) infectious episodes and 34 (64.1%) occurred in induction (P = 0.005). Twenty four (45.2%), 12 (22.6%) and 17 (32.07%) episodes were MDI, CDI and FUO respectively. Twelve of the 14 episodes with septic shock had MDI (P = 0.000). Forty one (77.3%) and 24 (45.2%) episodes

were associated with prolonged and profound neutropenia respectively. Gram negative bacteria (GNB) was isolated in 15 (62.5%), gram positive in 6 (28.5%) and fungi in 3 episodes of MDI. Blood stream infection (32%) followed by lung (11.2%) and gastrointestinal tract (5.6%) were the common sites of infection. Meropenam and colistin were given in 29 episodes while 14 episodes required oxygen and ionotrope support. Forty seven (77.7%) patients recovered and 6 (22.3%) died of which 4 had MDI (P = 0.045).

**Conclusions:** **Conclusion** In Indian setting there was high incidence of infectious episodes (70.6%) with predominance in induction. GNB was the most common pathogen. With good supportive care the recovery rate was 77.7% and mortality rate was 22.3%.

PO023 / #1457 | Publication Topic: AS05 SIOP Scientific Program / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes

#### SUCCESSFUL TREATMENT WITH RESPONSE-ADJUSTED (RA) VENETOCLAX DOSING COMBINED WITH AZACYTIDINE/GILTERITINIB IN A REFRACTORY AML-FLT3-ITD POSITIVE PATIENT

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**Background and Aims:** **Background:** Patients with relapse/refractory acute myeloblastic leukemia (AML) with FLT3 abnormality have a dismal prognosis. Venetoclax has been used as salvage chemotherapy but the optimal dosing/duration is undetermined. **Aim:** We presented a case of refractory AML-FLT3 abnormal treated with RA-Venetoclax dosing combined with Azacytidine/Gilteritinib which successfully induced remission and allow patient to received stem cell transplant (SCT) treatment.

**Methods:** **Methods and Results:** A 15 y.o. male complained of fever/fatigue and shortness of breath. Initial CBC showed mild leukocytosis, anemia, thrombocytopenia and 81% circulating blasts. Bone marrow (BM) aspiration confirmed Acute Myeloblastic Leukemia (AML) with no differentiation (AML-MO), positive for FLT3-ITD and trisomy 4. Received Induction 1 with Cytarabine/Idarubicin (7+3). BM assessment demonstrated flow MRD (F-MRD) at 34%. Induction 2 with Cytarabine BID/7d, Mitoxanthrone x3 doses, Etoposide x3 doses, and Midostaurin 50 mg/BID d8-21. BM evaluation demonstrated F-MRD at 57%. Patient arrived to our institution and BM demonstrated F-MRD of 91% blasts. Molecular studies showed only FLT3-ITD-1 {Allele Ratio (AR) 2.68} and trisomy 4. Re-induction with Azacytidine 75 mg/m<sup>2</sup>/d1-7, Gilteritinib 80 mg/daily and RA-Venetoclax day 1 (20 mg), day 2 (50

mg), and from day 3 onward at 100 mg/d to complete 7d. Venetoclax dose reduced due to concomitant azole antifungal administration. D14 BM F-MRD 2.5%, and FLT3-ITD-1 AR 0.03, then patient received Venetoclax for 7d more (14/days total). End of cycle BM showed F-MRD 0.93%, FLT3-ITD-1 AR <0.01. Second cycle Azacytidine/Venetoclax d1-7, and Gilteritinib/daily. Response assessment demonstrated BM F-MRD 0.02%, and negative FLT-ITD or trisomy 4. Patient went to receive a third cycle of chemotherapy (Venetoclax/Azacytidine d1-7 and Gilteritinib/daily with sustained remission and underwent SCT with a MUD with plan for Gilteritinib post SCT.

**Results:** See Methods.

**Conclusions:** We demonstrated that a RA-Venetoclax dosing combined with Azacytidine/Gilteritinib was successful and D14 BM response help to determine length of Venetoclax treatment without excessive myelosuppression.

PO024 / #1783 | **Publication Topic:** AS05 SIOP Scientific Program / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes

#### GEMTUZUMAB OZOGAMICIN FOR RELAPSED OR PRIMARY REFRACTORY ACUTE MYELOID LEUKEMIA IN CHILDREN - EXPERIENCE OF THE POLISH PEDIATRIC LEUKEMIA AND LYMPHOMA STUDY GROUP (PPLSSG)

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**Background and Aims:** Gemtuzumab ozogamicin (GO), one of the first targeted drugs used in oncology, consists of an anti-CD33 monoclonal antibody bound to a derivative of cytotoxic calicheamicin. After the drug was withdrawn in 2010 due to a significantly increased rate of early deaths, GO regained approval in 2017 for the treatment of adults and children with acute myeloid leukemia (AML) refractory or relapsed and de novo AML. The aim of the study is to analyze retrospectively the effects of treatment and the toxicity profile of GO in children with primary refractory or relapsed (r/r) AML.

**Methods:** From January 2008 to December 2022, 35 children were treated with GO in the Polish Paediatric Leukemia and Lymphoma Study Group centres (18 girls and 17 boys, mean age 6.3 years). Primary refractory disease was the indication for GO use in 13 children, the first early AML relapse in 15 children, the first late in 5, and the second early in 2 children. Thirteen children had poor risk genetics at the time of diagnosis of r/r leukemia.

**Results:** Most of the children (72%) had more than 5% bone marrow leukemic blasts (0.1-100%; median 22%) before the start of GO therapy. Most of the patients (30/35) received 1 administration of GO in combination with chemotherapy (IDA-FLA, DOXO-FLA, FLA, FLAG). Of the 35 patients, 18 (52%) achieved complete remission, 8 presented with progression, 6 with relapse. GO therapy was followed by haematopoietic stem cell transplantation in 19 children. Twenty-one children eventually died from disease progression, VOD, COVID, CMV. Fourteen patients (40%) live in the first or subsequent remission of the disease. Hematological toxicities and VOD were reported during GO therapy.

**Conclusions:** The use of GO in severely pretreated children with previous failure of failure of AML treatment is a possible and effective fusion therapy to SCT, with an acceptable toxicity profile.

PO025 / #70 | **Publication Topic:** AS05 SIOP Scientific Program / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes

#### PRESENCE OF TRANSCRIPTS OF THE BCR/ABL GENE IN THE PEDIATRIC POPULATION WITH CHRONIC MYELOID LEUKEMIA AT THE HOSPITAL REGIONAL DE ALTA ESPECIALIDAD DEL BAJÍO

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**Background and Aims:** Background: Chronic Myeloid Leukemia (CML) is associated with the presence of the Philadelphia chromosome (Ph), a product of translocation between chromosomes 9 and 22, reflecting the rearrangement of the BCR-ABL gene. It constitutes 2% of leukemias in children under 15 years and 9% in adolescents between 15–19 years, with an incidence of 1 and 2.2 cases per million, respectively. The increased tyrosine kinase activity of BCR-ABL participates in the leukemic hematopoietic transformation capacity, and molecular therapies target it. Objective: To determine the presence of BCR/ABL gene transcripts in the pediatric population of the Hospital de Alta Especialidad del Bajío (HRAEB) with CML.

**Methods:** A retrospective, observational, cross-sectional, and descriptive study was carried out by analyzing the medical records of patients diagnosed with leukemia from the Hematology and Oncology Service of HRAEB from 2008 to 2018. The genotyping of BCR/ABL transcript by qPCR and other data were collected.

**Results:** Of the 580 medical records of patients with leukemia, 51 had CML (8.8%), and 9 incomplete medical records were discarded, resulting in a final total of 42. Of these, 59.5% were male and 40.5% were female. Five pediatric patients were recorded (1.1% of the population with CML), 80% were male and 20% were female. The average age was 10.8 years (range 2–15 years). Clinically, splenomegaly (60%), hepatomegaly (40%), anemic syndrome (20%), and hemorrhagic syndrome (0%) were found. The presence of BCR/ABL was 80%, and the distribution of its transcripts in the pediatric population was b3a2 (75%), e1a2 (25%). All patients received tyrosine kinase inhibitors, and 60% are still alive.

**Conclusions:** The frequency of the BCR/ABL gene is lower than that reported in the literature, with a predominance of the b3a2 transcript. It helps to identify the presence of BCR/ABL transcript types in the pediatric population with CML given their utility in treatment, prognostic and survival.

PO026 / #1549 | Publication Topic: AS05 SIOP Scientific Program / AS05.b Myeloid Leukemias, Myelodysplastic and Myeloproliferative Syndromes

#### OUTCOMES OF SALVAGE CHEMOTHERAPY REGIMENS IN CHILDREN AND ADOLESCENTS WITH RELAPSED/REFRACTORY ACUTE MYELOID LEUKEMIA (AML)

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**Background and Aims:** Children with AML have high risk of relapse (30%) with probable overall survival of 16% to 34%. This can only be achieved with intensive salvage chemotherapy followed by hematopoi-

etic stem cell transplant (HSCT). The aim of this study is to assess toxicities and outcome associated with various salvage chemotherapy regimens.

**Methods:** This was a prospective observational study conducted over a period of one year. Seventeen children and adolescents less than 18 year with relapsed/refractory AML were enrolled in the study. Patients were treated with regimens based on the following drugs: cytarabine, granulocyte colony-stimulating factor (G-CSF), and fludarabine (FLAG) with Bortezomib (n = 10); cytarabine, cladribine and G-CSF (CLAG) with idarubicin (n = 4); FLAG with idarubicin (n = 3). Targeted therapy for FLT3 mutation : sorafenib (n = 1) and midostaurin (n = 5) were given. Their toxicities and outcomes were studied.

**Results:** Median age of patients was 11 years (IQR 3 to 14). Twelve (70.5%) were males and five (29.5%) were females. Cytogenetics were positive in three (17.6%) : trisomy 8, trisomy 21 and RUNX1-RUNX1T1 translocation. FLT3 mutations were most common and were present in six (35.3%) patients. Eleven (64.7%) had persistent leukemic activity and six (35.3%) had relapse after induction. All but one relapsed within six months. Most common toxicity was myelosuppression, all patients had grade 3 or more pancytopenia. Other grade 3 or more toxicities were febrile neutropenia (94.1%, n = 16), sepsis (41.1%, n = 7), enterocolitis (29.4% n = 5), bronchial infection (29.4% n = 5), hypokalemia (58.8%, n = 10). Seven (41.1%) achieved remission, two (11.7%) proceeded to HSCT, at last follow up four (23.5%) are alive without disease. Thirteen (76.4%) died, out of which six (35.3%) were treatment related mortality and seven (41.1%) deaths occurred due to disease.

**Conclusions:** Children and adolescents with relapsed/refractory AML have poor survival. Survival may be improved by anticipating toxicities associated with salvage chemotherapy regimens and selecting regimen with improved outcome

PO027 / #13 | Publication Topic: AS05 SIOP Scientific Program / AS05.c Lymphomas

#### MANAGEMENT AND OUTCOME OF CHILDREN WITH NON-HODGKIN'S LYMPHOMA NHL: A REPORT FROM A SINGLE INSTITUTION IN ALGERIA

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**Background and Aims:** Improvement of treatment results for NHL has been achieved during recent years, especially by intensifying therapy for advanced disease. However, is there a difference between these two decades before 2010 and 2022 periods? We aim to identify the clinical presentation, management and survival of patients with NHL.

**Methods:** A retrospective study including all patients aged less 16 years old diagnosed with NHL was performed from January 1998 to January 2023. Patients are staged and treated according to adapted LMB protocol regimens. Survival rate is studied by Kaplan-Meier method.

**Results:** A total of 86 patients is identified, 59 boys and 27 girls with an age ranging from 3.5 to 15.5 ys. Primary tumor sites were abdomen in 45.3%, mediastinum in 20%, tonsil in 12.7%, bone 3.4%, bone marrow 12.8% and oculo-cerebral 1%. Three patients had CNS involvement at diagnosis (3.4%). Burkitt's lymphoma was the most common histological type, 65% of the patients had stage 3, and 32.5% had stage 4 disease. High Dose methotrexate was administered at 3 or 5 g/m<sup>2</sup>/day. One underwent CNS radiotherapy. Sixteen patients (69.8%) achieved complete remission while eleven died rapidly of refractory disease (12.7%). Secondarily, nine patients died as a consequence of disease relapse (10.4%). Overall survival is 58% with a follow up time ranging 12 months to 23 years. Comparison between the two decades did not objective any difference in terms of progress.

**Conclusions:** The majority of Algerian patients are diagnosed with advanced disease (stage 3 or 4 of Murphy's Classification). More efforts should be performed for an early diagnosis to achieve appropriate management and a better outcome.

PO028 / #1587 | Publication Topic: AS05 SIOP Scientific Program / AS05.c Lymphomas

#### CLINICO-PATHOLOGICAL PROFILE AND TREATMENT OUTCOMES OF CHILDREN WITH HODGKIN LYMPHOMA AT TIKUR ANBESSA SPECIALIZED HOSPITAL (TASH), ETHIOPIA'S LARGEST TERTIARY REFERRAL HOSPITAL

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**Background and Aims:** Hodgkin's Lymphoma accounts for approximately for 6% of childhood malignancies and peaks during adolescence. It encompasses two basic diseases: Classical HL(CHL) and Nodular Lymphocyte predominant Lymphoma(NLPHL). Nodular Sclerosis HL is the commonest subtype of CHL in developed countries. Treatment of HL in pediatric patients is risk adapted. With the use of therapeutic regimens, patients with favorable prognostic factors and early staged disease in developed countries have EFS of 85 to 90% and 5 yrs overall survival of more than 95% This study aims to assess the clinico-pathological profile and treatment outcomes of children with HL at TASH.

**Methods:** TASH conducted a retrospective cross sectional study through self administered structured questionnaire on 106 children treated from 2014 to 2018 who met the inclusion criteria. Collected data was analysed using a statistical package for social science (SPSS) version 25. P value less than 0.005 was considered to be statistically significant. Kaplan-Meier estimate used for OS and EFS analysis

**Results:** Mean age of the patient was 8.36 years with a range of 3 to 15 years with a male to female ratio of 3.8:1. Peak age of HL was 5

to 10 years, accounting for 61.3%(n = 65). The commonest histologic sub type mixed cellularity, accounting for 62.3%(n = 66). more than half (54.6%) presented with stage 3/4 disease. Hb, LDH, ESR the presence of B symptoms(p<0.005 has a significant association with stage of the disease(p<0.005). The 5 yr OS AND EFS were 100% and 93.9% respectively

**Conclusions:** Our study shows the peak age is 5 to 10 years. Mixed cellularity is the commonest type. OS and EFS are comparable with the developed countries. Will continue with multi institutional study in Ethiopia.

PO029 / #553 | Publication Topic: AS05 SIOP Scientific Program / AS05.c Lymphomas

#### NIVOLUMAB EXPERIENCE IN REFRACTORY LYMPHOMA CASES WITH PD1, PDL1 POSITIVITY

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**Background and Aims:** In this study, 3 refractory lymphoma patients with PD-1 and PDL-1 positivity who were treated with nivolumab were presented.

**Methods: Case 1:** A 15-year-old female patient was treated with diagnosis of diffuse large B-cell lymphoma due to a mediastinal mass one year ago with NHL-BFM-2012 and R-ICE. She had refractory disease, her family used alternative medicine, and applied to our center on 02.01.2019. A mass lesion that started from the level of the cricoid cartilage located on the left lateral of the neck and extended to the sternum, fistulized to the skin of 5 × 6 cm, pushed the trachea and esophagus to the right and caused obstruction in the trachea, and multiple lymph nodes adjacent to the lesion were detected. Histopathology was confirmed, 3 courses of IGEB-B (Rituximab, Ifosfamide, Gemcitabine, Vinorelbine, Prednisolone, Bortezomide) was given due to refractory disease, and progression was detected. Subsequently, PR was achieved with brentuximab. Nivolumab was administered to the patient with PD1, PDL1, after 6 doses partial remission was achieved, ACT was performed in March 2020, and the patient has been followed in full remission for 34 months.

**Results: Case 2:** The 8-year-old patient admitted with the diagnosis of EBV-associated Hodgkin lymphoma stage 4 developing based on immunodeficiency, was administered 6 CHOP, 12 rituximab, and 4 AVD, respectively, but no response was obtained. Pulmonary toxicity developed after the first dose of brentuximab. The patient showed resistance to the anticancer chemotherapies. PD1 negative and PDL-1 positive (90%) in the tumor tissue and nivolumab treatment was started. She

has been using nivolumab for 21 months, and achieved complete remission. **Case 3:** The patient with a diagnosis of multi-metastatic stage 4 HL had received 1 OEPA, 1 OPPA, AVD+Brentixumab, and 5 ICE, respectively. Brentixumab was discontinued because of pulmonary toxicity. As PD-1 negative and PD-1 >95 positive in the patient who was unresponsive to all these treatments, nivolumab treatment was started, remission was achieved.

**Conclusions:** In the current literature, PD-1 and PDL-1 positivity has been reported in adult lymphomas. This is rarer for childhood lymphomas. PD-1, PDL-1 can be studied especially in cases with refractory disease.

PO030 / #774 | Publication Topic: *AS05 SIOP Scientific Program / AS05.c Lymphomas*

### ANAPLASTIC LARGE CELL LYMPHOMA IN CHILDREN

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**Background and Aims: Introduction:** Anaplastic large cell lymphomas (ALCL) are aggressive T-cell neoplasms of variable clinical expression. They are more frequent in children but represent only 10 to 20 % of all non-Hodgkin's lymphoma. While histologic features of ALCL subtypes have significant overlap, the use of cytogenetics is of primary interest. The aim of our work is to describe the epidemiological, clinical, and evolutionary profile of these lymphomas.

**Methods: Patients and Methods:** This is a retrospective study carried out in the department of haematology and paediatric oncology of Casablanca, spread over a period of ten years (from January 2013 to January 2023), concerning children with ALCL whose diagnosis was based on immunohistochemical study. A pre-established exploitation form allowed the collection of data from the patients' files.

**Results: Results:** Ten cases were collected, with a median age of 11 years [4-18 years] and a M/F sex ratio of 1.5. The mean time to consultation was three months. Clinically, our cases presented at an advanced stage with polyadenopathy, and mainly extra-nodal involvement; visceral, bone, otorhinolaryngeal sphere and skin. All patients had CD30+, EMA+. Anatomical correlation revealed 80% of ALK positive and 20% of ALK negative. There were 40% of null phenotype and 60% of T phenotype. Most of our patients expressed markers of cytotoxicity, notably B granzymes. The ALCL99HR protocol was used in all patients. Evolution was favourable in seven patients with complete remission, failure was noted in one patient, death due to progression occurred in another and one patient was still receiving treatment.

**Conclusions: Conclusion:** ALCL is a rare T-cell lymphoma. It is most common in children, 90% of whom are ALK-positive; the prognosis is good, due to the use of immunotherapy. Clinical expression is heterogeneous; hence the delay in consultation. Cytogenetics can confirm the diagnosis by the presence of many anomalies; whereas it is not requested in our current practice.

PO031 / #25 | Publication Topic: *AS05 SIOP Scientific Program / AS05.c Lymphomas*

### THE SCOPE IMPACT OF PATIENT NAVIGATION IN FACILITATING ACCESS TO PRIMARY CARE IN ONCOLOGY FOR AGGRESSIVE LYMPHOCYTE PATIENTS IN WESTERN KENYA

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**Background and Aims:** NHL is the fifth most common cancer among both men and women, with a slight predominance in men, and represents approximately 5% of all childhood malignancies. This study aims to evaluate the scope impact of patient navigation in facilitating access to primary care for Burkitt's lymphoma patients in the western region belt in western Kenya.

**Methods:** This was a retrospective chart review that abstracted record data collected that included clinical data, diagnostic procedures as well as treatment outcomes, and effective training that covered the basic knowledge of Burkitt's lymphoma; medical terminology of Burkitt's lymphoma, predisposing risk factors, disease progression, prevention, treatment options, referral guidelines, communication skills, barriers in accessing services and primary care, and how to overcome barriers.

**Results:** Patient navigation interventions at healthcare facilities have shown that patients received primary care in a more reduced time compared to when the intervention was not available. The patient navigation intervention both at the community level, peripheral facilities, health care centers, and the mainstream facilities raised their index of suspicion i.e., an increase in knowledge level on Burkitt's lymphoma leading to more referrals and access to primary care.

**Conclusions:** Patient navigators including clinical and lay navigators are responsible for influencing members of the community to raise and increase their index of suspicion on Burkitt's lymphoma with the main effort to access primary care promptly as they provide emotional support, screening services, education, and navigation cares such as escorting, scheduling appointments and referring patients to specialists. The patient navigators have fostered rapport with the patient in a manner that is culturally acceptable to the community members. Moreover, there is a need to attach great importance to health-care professionals and researchers to have comprehensive sustainable training for patient navigators on patient-centered health education with a great emphasis on chronic illness education about Burkitt's lymphoma.

PO032 / #581 | Publication Topic: AS05 SIOP Scientific Program / AS05.c Lymphomas

### CLINICAL OUTCOMES AND LONG-TERM EFFECTS OF CONSOLIDATIVE RADIOTHERAPY IN PEDIATRIC HODGKIN'S LYMPHOMA: A SINGLE-CENTERED RETROSPECTIVE COHORT STUDY

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**Background and Aims:** There is a high disease burden of pediatric Hodgkin's lymphoma (PHL), especially in developing countries like Pakistan. Even with improved survival rates, chemotherapy, and radiotherapy-related complications significantly alter the quality of life of such patients. Our study, therefore, aims to delineate the long-term effects and disease outcomes of consolidative radiotherapy in pediatric Hodgkin's lymphoma.

**Methods:** This retrospective cohort study was conducted on PHL patients (below age 18) treated between January 2014 till January 2018. All patients with the presence of residual disease on interim PET scan received radiation doses of 35 and 21 fractions respectively. Data regarding patient demographics, disease characteristics, and treatment details were collected from the institutional database.

**Results:** Of the 91 patients, 73 (80.2%) were males and 18 (19.8%) were females. The overall mean age at presentation was  $7.7 \pm 3.3$  years. High-risk disease was found in 81 (89%) while 44 (48.4%) had Stage IV disease. Complete remission was achieved in 70 (76.9%), loss to follow-up in 11 (12.1%), disease progression/relapse in 4 (4.4%), and death during treatment in 6 (6.6%). The five-year overall survival was 90% and event-free survival was 76.9%. During treatment, a total of 9 patients had moderate-to-severe left ventricular dysfunction, 6 patients had altered thyroid profile (hypothyroidism), 3 developed pulmonary fibrosis, and 1 patient developed cerebellar ataxia.

**Conclusions:** Our analysis shows good 5-year overall and event-free survival. Cardiotoxicity, hypothyroidism, and pulmonary fibrosis were common long-term chemotherapy/radiotherapy-related side effects. A prospective randomized controlled trial is needed to reduce the dose of radiotherapy by giving it to PET-positive residual disease at end of treatment rather than at mid-assessment.

PO033 / #1035 | Publication Topic: AS05 SIOP Scientific Program / AS05.d Stem Cell Transplantation

### PREDICTING THE COST OF ALLOGENIC HEMATOPOIETIC STEM-CELL TRANSPLANTATION IN MOROCCO (CHILDREN HOSPITAL OF RABAT)

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**Background and Aims:** Hematopoietic stem-cell transplantation (HSCT) requires highly specialized, resource-intensive care. The number of HSCTs has increased constantly in the past 20 years, mainly due significant changes in the practice of HSCT. In Morocco, HSCT started in 2012 with 110 cases, there were no studies on the cost of transplantation. **Aims:** To estimate the costs associated with allogenic HSCT for aplastic anemia in Morocco.

**Methods:** We prospectively collected all in and outpatient costs (from transplant indication until six months post-graft) for patient with very severe idiopathic aplastic anemia, who has allogenic HSCT at the pediatric hematology and oncology center in the children's hospital of Rabat (Morocco).

**Results:** We identified a case of a 14-years-old boy with very severe idiopathic aplastic anemia, who has allogenic HSCT. Data of cost are including pre-transplant evaluation, inpatient HSCT and post-transplant follow-up. Based on this work, the estimated cost of allogenic HSCT was \$66,486 (689 695 MAD). A greater cost burden was associated with inpatient services for higher-intensity preparative conditioning regimens (78%). The cost of HSCT is very variable, it changes mainly according to the type of hemopathy, the conditioning regimen used, the transplant type and especially the different complications presented by the patient in post-graft study period.

**Conclusions:** Allogenic HSCT is one of the most expensive treatments in the world; nevertheless this is due to the complexity of the technique, the need for a multidisciplinary team, the skills, and the medical and paramedical expertise necessary for its realization and its success.

PO034 / #1523 | Publication Topic: AS05 SIOP Scientific Program / AS05.d Stem Cell Transplantation

### HEMATOPOIETIC STEM CELL TRANSPLANT IN LOW AND MIDDLE INCOME COUNTRIES WITH FOCUS ON HAPLOIDENTICAL TRANSPLANTATION

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**Background and Aims:** The implementation of transplant in low and middle income countries is a challenge due to the problems of premises, human resources and the difficulty of access to drugs for

transplant. The choice of donor is most often made towards genoidentical transplant, because of the absence of a file bank and placental cord blood. Haploidentical transplant with post-transplant cyclophosphamide remains a solution in the absence of a geno-identical donor, but is much more difficult to implement in our conditions. The Rabat center and our hematopoietic stem cell transplantation unit are supported by the GFAOP and uses the therapeutic protocols of this group.

**Methods:** To report the experience of the Pediatric Hematology and Oncology Center (CHOP) of the Rabat Children's Hospital (HER) in hematopoietic stem cell transplant (HSCT) by focusing on the first case of haploidentical transplantation in Morocco.

**Results:** A total of 12 allogeneic hematopoietic stem cell transplantation (HSCT) were performed at the pediatric hematology and oncology center of the children's hospital of Rabat (Morocco) between 2018 and 2022. These are 3 cases of severe congenital immune deficiency (SCID), 2 cases of leukemia, 6 cases of aplastic anemia and one case of Fanconi anemia. The haploidentical transplant was performed in an 18-month-old child with SCID T-B+NK- type with mutation in the gene *Jak3*. This is the first experience of this type of transplant in Morocco. In our context, this protocol becomes the only choice for transplanting children with SCID who do not have a geno-identical donor and possibly other types of primary immunodeficiency. This allows us to offer an immediate donor for all patients who have an indication for HSCT.

**Conclusions:** This technique appears to be simple and widely applicable and avoids the high cost of other procedures, including searching for potential donors on file, obtaining the graft and depleting the T graft.

PO035 / #1069 | Publication Topic: AS05 SIOP Scientific Program / AS05.d Stem Cell Transplantation

#### EXPERIENCE IN ALLOGENEIC HEMATOPOIETIC STEM CELLS TRANSPLANTATION FOR THE TREATMENT OF SEVERE COMBINED IMMUNODEFICIENCY (OMENN SYNDROME) COMPLICATED BY CYTOMEGALOVIRUS INFECTION

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**Background and Aims:** Omenn syndrome (OS) is a variant of severe combined immunodeficiency caused by mutations in RAG genes. Nowadays, hematopoietic stem cell transplantation (HSCT) is the unique curative treatment available.

**Methods:** A 7-month-old female patient with OS (mutation RAG1 was genetically confirmed) received treatment at the Belarusian Research

Center for Pediatric Oncology, Hematology, and Immunology, where she underwent cytomegalovirus (CMV) infection treatment and further allogeneic HSCT from HLA-compatible (10/10) senior sibling.

**Results:** The patient was born prematurely (35 weeks of gestation, weight 2 kg) with a violation of the pace of motor development due to encephalopathy of prematurity of mixed genesis and congenital CMV infection. Before transplantation, the child received treatment for generalized CMV infection (the number of copies of the virus in the peripheral blood exceeded  $1 \times 10^6$ ), including CMV encephalitis, hepatitis, pulmonitis, and received therapy with ganciclovir, neocytotect, cidofovir. Given the primary diagnosis, positive dynamics in CMV status, febrile fever episodes, and refractory to antipyretics (NSAIDs), and to prepare for subsequent HSCT, a course of immunosuppressive therapy with cyclosporine was performed. In preparation for HSCT and treatment of CMV infection, donor lymphocyte infusions (DLI) were performed twice (donor CMV IgG-positive). After allogeneic-related bone marrow HSCT and despite the prevention of "graft-versus-host" disease (GVHD) in the early post-transplant period, the patient developed engraftment syndrome (enterocolitis, hepatitis, dermatitis) and acute GVHD grade 1 (skin stage 1-2). Transplantation of mesenchymal stem cells from the same donor was performed to resolve GVHD. In the post-transplant period, CMV reactivation, enterocolitis of mixed etiology, chronic liver GVHD, and bilateral focal pneumonia of fungal etiology were observed.

**Conclusions:** Currently (day +480), the patient demonstrates stable 100% donor chimerism. There is a restoration of T- and B-lymphocytes to normal values, and a gradual resolution of CMV infection and liver GVHD, which indicates the effectiveness of HSCT approach for OS treatment.

PO036 / #533 | Publication Topic: AS05 SIOP Scientific Program / AS05.d Stem Cell Transplantation

#### HAPLOIDENTICAL HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR RELAPSED ACUTE LYMPHOBLASTIC LEUKEMIA IN CHILDREN TREATED IN URUGUAY

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**Background and Aims:** Background: The prognosis of relapsed Acute Lymphoblastic Leukemia (ALL) remains poor due to resistance to chemotherapy agents. This study evaluate the efficacy and feasibility of Haploidentical Hematopoietic Cell Transplantation (Haplo HSCT) for pediatric relapsed ALL.

**Methods:** 41 patients with relapsed ALL, 14 underwent Haplo HSCT between 2010 and 2021 at the Hospital Pereira Rossell (Montevideo-Uruguay). All patients were transplanted in Complete Remission (CR) following different protocols, only 3 had positive MRD(0.1%,0.6%,1.9%). Conditioning regimens employed were TBI based in 11 patients. Graft versus host disease (GVHD) prophylaxis was administered with cyclosporine and methotrexate.

**Results:** 8 patients received peripheral blood and 6 received bone marrow as the stem cell source. Among 14 patients who achieved engraftment, acute GVHD occurred in 8 patients. (GI6, GII4, GIII1, GIV 1, skin was the most common organ involved) and chronic GVHD was observed in 6 (GI 2, GII 2, GIII 2, GIV 2 Skin was involved in the majority of cases and severe cases were because of the Lung). The 5 year overall survival (OS) was 33% and 32% and leukemia free survival rates were 20% and 16% in patients without transplant.

**Conclusions:** This abstract shows the feasibility of performing haplo in LAL realpsed with TBI an CFM post infusion in a small center.

PO037 / #141 | Publication Topic: AS05 SIOP Scientific Program / AS05.d Stem Cell Transplantation

#### CLINICAL IMPACT OF THE BLOOD BANK ON THE MANIPULATION OF HEMATOPOIETIC PROGENITOR CELLS IN TRANSPLANTATION PROGRAM OF THE TELETON ONCOLOGY CHILDREN'S HOSPITAL

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**Background and Aims:** Stem Cell Transplantation (SCT), therapeutic option for malignant and benign diseases, only 20–25% of patients have a match sibling donor, then, unrelated or haploidentical donor should be considered. Several, donor and patient factors, can influence blood engraftment, immune reconstitution, and blood component required. Harvest Manipulation (HM) is performed in some cases: ABO Incompatibility: erythrocyte depletion and desplasmatization Autologous and Unrelated donor Cryopreservation Using DMSO 2.5% : Results of intervention and source manipulation in relation to bone marrow transplantation in Mexico are not known, The aim of study is to evaluate the role of procedures performed in blood banks., evaluating clinical impact on grafting time, as well as the decrease in the cell count and cell viability due to quality and standardization of the procedures.

**Methods:** Cohort Study: Prospective, Observational, Analytical. Carried out in the blood bank and SCT Program in Teletón Children's Oncology Hospital : Two groups were divided by challenge-solution 1.- ABO incompatibility: erythrocyte depletion and desplasmatization 2.- Cryopreservation need. Autologous and Unrelated donor Cultures for contamination / Total nucleated (TNC) / Mononuclear Cell (MNC) / CD34+ / Viability were performed before and after manipulation, also hematocrit for erythrocyte depletion and DMSO dose for autologous

**Results:** The HM events were: Fifty procedures: 52.5 % bone marrow, 47.5% peripheral blood. A.- cryopreservation 54%, erythrodepletion in 24%, desplasmatization in 22% . The processing with the greatest decrease in cell count was with desplasmatization. The median myeloid engraftment recorded in the manipulated harvests was 13.1 days. Complications due (DMSO): pulmonary 62.5% . No intensive care contamination after handling was recorded in 2% of cases

**Conclusions:** Harvest Manipulation is safe No contamination Loss of Cell count 20% above comparing other groups No graft failure.

PO038 / #403 | Publication Topic: AS05 SIOP Scientific Program / AS05.d Stem Cell Transplantation

#### ALLOGENEIC BONE MARROW TRANSPLANTATION AS CONSOLIDATION THERAPY FOR MEXICAN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA WITH EARLY RELAPSE

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**Background and Aims:** Acute lymphoblastic leukemia (ALL) it's a curable disease in more than 90% of cases in developed countries, however in Mexico a high percentage of children with ALL have high-risk relapses and the prognosis is less than 16% with conventional treatments only with chemotherapy, the objective of the present was to determine the survival of this patients treated with bone marrow transplant.

**Methods:** An observational, analytical and retrospective study for patients from 0 to 19 years old who had received hematopoietic progenitor cell transplantation with a diagnosis of "ALL" and high-risk relapse were included. They received an allogeneic transplant with conditioning based on TBI / CFM / VP16: With SPSS version 25, descriptive statistics were obtained. A Kolmogórov-Smirnov test used to fit a normal distribution. Of the qualitative variables, absolute frequencies and percentages were obtained. Survival curves were performed using the Kaplan Meier method and the risk factors will be evaluated using the log-Rank method.

**Results:** A total of 47 patients were included, male: female ratio 3: 1, minimum age 3 years, maximum of 19 years old, in 47% the transplant was performed after the first relapse, in 89% the leukemias were precursors B. The overall survival was 79 and the event-free survival was 71 with a 5-year follow-up, among the variables that were analyzed

as: Initial risk assigned (0.112), Hypodiploidy (0.133), Development of EICHa (0.242), ALL Ph + (0.312), Year in which the TCPH was carried out (0.348), source cell (0.570), Remission number (0.598), CNS + (0.694), 100% compatibility (0.738), Immunophenotype of ALL at Dx (0.825), Relapse rate (0.911). No statistical significance was found.

**Conclusions:** The survival of children with high-risk relapse ALL in the study was 71% at 5 years compared with the survival of less than 16% of children who received 2nd-line chemotherapy treatment reported by other groups in Mexico.

PO039 / #1365 | Publication Topic: AS05 SIOP Scientific Program / AS05.e Neuroblastoma

### MULTIFOCAL PRIMARY NEUROBLASTOMA-CASE REPORT AND REVIEW OF LITERATURE

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**Background and Aims:** Neuroblastoma, the most common extracranial solid tumours of childhood, has a varied spectrum from low-risk focal tumours to metastatic aggressive poorly differentiated tumours. Multifocal tumours are rare and can often confuse the risk stratification if they are synchronous.

**Methods:** Retrospective review of case study

**Results:** Miss. D, 2year old girl, presented with abdominal mass of 3 weeks duration without any hematuria or constitutional symptoms.

Investigations revealed normal complete blood counts, liver and renal functions; elevated urinary VMA(218mg/L), normal Serum ferritin and LDH, AFP and B-HCG levels.

PET-CT showed mass arising from upper pole of left kidney with local extensions/mass effect and a pleural based nodule in left lower hemithorax with FDG-avid lymph node in right para-aortic region (Fig-1). Trucut biopsy from abdomen and thoracic lesion showed ganglioneuroblastoma maturing type with Ki-6%. N-MYC was not amplified and bone marrow was not infiltrated.

Though her age and metastatic lesion favoured a high risk, histopathology and N-MYC were pointing against. She was started on neoadjuvant chemotherapy and reassessed after 2 cycles; no interval change in size of lesion was noted. Hence, after a detailed multidisciplinary discussion, surgical excision was performed. Intraoperatively three separate masses were found; one in left suprarenal area necessitating partial nephrectomy and DJ stent, one paracaval mass encasing inferior mesenteric artery excised completely and one in thorax with small intraspinal extension at D6 level was excised 95%. Postopera-

tive histopathology confirmed ganglioneuroblastoma and there were no segmental chromosomal anomalies. She received 2 cycles of adjuvant chemotherapy and is doing well for last 8-months on follow-up.

**Conclusions:** Multifocal neuroblastomas are rare and carry favorable biologic features; hence Surgery remains mainstay of treatment. Genetics studies might be warranted to look for syndromic association; presence of a PHOX2B deletion and NF1 mutation has been associated with familial predisposition.

PO040 / #62 | Publication Topic: AS05 SIOP Scientific Program / AS05.e Neuroblastoma

### ISOLATED LEPTOMENINGEAL RECURRENCE IN NEUROBLASTOMA IV: CASE REPORT

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**Background and Aims:** CNS recurrence in neuroblastoma is rare, with an incidence of 2 to 5% and very low survival. Intracranial mass or leptomeningeal involvement with neoplastic cells in the cerebrospinal fluid or anatomopathological are the presentations. There are no reports of isolated recurrence in leptomeninges. We report a case of a patient with late isolated recurrence in the leptomeninges without presence of intracranial mass or bone involvement, treated with radiotherapy and dinutuximabe.

**Methods:** Patient chart, laboratory tests and images were reviewed, paraffin blocks and slides were stained with H&E and immunohistochemistry was performed.

**Results:** 13-year-old female patient, who was off treatment for Neuroblastoma IV, presented vomiting and headache for 2 weeks associated with slowed speech and seizure. Magnetic resonance imaging of the skull and neuroaxis showed diffuse and regular leptomeningeal thickening and cerebrospinal fluid with the presence of proteinorrachia and 4% of neoplastic cells. Myelogram and bone marrow biopsy with no evidence of disease and bone scan with MIBG showing uptake in leptomeninges. The patient had as a past medical history of Neuroblastoma IV paravertebral and bone marrow, underwent chemotherapy, autologous bone marrow transplant, isotretinoin, radiotherapy in paravertebral lesion and resection of residual mass. She had been off treatment for 2 years and 7 months. It was decided to perform radiotherapy to the skull and neuroaxis, followed by dinutuximabe. At the last assessment, 1,5 years after the diagnosis of recurrence, asymptomatic patient with no uptake by MIBG on scintigraphy.

**Conclusions:** CNS recurrence is usually early and presents with neurological symptoms. Magnetic resonance imaging is highly sensitive, and MIBG scintigraphy is highly specific for the diagnosis of Neuroblastoma. Standard treatment consists of cranial and channel radiotherapy, chemotherapy, and immunotherapy.

PO041 / #299 | Publication Topic: AS05 SIOP Scientific Program / AS05.e Neuroblastoma

### MUC16 GENE MUTATION AND RECURRENCE OF HIGH-RISK NEUROBLASTOMA : A CASE REPORT

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**Background and Aims:** MUC16基因是粘蛋白基因家族的一员,参与肿瘤复发。本研究的目的是研究 MUC16 遗传表型特征与复发性高危神经母细胞瘤 (NB) 患儿的病例特征和预后之间的相关性。

**Methods:** A retrospective analysis of the whole genome exon analysis and clinical data was performed on the tumor tissue samples and cDNA samples extracted from peripheral blood of a child with recurrent high-risk NB.

**Results:** The boy was 4 years old and 2 months old. The onset of the disease was "pain in the right chest wall", which was originally caused by "right peritoneum involving the right posterior lower mediastinum", with lymph node metastasis, and was diagnosed as a high-risk group of stage 4. After surgery, 6 cycles of chemotherapy, radiotherapy, and 4 cycles of 3F-8 immunotherapy, the children obtained CR. At the beginning of the disease, N-MYC gene was not amplified. The patient came to the hospital for treatment because of multiple metastasis and recurrence of right chest wall soft tissue, local lymph nodes and neck lymph nodes 6 months after stopping treatment. The whole genome exon sequencing of cDNA from tumor tissue and peripheral blood showed that there was a mutation in the promoter region of MUC16 gene in children: c.38864 (exon36) - c.38865 (exon36) del AA ins CT; c.13132(xeon3)A>G. The HLA typing of the children was HLA-A/B/C heterozygous. Tumor tissue samples also showed that there were site mutations in ARIDB and SMARCA4 genes in the regulatory pathway of SWI/SNF chromatin remodeling complex: (1) ARIDIB genes: c.1351 (exon1) T>G, c.644 (exon1) T>G, c.986 (exon1) C>G; (2) SMARCA4 gene: c.2779 (exon20) C>T. After recurrence, 4 cycles of chemotherapy suggested that the child obtained PR.

**Conclusions:** MUC16 gene mutation may be involved in the mutation of children, while SWI/SNF chromatin remodeling complex regulatory genes ARIDB and SMARCA4 may be involved in the occurrence of tumor proliferation and immune escape.

PO042 / #1683 | Publication Topic: AS05 SIOP Scientific Program / AS05.e Neuroblastoma

### MANAGEMENT OF LOCALIZED NEUROBLASTOMA :EXPERIENCE OF THE PEDIATRIC ONCOLOGY DEPARTMENT IN CASABLANCA

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**Background and Aims:** Neuroblastoma is the most common extracranial solid tumor in children.It results from neural crest stem cells.The aim of our study is to show the importance of local treatment in localized neuroblastoma.

**Methods:** This is a Retrospective study of localized Neuroblastoma at the pediatric oncology department In August 20th Hospital-Casablanca,from January 2014 to March 2018.The diagnosis was based on CT,anatomopathologic study,urinary catecholamines dosage and MIBG scintigraphy.

**Results:** We found 11/41 of localized cases which is 27% of global series of Neuroblastoma.The median age was 01year[38 days-3.5 years].Sex ratio(F/M)was1.2.The average consultation time was 02 months[3days-6months]. The site of primary tumor was abdominopelvic in 09cases which 07 surrenal and 04 median, thoracic and intramedullary in 1 patient respectively.Spinal cord compression,dysuria,isolated fever were respectively inaugural in 1 case. The diagnosis of Neuroblastoma was guided by CT-SCAN and elevated urinary catecholamines.The MIBG scintigraphy was performed in 02 patients showing fixation. Histological confirmation was performed in 06 patients showing favorable histology in 5cases. 3 patients had a first surgery with complete tumor removal and did not require adjuvant chemotherapy. Preoperative chemotherapy was administered in 08cases including standard-risk neuroblastoma protocol(carbo-VP16, CADO)with an average of 4 cures[3-6]. This chemotherapy allowed tumor reduction in 6 cases. One patient died due to sepsis.After chemotherapy,complete resection was performed in 04 patients showing favorable histology in 03cases.Post-operative chemotherapy was administered in 04 cases. 03 patients,in whom surgery was not possible or complete,received radiotherapy. Overall survival at 5 years was 73% of which 87.5% were in complete remission.

**Conclusions:** Neoadjuvant chemotherapy in neuroblastoma makes the tumor totally resectable and thus control the disease.

PO043 / #1297 | Publication Topic: AS05 SIOP Scientific Program / AS05.e Neuroblastoma

### PRIMARY OCULAR NEUROBLASTOMA: A RARE PRESENTATION

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**Background and Aims:** Neuroblastoma is one of the commonest paediatric malignancy. Most common primary sites being abdominal, pelvic, thoracic and cervical locations. Although orbital metastases are common in neuroblastoma, primary ocular neuroblastoma



is an uncommon entity. We describe a case of primary ocular neuroblastoma.

**Methods:** A 3 year old girl child presented with history of left eye swelling since one month with associated fevers. On examination, child had a unilateral periorbital swelling and ecchymosis with ptosis. general examination showed no hepato-splenomegaly with only multiple cervical lymphanodes palpable. Routine blood tests were suggestive of slightly low haemoglobin with normal white cell count and platelets. PET CT was was suggestive of metabolically active permeative bony lesion of left frontal bone with associated infiltration of left supraorbital margin, superior rectus muscle resulting in proptosis.

**Results:** It was a localised with no disease elsewhere. A differential diagnosis of rhabdomyosarcoma was thought of. As routine workup in all pediatric solid tumors, bilateral bone marrow studies was performed, showing small round blue cells, confirming neuroblastoma. MYCN was non amplified. The child recieved 8 cycles of RAPID COJEC, followed by 1 cycle of TVD as unilateral marrow was still positive for metastasis. She is now being worked up for a Haploidentical stem cell transplant (HSCT) for possible GVL effect.

**Conclusions:** Orbital tumors in children are rare and present with unspecified symptoms like proptosis, diplopia not well described by children themselves. Benign causes include congenital cysts, hemangiomas etc. Rhabdomyosarcoma is commonest primary orbital and retinoblastoma, intraocular malignancy. It is vital to recognize the signs and symptoms of pediatric ocular tumors so that prompt ophthalmologic evaluation can preserve vision and in case of malignancy, can prove life saving. We wish to highlight the importance of bilateral bone marrow studies in solid tumors as in this case, it detected marrow metastasis of neuroblastoma (PET negative).

PO044 / #1649 | **Publication Topic:** AS05 SIOP Scientific Program / AS05.e Neuroblastoma

#### CHARACTERIZATION OF ONSET AND RESOLUTION OF ADVERSE EVENTS IN PATIENTS TREATED WITH NAXITAMAB IN TRIAL 201

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Medicine, Mainz, Germany, <sup>7</sup>Riley Hospital for Children, Pediatric Hematology-oncology, Indianapolis, United States of America, <sup>8</sup>Hospital Infantil Universitario Niño Jesus, Department Of Pediatric Hemato-oncology, Madrid, Spain, <sup>9</sup>Memorial Sloan Kettering Cancer Center, Pediatric Oncology, New York, United States of America, <sup>10</sup>Y-mAbs Therapeutics, Medical Affairs, Horsholm, Denmark

**Background and Aims:** Several anti-GD2 monoclonal antibodies are used for high-risk neuroblastoma (HR-NB), each with unique administration rates, various onsets and resolution of adverse events (AEs). Ongoing Trial 201 (phase II, NCT03363373) evaluates naxitamab with granulocyte-macrophage colony-stimulating factor (GM-CSF) to treat patients with refractory/relapsed HR-NB in bone and/or bone marrow. We report Grade 3/4 (G3/4) infusion-related reactions (IRRs) incidence, median time to onset (mTTO) and duration (mD) to help clinicians with patient care.

**Methods:** Naxitamab was administered at 3mg/kg/dose (~90mg/m<sup>2</sup>/dose) intravenously over 30–60mins on Days 1/3/5 with GM-CSF subcutaneously on Days -4 to 5. IRRs were defined as AEs related to naxitamab occurring on a naxitamab infusion day. Duration of IRRs was calculated from IRR onset to IRR resolution, regardless of IRR grade. Time to onset was calculated from start of naxitamab infusion. IRR severity was graded according to CTCAE version 4.0 and assessed as related or unrelated to naxitamab. If IRR severity varied, the most severe grading was assigned. IRRs of pain were IRRs reported with preferred terms including the word "pain", excluding pain from procedures or vessel puncture.

**Results:** At pre-planned interim analysis (data cut-off 31-Dec-2021), 57/74 (77%) patients experienced G3/4 IRRs; only 0.8% IRRs were grade 4. Incidence, mTTO, and mD for G3/4 IRRs occurring in ≥10% of patients were as follows: hypotension incidence = 60%, mTTO = 23min (range:0-223min), mD = 23min (range:0-31days); pain incidence = 58%, mTTO = 12min (range:0-132min), mD = 58min (range:0-6 days); urticaria incidence = 19%, mTTO = 12min (range:6-117min), mD = 23min (range:0-4days); bronchospasm incidence = 18%, mTTO = 27min (range:8-89min), mD = 5min (range:0-11hrs).

**Conclusions:** Naxitamab-related IRRs of hypotension, pain, urticaria and bronchospasm with worst severity of G3/4 generally started within 30 minutes of infusion initiation. These G3/4 IRRs were generally manageable with most resolving within one hour of onset.

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PO045 / #1684 | **Publication Topic:** AS05 SIOP Scientific Program / AS05.e Neuroblastoma

#### NAXITAMAB FOR REFRACTORY OSTEOMEDULAR NEUROBLASTOMA. DEVELOPMENT OF A REFERENCE CENTER AND CLINICAL CASE IN MEXICO

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**Background and Aims:** Neuroblastoma is ninth cause of cancer in Mexico. Incidence 2.3/million Osteomedular refractory neuroblastoma is rare disease Therapy with antibodies are not available due to government regulations Naxitamab (Danyelza®) in osteomedular refractory neuroblastoma is option treatment.

**Methods:** Clinical case Female 5 y/o: Abdominal mass and pain. ultrasound was performed: retroperitoneal and pancreas mass. DOPA PET multiple lesions in humerus, femur, pelvis and temporal skull was reported, . Urine catecholamines elevated . Initial primary tumor was done and bone marrow (BM) biopsy 90% infiltration: Pathology report: NEUROBLASTOMA. Poorly differentiated, with N MYC amplification positive, intermediate karyorrhexis mitosis index, with unfavorable histopathology. KI67 positive in 60%, ALK and neurofilament positive in neoplastic cells.High Risk group was assigned CHILDREN'S ONCOLOGY GROUP ANBL12P1 protocol began and macroscopic complete resection (primary tumor) performed at surgery time Evaluation prior to tandem stem cell transplantation was done. BM 5% undifferentiated and lesions at pelvis, femur, humerus and skull still persist. Second line began with Ifosfamide, carboplatin and etoposide. Hematologic toxicity and after 2 cycles nort response. At the same time: Naxitamab Danyelza® (Ymab) arrived to Hospital. Training for nurses, Intensive care phisicyans and pharmacists was done. Protocol for administration was designed. HITS Therapy: Irinotecan 50 mg/m<sup>2</sup>/d Day1-5 Temozolomide 150 mg/m<sup>2</sup>/d . Naxitamab 2,25 mg/kg IV day 2, 4, 8 y 10. GM-CSF 250 mcg/m<sup>2</sup>/día days 6–10

**Results:** 4 cycles of HITS were applied after 2 cycles BM biopsy no infiltration PET- DOPA only pelvis and skull persist 2 cycles more: complete response Secondary effects: cycle 1 .- hipertension, diaphoresis, pain, broncoespaism and subcutaneous nodules cycle 2.- diaphoresis and subcutaneous nodules cycle 3 and 4 .- diphoresis and pain

**Conclusions:** Naxitamab administration is feasible in Low and middle income countries Government Regulation are a limitation for administration Requirements are necessary to complete as infusion center: Hospital Pharmacy, Personnel Training, Protocol for administration.

PO046 / #1865 | Publication Topic: AS05 SIOP Scientific Program / AS05.f Renal Tumours

### UNCOMMON PRESENTATION OF WILM'S TUMOUR, A CASE SERIES REPORT AT THE PAEDIATRIC ONCOLOGY UNIT, KORLE-BU TEACHING HOSPITAL

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**Background and Aims:** BACKGROUND Wilms tumor (WT), the commonest pediatric renal neoplasms with majority being unilateral, but 6% have bilateral Wilm's tumour(BWT). (1) The survival rate of WT in high income countries (HICs) is about 90% with a recurrence of 15%; lung lesions as the commonest site.(4) The risk of relapse is dependent on an interplay of factors : age, stage and histology type of disease.(5) AIM 1. To identify the risk factors associated with disease relapse in patients with WT at POU, KBTH. 2. To identify predisposing factors to rare presentation of patients with WT at POU, KBTH.

**Methods:** METHODS Patients folders were audited and assessed clinical presentation, radiological imaging, pre and post-operative chemotherapy, surgical and pathological staging, radiotherapy and the time taken for disease relapse. A case series of 3 cases, a BWT, relapsed hepatic WT and brain metastasis.

**Results:** Case 1 : The prevalence of BWT is higher in children with genetic syndromes-WAGR, Beckwith Wiedemann, no features suggestive of overgrowth syndrome in child. Child had histological mixed type of tumour, partial nephrectomy and on 4drug regimen for 34weeks. Case 2 : Child more than 4 years old and had relapse within 5years post treatment.(9)(10) and given a second line therapy with radiotherapy. Case 3 : Brain metastases rare in Wilm's tumour, 1% of cases(11) and associated with prior lung lesions. Child had cranio-spinal radiotherapy and chemotherapy, but unfortunately did not survive.

**Conclusions:** A wholistic approach in WT results in a high overall survival rates in children (90%). Some patients with BWT, advanced stage, anaplastic histological type and genetic aberration have increased risk of uncommon presentations. There should be a global synchrony of definitions, radiological, pathological diagnosis and therapy aimed at cure and improvemet of the quality of life.

PO047 / #703 | Publication Topic: AS05 SIOP Scientific Program / AS05.f Renal Tumours

### HEPATOPATHY-THROMBOCYTOPENIA SYNDROME AFTER ACTINOMYCIN D TREATMENT IN CHILDREN WITH WILMS TUMOR, A SINGLE INSTITUTION EXPERIENCE

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**Background and Aims:** Actinomycin D is a chemotherapy drug that is commonly used in the treatment of Wilms tumor (WT). However, one of the potential side effects of actinomycin D is hepatopathy-thrombocytopenia syndrome (HTS), which is a rare but life-threatening complication that characterized by liver dysfunction, thrombocytopenia, and coagulopathy. While the survival rates of children with localized Wilms tumor are favorable, it is important to be aware of the potential complications associated with treatment, including HTS.

**Methods:** A retrospective, observational study of WT was conducted from 2001 to 2021 at a tertiary care setting in central Taiwan. The records were reviewed for age at diagnosis, sex, stages, agents of chemotherapy, type of surgery, tumor characteristics, postoperative treatment, treatment complications and outcome.

**Results:** During the study period, 23 children with previously untreated WT were registered at our center were included. The median age was 3 years (1–11 years) with a male predominance (Male: Female ratio of 1.3:1). The most common stage was Stage II (9/23, 39.1%), followed by Stage I (7/23, 30.4%), Stage III (5/23, 21.7%), Stage IV (1/23, 4.3%) and Stage V (1/23, 4.3%). Two stage III patients developed HTS during the courses of treatment, which presented with fever, markedly elevated liver function enzymes, hepatomegaly, thrombocytopenia and coagulopathy. Both patients recovered after receiving intensive care and were able to continue with their treatment.

**Conclusions:** In spite of the good prognosis of WT in children, we should be aware of the treatment associated complications in the management of WT.

PO048 / #1673 | Publication Topic: AS05 SIOP Scientific Program / AS05.f Renal Tumours

#### CLINICAL FEATURES AND OUTCOMES OF WILMS TUMOUR IN CHILDREN WITH WAGR SPECTRUM DISORDER IN RUSSIA

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**Background and Aims:** Wilms tumour (WT) is the most common childhood kidney cancer. In up to fifteen percent of cases, WT appears as a part of a predisposition syndrome, including WAGR, Beckwith-Wiedemann and Denys-Drash syndrome. WAGR syndrome is a rare genetic disorder characterized by a deletion of 11p13 and is clinically associated with WT (in fifty percent of children), aniridia, genitourinary anomalies, and intellectual disability. In the present study, we collected data from thirteen cases of WT associated with WAGR enrolled in the registry to explore the clinical characteristics and treatment outcomes.

**Methods:** We analyzed thirteen patients with WAGR syndrome and WT from International Society of Patients with Aniridia in Russia. Clinical characteristics and outcomes were evaluated in our study.

**Results:** The median age at WT diagnosis was 15 months (3-29 months). Five (38,5%) patients had bilateral disease and one (7,7%)

had metastatic disease. Two out of the five patients with bilateral WT had nephroblastomatosis in contralateral kidney. Histology was mentioned in 11 patients: stromal in six cases (55%), three mixed WT (27%), blastemal type in one case (9%) and one tumour with indeterminable type (9%). Anaplasia type was not presented. Two patients (18%) had nephrogenic rests in the kidneys. Despite a large spread of time to follow-up (8-216 months), no deaths or relapses observed.

**Conclusions:** Patients with WAGR spectrum disorder have a high risk (50%) of developing WT. Metastatic disease and relapses are rare in this group of patients. Because of the high risk of toxicity and chronic kidney disease, patients with WT and WAGR syndrome need to be treated by multidisciplinary team and closely monitor the renal function.

PO049 / #1028 | Publication Topic: AS05 SIOP Scientific Program / AS05.f Renal Tumours

#### TREATMENT OUTCOME OF WILMS TUMOUR IN CHILDREN IN BANGLADESH

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**Background and Aims:** Wilms' tumor is the most common malignant kidney tumor in children. The histopathology subtype of the tumor is the most important factor in determining the prognosis. However, the outcome of treatment is still poor in many developing countries. The aim of this study was to determine the outcome of children with Wilms' tumor in our hospitals over a period of 12 years.

**Methods:** This is a prospective study and the target population included childrens (upto eighteen years) with Wilms' tumor admitted in Dhaka Medical College Hospital and Dr. Azmol Hospital Limited from January, 2009 to December, 2022 and were treated according to the International Society of Pediatric Oncology (SIOP) protocol. Diagnosis was based on clinical, radiologic, surgical, histologic findings and confirmed by histological evaluation of the resected specimen. Data on age at presentation, sex, clinical features, investigations, findings at operation, other modalities of treatment applied, complications of treatment, outcome, duration of follow up and difficulties encountered in the management were obtained. Overall survival and event-free survival (EFS) were analyzed by the Kaplan Mayer method in the SPSS software, version 23.

**Results:** One hundred and fifty children with Wilms tumor with female preponderance and left laterality were most common. The mean age of children with this tumor was 30 months. The most common stage among boys and girls was stage III. The most common presenting features was mass in the abdomen. Four cases were bilateral and rest were unilateral. Fifteen children died of complications of treatment, while ten relapsed with poor outcome. Our findings revealed that the overall five-year survival of patients was 78%.

**Conclusions:** The outcome of Wilms tumor in children has improved dramatically due to the improvement of therapeutic strategies,

multidisciplinary team approach, reduction of refusal and abandonment of treatment.

PO050 / #1178 | Publication Topic: AS05 SIOP Scientific Program / AS05.f Renal Tumours

### EWING RENAL SARCOMA: A ANALYSIS OF REGISTERED CASES IN THE BRAZILIAN RENAL TUMORS GROUP

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**Background and Aims:** Ewing's sarcoma of kidney (ESK) is a rare primary renal tumor in the pediatric population, with few cases being documented. This type of cancer generally presents with aggressive behavior and rapid growth, as well as non-specific clinical presentation, making it necessary to distinguish from other small round blue cells renal tumors.

**Methods:** Between July 2019 and January 2023, three cases were registered by the Brazilian Renal Tumors Group in the UMBRELLA-RTSG-SIOP 2.016. A retrospective analysis of clinical, radiological and anatomopathological characteristics was performed.

**Results:** ESK represented 0.6% of the cases registered in the Brazilian Renal Tumors Group. The patients were between 8 and 15 years old, being two males and one female. None of them were metastatic at diagnosis. Family history was negative for renal tumors or congenital anomalies. One patient presented with asymptomatic abdominal mass and two had abdominal pain. Other signs and symptoms described among the patients were vomiting, hematuria and hypertension. The first patient underwent needle biopsy before starting chemotherapy treatment for ESK, the second was submitted to primary nephrectomy and the third received preoperative chemotherapy with dactinomycin and vincristine for four weeks with posterior nephrectomy. Tumoral volume ranged between 297 and 426 cm<sup>3</sup>. Immunohistochemical markers in common were positive CD99 and negative WT1. All patients were positive for the EWSR1-FLI1 fusion.

**Conclusions:** The histological and molecular confirmation is essential to a accurate diagnosis of ESK, avoiding delays in proper treatment. Due to the differential diagnosis of renal tumors, the development of strategies to better determine identification ESK are extremely important. The patient registration in collaborative groups, such as the Brazilian Renal Tumors Group contributes to improve knowledge of rare renal tumors.

PO051 / #1352 | Publication Topic: AS05 SIOP Scientific Program / AS05.f Renal Tumours

### BILATERAL RENAL MUCINOUS TUBULAR AND SPINDLE CELL CARCINOMA (MTSCC)- AN EXTREME RARE OCCURRENCE IN CHILDREN

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**Background and Aims: Introduction** Mucinous tubular and spindle cell carcinoma of kidney (MTSCC) is extremely rare entity in children. Management of these tumors involve complex issues. Herein, we present a rare case with bilateral renal involvement who later developed progressive disease (bilateral lung, liver and bony metastases).

**Methods: Methods** A thirteen-year-old boy presented to us with episodes of hematuria and bilateral dull-aching flank pain for last 9 months. On examination, there is presence of a large, 10 × 10 cm sized, firm mass occupying the right lumbar and right hypochondrium regions with extension beyond the midline. Contrast enhanced computed tomography (CECT) scan of abdomen confirmed the presence of a large heterogeneous mass arising from right kidney with areas of calcification and displacement of inferior vena cava (IVC) to the left. Similar masses were seen involving the left kidney. Core biopsy of the right sided tumor was consistent with features of MTSCC. Intra-operatively, large 13 × 11 cm sized mass arising from right kidney with multiple dilated tortuous overlying vessels resulted in abandoning surgery. Tumor biopsy confirmed the presence of MTSCC of kidney. Post-operatively, child was started on metronomic therapy but showed poor response and developed progressive disease with bilateral lung, liver and bony metastases.

**Results: Results** Child developed progressive disease and died while on metronomic therapy.

**Conclusions: Conclusions** MTSCC of kidney is a rare tumor that can pose as both a diagnostic and therapeutic challenge. Metastases, even in cases with low-grade morphology, have been reported. While surgical resection (partial or radical nephrectomy) is usually preferred modality for localized disease, no systemic treatment guidelines are established for metastatic disease. Few cases of metastatic MTSCC have shown response to Sunitinib.

PO052 / #1448 | Publication Topic: AS05 SIOP Scientific Program / AS05.g Bone Tumours

### CLINICAL PROFILE OF PEDIATRIC MALIGNANT BONE TUMOR – 10 YEARS EXPERIENCES FROM A TERTIARY LEVEL CANCER HOSPITAL, BANGLADESH

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**Background and Aims:** Malignant bone tumor constitutes approximately 6% of all childhood malignancies. The most frequent pediatric bone tumor is Osteosarcoma 56%, Ewing sarcoma family of tumor 34% & Chondrosarcoma 6%. The incidence of bone cancer peak at age 15. Most published data is from developed countries. National Institute of cancer research & Hospital (NICRH), Bangladesh is a tertiary cancer center where a child with bone tumor get the opportunity of all multi-modal treatment facility. So, primary bone tumor is one of the commonest pediatric malignancies here. The aim of the study is to see the clinical profile of this bulk of primary pediatric bone tumors, that was not find out yet.

**Methods:** We did a 10-year hospital based cross sectional study, collecting data from the year of 2012 to 2021 registered in the pediatric hematology and oncology outpatient department of NICRH. Age up to 18 years of both sexes diagnosed with primary malignant bone tumor were included in the study. Reviewed data were analyzed by using SPSS version 25.

**Results:** The study found 5,427 cases with pediatric malignancy, bone tumor constitute 16.7% (n = 909). Ewing's Sarcoma was 50% (n = 455/909), Osteosarcoma 48% (n = 433/909) & Chondrosarcoma 2% (n = 21/909). Localized bone tumor was 68% and metastatic tumor 32%. Male, 58.8% (n = 534) and Female, 41.2% (n = 375) with M:F = 1.42:1. Frequent cases (43.9%) was found from 15-18yrs, 38.2% from 10-<15 yrs and 17.9% from <10 years age. Frequent age group for ES (31.9%) was <15 years but for OS frequent (24.1%) cases were found from >15yrs. Commonest presentation was pain (90%) and swelling (80%) with duration of symptoms varied 3-12 months. Site of tumor was 75.5% in lower extremity, 14% in pelvis, 6% in upper extremity, rib 2%, Scapula/Clavicle 1%, Head&neck 1%, vertebrae/spine 0.50%.

**Conclusions:** The study found commonest bone tumor for pediatric age group was ewings sarcoma followed by osteosarcoma.

PO053 / #1675 | Publication Topic: AS05 SIOP Scientific Program / AS05.g Bone Tumours

#### FIRST SYMPTOMS AND TIME TO DIAGNOSIS IN PEDIATRIC PATIENTS WITH OSTEOSARCOMA IN KINSHASA

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**Background and Aims:** Osteosarcoma is the most common primary malignant bone tumor in children. In HIC, most patients come at early stages and this contribute to the high survival rate. However, the survival rate is much lower in LMIC due to diagnosis delay and limited access to appropriate treatment. Since 2021, the French African Pediatric Oncology Group (GFAOP) has been collaborating with our hospital to improve early diagnosis of childhood cancer. The aim of this

study is to assess the diagnosis delay and analyze its associated factors in patients with osteosarcoma in Kinshasa.

**Methods:** We conducted a retrospective study of children with osteosarcoma diagnosed between 2016 and 2022 at Kinshasa University Hospital. Children with osteosarcoma diagnosed by clinical and imaging findings were also included.

**Results:** A total 30 patients was registered during the study period. The mean age at diagnosis was 13.1 years. The most common presenting sign was painful and large bone mass. The primary tumor was located predominantly at the femoral site. Metastatic workup was positive in 57% and lung was the common site of metastasis in all patients. The median time to diagnosis was 144 days. Diagnosis delay was associated with metastasis and malnutrition (p = 0,003; p = 0, 04 respectively). However, gender, age, distance to the hospital, parental level of education did not have a significant statistical correlation with the time to diagnosis. The evolution after diagnosis found that 14 patients received palliative care just at diagnosis, 12 patients abandoned curative treatment (6 at diagnosis and 6 refused amputation). The 4 remaining patients had progression of the disease during treatment.

**Conclusions:** The management of osteosarcoma in Kinshasa is a challenge because of advanced stage and abandonment of treatment. There is a clear need to identify the reasons behind late presentation and abandonment while increasing awareness on early signs of childhood cancer.

PO054 / #1768 | Publication Topic: AS05 SIOP Scientific Program / AS05.g Bone Tumours

#### IMPACT OF LATENCY TO DIAGNOSIS AND CLINICAL FACTORS ON THE SURVIVAL OF CHILDREN AND ADOLESCENTS WITH OSTEOSARCOMA: EXPERIENCE FROM A TERTIARY CARE CENTER IN MÉXICO

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**Background and Aims:** Multiple clinical factors may influence survival outcomes in patients with osteosarcoma. The objective of this study was to evaluate the relationship of latency to diagnosis and clinical factors with the prognosis.

**Methods:** Retrospective study. Seventy-four patients were included (From 2007 to 2022).

**Results:** The median age was 13 years, male predominance was 63.5%, the most affected anatomical site was the femur (52.7%), and the

median size of the primary tumor was 10 cm. The most frequent osteoblastic histological subtype was 70.3%.

The latency to diagnosis was  $13.2 \pm 6.2$  weeks. 51.4% of the patients had latency to late diagnosis. (Defined as more than 13 weeks between symptom onset and histopathologic diagnosis.)

Metastatic disease was 35%, with a statistically significant relationship between latency to late diagnosis. ( $p = 0.024$ ).

Neoadjuvant chemotherapy was administered to 85% and adjuvant chemotherapy to 78.4%.

Local control performed: amputation 44.8%, disarticulation 37.9%, limb salvage 12.1%. Good histological response in 24.3%.

Abandonment of treatment was 19%, mainly in the referral to surgery for local control, with a statistically significant relationship between the abandonment of treatment, with the distance  $\geq 50$  km from the place of residence of the patient to the hospital ( $p = 0, 01$ ).

The following factors were associated with an unfavorable prognosis: late latency to diagnosis ( $p = 0.001$ ), tumor size  $>8$  cm (0.001), metastatic disease ( $p = 0.01$ ), and poor histological response to treatment ( $p = 0.009$ ).

With a median of 60 months of follow-up in patients with metastatic disease OS was  $26 \pm 10\%$  and EFS  $13.5 \pm 7.2\%$  compared to patients with a localized disease with  $61 \pm 9.2\%$  OS and  $42.5 \pm 7.9\%$  EFS.

**Conclusions:** There is a need to design adequately to strengthen patient referral systems and establish strategies for greater adherence to treatment, due to the high impact of delays to diagnosis and abandonment of treatment on the survival of patients with osteosarcoma.

PO055 / #1591 | Publication Topic: AS05 SIOP Scientific Program / AS05.g Bone Tumours

#### OSTEOSARCOMA IN CHILDREN: EXPERIENCE OF THE SERVICE AND CHALLENGES. DEPARTMENT OF HEMATOLOGY-ONCOLOGY PEDIATRIC (SHOP)- AUGUST 20 HOSPITAL - CASABLANCA MOROCCO

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**Background and Aims:** Osteosarcoma is the most common bone cancer. Survival was completely improved by early diagnosis and poly-chemotherapy. Our study describes the clinical presentation, diagnosis and treatment in our context.

**Methods:** A monocentric descriptive retrospective study conducted at the SHOP between 2015 and 2020, including 32 patients with anatomopathological diagnostic confirmation, treated by Doxorubicin/Cisplatin or Protocol OS 2005. Patients who refused amputation are excluded.

**Results:** The median age at diagnosis is 11 years [05-17 years]. The sex ratio is 1.2. The clinical presentation was dominated by the association of swelling in 88% with functional impotence and localized pain. The seat of the lesion is predominant at the distal end of the right femur in 50% of cases. 100% of patients had a bone MRI showing a tumor process with advanced localized stage. Bone scintigraphy performed in 90% of patients revealing secondary bone localizations in 5%. CHEST CT was done in 70% of patients, 35% had pulmonary nodules. The average delay for histological confirmation is 2 months [01-06 months]. The results showed: 71% osteoblastic osteosarcoma, 13% chondroblastic, 10% fibroblastic and 6% telangiectatic. 75% of patients are non-metastatic at diagnosis. The patients are all included in neoadjuvant chemotherapy, 85% received Doxorubicin/Cisplatin against 15% OS2005 Protocol. At evaluation, 75% of all patients showed a radiological progression, 15% stable and 10% noted a reduction in tumor volume. The median time between the end of chemotherapy and surgery is 35 days. The histological response was marked by 80% of poor responders with a Huvos grading of 1/2. The evolution was marked by a relapse at the pulmonary level in 8 patients. The protocol adopted is metronomic chemotherapy. The overall survival at 03 years was 35%.

**Conclusions:** Management still faces many challenges in developing countries, in particular the delay in diagnosis and therapeutic as well as the refusal of amputation.

PO056 / #742 | Publication Topic: AS05 SIOP Scientific Program / AS05.g Bone Tumours

#### TREATING OSTEOSARCOMA IN CHILDREN AND ADOLESCENTS IN A RESOURCE-LIMITED SETTING: THE REALITY OF METASTASES, TREATMENT ABANDONMENT, AND SURGICAL CHALLENGES

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**Background and Aims:** Low-income countries (LICs) have not been able to replicate the same survival outcomes achieved in high-income countries due to constrained treatment resources and a high number of late presentations. There is a dearth of literature on the management of osteosarcoma in LICs such as Uganda. We described the clinicopathological features, treatment, and outcomes of osteosarcoma in Ugandan children and adolescents.

**Methods:** We retrospectively reviewed records of children and adolescents diagnosed with osteosarcoma at the Uganda Cancer Institute

from January 2016 to December 2020. Patient and tumour characteristics and treatment outcomes were analyzed. The Kaplan-Meier survival analysis was done. Statistical significance was determined at  $p < 0.05$ .

**Results:** Seventy-four osteosarcoma cases were identified, with a median age of 13.0 years (IQR: 9.8–15.0). The majority ( $n = 41$ ; 55.4%) were male; the median duration of symptoms was five months (IQR 3.0–8.0). At diagnosis, 37 (50.0%) patients had metastatic disease, mostly to the lungs ( $n = 43$ ; 91.9%). Only 43 patients (58.1%) underwent surgery that was radical in all but one patient. Two-thirds (67.4%; 29/74) of the surgeries were performed upfront, and 14 (32.6%) followed neoadjuvant chemotherapy. No patient had a metastasectomy. Thirteen patients (17.6%) were palliated - 2 upfront. The median follow-up time was 16.8 months (IQR 7.6–23.1). Twenty-six (35.1%) patients abandoned treatment, including radical surgery (18/26; 69.2%). Only 17.6% ( $n = 13$ ) were alive; 45.9% ( $n = 34$ ) had died, and 36.5% ( $n = 27$ ) had an unknown status. The median overall survival (OS) and event-free survival (EFS) were 1.8 and 1.4 years, respectively. The 3-year OS and EFS rates were 22.0% and 16.7%, respectively. Patients with metastatic disease ( $p = 0.009$ ), Enneking stage IIB/III ( $p = 0.007$ ), no surgery ( $p = 0.025$ ), delayed adjuvant chemotherapy  $> 21$  days ( $p = 0.004$ ), and tumour size  $> 12$ cm ( $p = 0.023$ ) had lower survival.

**Conclusions:** High rates of metastatic disease, treatment abandonment, and surgical challenges thwart treatment outcomes of Ugandan children diagnosed with osteosarcoma.

PO057 / #879 | Publication Topic: AS05 SIOP Scientific Program / AS05.g Bone Tumours

#### MAXIMIZING RESOURCE UTILIZATION IN AN LMIC; A DAYCARE-BASED MODEL FOR LOCALIZED OSTEOSARCOMA USING A CARBOPLATIN & IFOSFAMIDE PROTOCOL

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**Background and Aims:** Historically, the management for Osteosarcoma (OS) in pediatric patients involved only surgical resection with event free survival (EFS) estimated at 20%. The revolutionary introduction of multi-agent adjuvant chemotherapy significantly improved survival rates up to 66%. The current OS99 protocol comprises the combination of doxorubicin, ifosfamide, and carboplatin and has been found to exhibit reduction in toxicities associated with the conventional treatment regimen. This study evaluates the toxicity and outcomes of the OS99 protocol in patients with Osteosarcoma treated in a daycare setting of a tertiary hospital.

**Methods:** A retrospective study was conducted by Indus Hospital and Health Network to evaluate the outcomes of patients up to 16 years of age, diagnosed with localized osteosarcoma and treated with curative

intent as per the OS99 protocol between October 2017 and February 2022.

**Results:** A total of 26 patients with localized osteosarcoma were included of which 16 (61.5%) were 9–12 years of age and 18 (69.2%) were male. The most frequently involved bones were the femur and tibia with 11 (42.3%) patients each. The most common presenting symptoms were swelling (92.3%,  $n = 24$ ) and pain (77%,  $n = 20$ ). Cardiac toxicity was the most frequently observed ( $n = 7$ , 26.9%) followed by febrile neutropenia ( $n = 3$ , 11.5%). Delay in chemotherapy due to thrombocytopenia was observed in 3 (11.5%) patients. Completion of treatment was achieved by 17 patients, 13 (76.5%) of which were cured and 3 (17.65%) relapsed at the primary site and lungs while only 1 patient presented with relapse in lungs. One patient expired during the course of the study due to sepsis during treatment.

**Conclusions:** The OS99 protocol showed promising outcomes in terms of event free survival rates (EFS) with manageable treatment-related toxicities. Further studies should be conducted to evaluate the efficacy of treating osteosarcoma solely in a daycare setting.

PO058 / #1107 | Publication Topic: AS05 SIOP Scientific Program / AS05.h Soft Tissue Sarcomas

#### CHILDHOOD HEAD AND NECK RHABDOMYOSARCOMA IN PEDIATRIC HEMATOLOGY AND ONCOLOGY CENTER OF RABAT (MOROCCO)

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**Background and Aims:** Pediatric rhabdomyosarcoma (RMS) is the most common malignant mesenchymal tumor of the child. It represents 5% of all pediatric cancers. The head and neck location of the childhood RMS is the most frequent location. The aim of our study is to describe the clinicopathological characteristics and therapeutic results of a series of head and neck rhabdomyosarcoma.

**Methods:** Cases diagnosed as RMS affecting the head and neck region were retrospectively retrieved from the files of pediatric hematology and oncology center of Rabat (Morocco) from January 2014 to December 2018. Data on clinical features (sex, age and affected site), microscopic subtype, immunohistochemical results, treatment employed and follow-up status were obtained from the patient's medical charts.

**Results:** Twenty one patients were diagnosed with rhabdomyosarcoma of the head and neck. The median age of patients was 5 years, the sex ratio was 2.5. The main diagnostic time is 2 months. The diagnosis of RMS was guided by imaging (CT and / or MRI) and confirmed by histology coupled with immunohistochemistry. The embryonal form was the most common. The location of the primitive tumor was parameningeal in 62%, orbital in 33% and non parameningeal in 5% of cases. The treatment consisted of chemotherapy in all cases, radiotherapy in

13 patients and surgery in 7 patients. Ten patients were alive in their last follow-up, whereas 8 patients died due to the disease and 2 lost to follow-up and 1 discontinued treatment.

**Conclusions:** Head and neck RMS is an aggressive malignant neoplasm which demands special concern to achieve early diagnosis and successful treatment. Its prognosis depends mainly on the initial location of the primitive tumor: orbital and non-parameningeal tumors have a better prognosis than parameningeal tumors.

PO059 / #870 | Publication Topic: AS05 SIOP Scientific Program / AS05.h Soft Tissue Sarcomas

#### PEDIATRIC ABDOMINOPELVIC EWING'S SARCOMA: A RETROSPECTIVE 10-YEAR SINGLE-CENTER STUDY AND BIOINFORMATIC ANALYSIS

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**Background and Aims:** Ewing's sarcoma (ES) is a rare but aggressive type of bone and soft-tissue cancer in children and adolescents. Abdominopelvic ES (apES) accounts for <3% cases of total ES and <10 annual cases of pediatric apES (<18 years) were reported across the world. The study was conducted to facilitate the understanding of prevalence, clinical features, pathological characteristics and outcomes of pediatric apES and construct a prognostic model and nomogram based on metastatic ES datasets.

**Methods:** Three pediatric apES patients in Shanghai Children's Hospital were included between 2013 and 2023. Prevalence of apES was calculated in our center. Clinicopathological data and prognostic outcomes were compared between apES and abdominopelvic inflammatory myofibroblastic tumor (apIMT). Datasets of metastatic ES tumors were applied to develop a prognostic nomogram combined with STAG2-based gene signature.

**Results:** A total of 452 malignant abdominopelvic tumors were identified and apES accounts for 0.6% among all cases in our center. Tumor volumes were larger in apES relative to apIMT ( $1558.65 \pm 904.67$  vs.  $290.00 \pm 173.58$  cm<sup>3</sup>). Higher proportion of Ki-67 cells were stained in apES slides ( $63.33 \pm 4.71$  vs.  $11.67 \pm 9.43$  %). Shorter follow-up days were shown in apES ( $34.28 \pm 7.10$  vs.  $77.17 \pm 42.80$  months). STAG2 in-frame mutation had been detected in one very severe case with multiple metastatic lesions. A STAG2-associated gene network indicated DNMT1, LIN9 and SMC1A as risky genes and STAG2, SUZ12 and PDS5B as protective genes, and the STAG2-based prognostic model was built and externally validated. The nomogram showed that younger age, male gender, tumor relapse and STAG2-based risky score decreased the survival probability.

**Conclusions:** Pediatric apES is a rare but extremely aggressive mesenchymal neoplasm and requires multi-modal diagnostic and therapeutic strategies. STAG2-associated network plays a dominant role in suppressing ES and its related agents such as EZH2 inhibitor might be promising.

PO060 / #1623 | Publication Topic: AS05 SIOP Scientific Program / AS05.h Soft Tissue Sarcomas

#### EXTRAOSSEOUS EWING SARCOMA: PRESENTATION OF A SERIES OF PEDIATRIC CASES AND EXPERIENCE OF AN INSTITUTION

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**Background and Aims:** Extraosseous Ewing sarcomas (EES) are rare, fast growing and very aggressive malignancies. The most frequent sites are paravertebral regions, lower extremities, buttocks, pelvis and retroperitoneum. The objective of this study is to describe the epidemiological data and clinical characteristics of patients, their clinical response to treatment and their prognosis.

**Methods:** Clinical findings, response to treatment, and prognosis of 5 EES cases diagnosed and treated between 2017 and 2022 are analyzed retrospectively.

**Results:** M:F ratio of 1.5:1. The median age was 11.6 years (2.4 years-18.25 years). Case 4 is a second neoplasm, embryonal rhabdomyosarcoma of the prostate as the primary neoplasm at 3 years. Case 5 is the youngest patient and 2 months earlier she was diagnosed and managed as a hemangioma with 2 previous embolization. In 2 of the 5 patients the primary site was the paravertebral region (1 cervical-thoracic and another thoraco-lumbar), 1 in pelvis, 1 patient in thigh and the last case in buttock. The average time of clinical evolution was 5.6 months (17 days – 15 months). Of the 5 patients, 3 had metastatic disease at diagnosis and all to lungs. Primary surgical resection was performed in 2 patients (case 1 and 3). The other 3 cases received neoadjuvant chemotherapy. Of the 5 patients, 3 of them are under clinical surveillance, without recurrence or sequelae and cases 4 and 5 are still on adjuvant treatment and a resection was achieved with negative margins.

**Conclusions:** EES are rare malignancies, with a better prognosis than primary bone malignancies. Early detection is required by including them in the differential diagnosis of soft tissue masses in the



paravertebral regions and lower extremities. Complete resection with negative margins and chemotherapy are very important elements in prognosis.

PO061 / #899 | Publication Topic: AS05 SIOP Scientific Program / AS05.h Soft Tissue Sarcomas

#### DIAGNOSTIC CHALLENGES OF PRIMARY EXTRASKELETAL EWING SARCOMA IN PEDIATRICS FROM A LIMITED RESOURCE SETTING: A CASE SERIES

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**Background and Aims:** Ewing sarcoma is an aggressive, small round blue cell tumor commonly seen in the bones but primary extraskeletal sites are rare. Definite diagnosis is based on histopathology with immunohistochemistry while cytogenetic studies demonstrating the pathognomonic t(11;22)(q24;q12) leading to EWSR1-FLI1 fusion gene will confirm the diagnosis. This poses as a challenge in limited resource settings and often lead to delays in treatment due to lack of capacity for further tests. This study reported three cases of cytogenetically confirmed primary Extraskeletal Ewing sarcoma (EES) in pediatrics.

**Methods:** Hospital records, including histopathology reports offsite, were reviewed for pediatric patients diagnosed with primary EES.

**Results:** Three cases were identified with ages 12–18 years old at diagnosis. All cases had specimens sent out to an international referral institution from a high-income country. The first two cases were females with initial consideration of Renal cell carcinoma but review of specimen detected EWSR1-FLI1 confirming renal Ewing sarcoma. The third case was male with posterior neck mass and initially managed as lymphoma but EWSR1 rearrangement was seen upon review and was shifted to Ewing sarcoma protocol. Bone scans were all negative for skeletal involvement. Diffuse membranous positivity for CD99 was demonstrated in all cases. All patients already underwent tumor resection when seen at the cancer institute but two already had tumor recurrence upon initiation of chemotherapy. The adapted Ewing sarcoma regimen was given consisting of induction with Vincristine, Doxorubicin, Cyclophosphamide alternate with Ifosfamide, Etoposide every 3 weeks, which will be followed by local control and maintenance phase. Only one case of renal Ewing sarcoma continued treatment while the other two who were initially started on different protocols, abandoned treatment and did not survive.

**Conclusions:** Diagnosis of EES is challenging in resource-limited countries that lack cytogenetic tests. Clinical correlation with high index of suspicion may aid in early detection and improve outcome.

PO062 / #1205 | Publication Topic: AS05 SIOP Scientific Program / AS05.h Soft Tissue Sarcomas

#### PRIMARY INTRACRANIAL SARCOMA WITH MENINGEAL INVOLVEMENT AT DEBUT: TWO PEDIATRIC PATIENTS CASE REPORTS

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**Background and Aims:** Primary Intracranial Sarcoma (IS) is an uncommon tumor. However, the possibility of a spinal presentation should be considered.

**Methods:** We report two cases of IS with leptomeningeal infiltration at diagnosis in a 9-year-old girl (case 1) and 7-year-old boy (case 2).

**Results:** Case 1 cranial CT reveals a 66 × 82 × 87mm tumor in the left frontal lobe. Tumor was totally removed, histopathology reports fusocellular sarcoma. 2-weeks post-surgical MRI showed discrete foci of pathological contrast enhancement on pial arachnoid surface on cervical and dorsal spinal cord. Multidisciplinary board established leptomeningeal involvement at debut. She received 2 cycles of chemotherapy with ifosfamide, carboplatin and etoposide (ICE), followed by MRI that shows discrete leptomeningeal dissemination. In case 2 the diagnostic CT showed two confluent rounded lesions in the right frontotemporal region of 40 × 27mm and another 17 × 35mm. Complete resection surgery was planned, and the histopathological diagnose was fusocellular sarcoma. Two-weeks post-surgical brain/spine CT showed a 27 × 46mm secular image in brain and a nodular enhancement of 5.6 × 4mm located in the spinal cord at D2 level. Patient started 2 cycles of ICE and after 2 months cranial-spine MRI reported a small focus of frontotemporal leptomeningeal enhancement of 7 × 3mm. Both patients received cranio-spinal axis irradiation (CSI) at a dose of 36Gy and a surgical bed boost of 23.4Gy, with 3D conformational technique. They also received oral etoposide during treatment. Posteriorly, they continued 3 and 5 ICE cycles respectively and cranial-spine MRI control every 6 months. Case 1 remains in follow-up after 33 months without evidence of tumor or leptomeningeal recurrence in the MRIs, and Case 2 is asymptomatic at 2 months after treatment.

**Conclusions:** Leptomeningeal involvement of the IS is seen at recurrence scenario and carries worse prognosis. Nevertheless, we report this clinical presentation at debut and a satisfactory therapeutic response after standard therapeutic scheme with an individualized radiotherapy indication.

PO063 / #1497 | Publication Topic: AS05 SIOP Scientific Program / AS05.h Soft Tissue Sarcomas

### CHILDHOOD RHABDOMYOSARCOMA: A MONOCENTRIC EXPERIENCE

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**Background and Aims:** Rhabdomyosarcoma (RMS) is a childhood tumor that has benefited from nearly 30 years of multimodality therapy culminating in a greater than 70% overall current 5-year survival. The aim of our study is to describe the epidemiological, clinical and para-clinical aspects and the therapeutic strategy followed.

**Methods:** This is a retrospective descriptive study from January 2017 to December 2020 collecting patients under 15 years of age had histologically proven rhabdomyosarcoma, treated according to the Protocol RMS 2005 treatment group.

**Results:** During this period 25 patients were treated, a male predominance was noted with a sex ratio of 2.1, median age of 4 years (1.5-14 years), history of neoplasia in the family in 16% of cases, and an average delay in diagnosis of 2.5 months. The most frequent site was urogenital in 48% of cases, and head and neck in 24%. The histological type was embryonic in 84% of cases, alveolar in 16%. According to Risk Group Classification 20% (5) of the patients were classified as low risk, 36% (9) patients belonged to the standard risk and 44% (11) patients were classified as high-risk and very-high-risk group. The treatment consisted of chemotherapy in all cases, surgery was performed in 68% (17) and 32%(8) was not operable, 32%(8) of patients had received radiotherapy .At the end of treatment 48% of patients were in complete remission, 32% in partial remission and 16% in therapeutic failure, chemotherapy second line was received by 40% (10), 32% (8) of which were declared as palliative,11 patients were alive at final status, for an overall survival of 44%.

**Conclusions:** The prognosis of RMS depends on several factors that will condition the therapeutic management, the predominance of the high and very-high risk group in our series explains the therapeutic failure rate and our low overall survival.

PO064 / #1566 | Publication Topic: AS05 SIOP Scientific Program / AS05.i Retinoblastoma

### RETINOBLASTOMA FREQUENCY AT THE PEDIATRIC ONCOLOGY UNIT OF NIAMEY A 3 YEARS RETROSPECTIVE STUDY UNDERTAKEN AT THE PEDIATRIC ONCOLOGY UNIT OF NIAMEY

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**Background and Aims:** IN NIGER THE RETINOBLASTOMA IS THE MOST COMMON PEDIATRIC SOLID TUMOR SINCE THE CRÉATION OF THE PEDIATRIC ONCOLOGY UNIT IN 2016. UNFORTUNATELY THE PATIENTS CAME LATELY IN THE UNIT AND MAKE DIFFICULT ITS TREATMENT . IITS TREATMENT HAVE A LOT OF PSYCHOLOGICA IMPACT BECAUSE OF THE ENUCLEATION WHICH LEADS THE PARENTS TO THE TREATMENT ABANDONMENT. IN ORDER TO ÉVALUÂTES ITS FREQUENCY, WE REALIZED A RETROSPECTIVE STUDY FROM 2016 TO 2018 AT THE PEDIATRIC ONCOLOGY UNIT OF NIAMEY. AIM OF THE STUDY : KNOWING THE RETINOBLASTOMA FREQUENCY DURING THE FIRST 3 YEARS ACTIVITY OF THE PEDIATRIC ONCOLOGY UNIT AND CONTRIBUTE TO MAKE ITS DIAGNOSIS ITS EARLIER.

**Methods:** IT WAS A RETROSPECTIVE STUDY FROM MARCH 1st 2016 TO OCTOBER 31, 2018. THE STUDY HAD CONCERNED 63 CASES OF RETINOBLASTOMA RECORDED IN THE PEDIATRIC ONCOLOGY UNIT DURING THIS PERIOD. ALL THE CHILDRENS AGED 0 TO 15 YEARS OLD, OF BOTH SEX WHO WERE FOLLOWED IN THE UNIT FOR RETINOBLASTOMA ARE INCLUDED IN THE STUDY.

**Results:** THE STUDY SHOWED THAT OUT OF 220 CASES OF PEDIATRIC CANCERS RECORDED IN THE UNIT, THE RETINOBLASTOMA WAS THE FIRST PEDIATRIC SOLID TUMOR WITH 63 CASES (28,63%). THE MALE SEX PREDOMINATE WITH 34 CASES (53,96%). OVER THE 63 CASES OF RETINOBLASTOMA, 3 CASES OF LEUCOCORIA WERE OBSERVED AND 1 case of bilateral localization. 8 CASES OF DEATH (12, 69%). 10 CASES OF TREATEMENT ABANDONMENT (15,87%) WERE RECORDED. A TOTAL OF 45 CHILDRENS WERE ALIVE INCLUDING 8 WITH BRAIN TUMOR AND WERE REFERRED TO THE REGION FOR PALLIATIVE CARE.

**Conclusions:** AT THE END OF THIS STUDY, WE CAN CONCLUDE THAT THE RETINOBLASTOMA RANKS FIRST AMONG PEDIATRIC CANCERS IN NIGER. THESE FIRST RESULTS ON RETINOBLASTOMA FREQUENCY SHOWED THAT ITS PROGNOSIS CAN BE GOOD IF WE FOCUSED ON EARLY DIAGNOSIS. ITS CURABILITY CAN BE IMPROVED DESPITE ITS SURGICAL TREATMENT WHICH PUCHES PARENTS TO THE ABANDONMENT OF TREATMENT, SO PARENTS MUST BE SENSIBILIZED.

PO065 / #1662 | Publication Topic: AS05 SIOP Scientific Program / AS05.i Retinoblastoma

EVALUATION OF THE CLINICAL PRESENTATION, TREATMENT, AND OUTCOME OF CHILDREN WITH RETINOBLASTOMA AT TERTIARY REFERRAL HOSPITAL, ETHIOPIA

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**Background and Aims:** Retinoblastoma is the most common primary ocular malignancy in childhood. It can present as unilateral, bilateral, and rarely as trilateral. Retinoblastoma is hereditary in 40% of cases, and it can be bilateral with a median age at diagnosis of one year. Our study assessed the treatment delay, clinical profile, and outcome of patients with retinoblastoma treated at Tikur Anbessa Hospital, Ethiopia's largest tertiary referral hospital.

**Methods: Materials and Methods** We conducted a retrospective cross-sectional study through a self-administered structured questionnaire on children treated with a confirmed diagnosis of retinoblastoma from January 2014 to January 2019. Collected data were analyzed using SPSS version 20. Kaplan Meier's estimate was used for OS analysis.

**Results:** Eighty-nine patients with retinoblastoma were included. The disease was unilateral in 71%, bilateral in 25.8%, and trilateral in 2.2%. The mean age at the first visit to the primary health care service was 28.9 months, and 15 months for unilateral and bilateral RB with a range of 2–74 months. The mean duration of symptoms to reach the retinoblastoma treatment center was 7.6 months in unilateral and 9.6 months in bilateral RB. 86.3% of patients presented with advanced disease; 64.2% were extraocular, and 35.2% of the patients had metastatic disease at the time of diagnosis. The one and two-year overall survival rate was 70% and 60% respectively.

**Conclusions:** Our study showed the mean age at the time of diagnosis at the treatment center was 36.5 months and 24.6 months for unilateral RB and bilateral RB respectively. Most patients presented with an advanced stage. There was a significant delay in referral from primary health care facilities to the treatment center. Emphasis has to be given to early detection and early referral of children with RB.

PO066 / #469 | Publication Topic: AS05 SIOP Scientific Program / AS05.i Retinoblastoma

CONTRIBUTION OF MULTIDISCIPLINARITY IN THE MANAGEMENT OF RETINOBLASTOMA IN PEDIATRIC ONCOLOGY UNIT IN NIAMEY, NIGER

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**Background and Aims: Introduction:** In Niger, delay in consultation, diagnosis at an advanced stage of the disease and limited means of management are the fundamental reasons responsible for the poor prognosis of retinoblastoma. **The objective of this work is to evaluate the stage at presentation and the outcome of retinoblastoma**  
**Methods: Materials and methods:** this is a preliminary retrospective and descriptive study over a 24-month period from January 2019 to December 2020. Data were collected from the database at the unit and at the ophthalmology department of the HNABD. All diagnosed cases of retinoblastoma were included.

**Results: Results:** 34 patients were registered, the mean age was 3.4 years. Leukocoria was the presenting sign in 70.7% of patients. The delay of more than 1 year between leukocoria and consultation was 53.6%. 38.2% of patients had vitreous swelling and exophthalmos represented 54.3%. A CT scan was performed in 60% of cases and 38.2% of histological results were obtained within 14 days. Preoperative chemotherapy was performed in 73.5% of patients within 17.5 days and postoperative chemotherapy in 26.5% within 18.9 days. The evolution was marked by 47% of death, 18% of abandonment and 35% of living

**Conclusions: Conclusion:** Early diagnosis of and multidisciplinary group workshop setted by GFAOP since 2019 in the sub-Saharan pediatric oncology units, public awareness are essential tools in the management of retinoblastoma for effective treatment and to improve survival of patients in low income countries. **Key words:** retinoblastoma, multidisciplinary, Niger

PO067 / #1735 | Publication Topic: AS05 SIOP Scientific Program / AS05.j Liver Tumours

CLINICAL SPECTRUM AND BEHAVIOUR OF PEDIATRIC MALIGNANT LIVER TUMORS; A SINGLE TERTIARY CARE CENTRE EXPERIENCE

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**Background and Aims:** Hepatoblastoma (HB) is the most common primary malignant hepatic tumor followed by hepatocellular carcinoma (HCC). The main objective of this study is to analyze clinical presentation, behavior and outcome of children with malignant liver tumors presenting to our center.

**Methods:** This retrospective study conducted from January 2018 to December 2022. All children diagnosed as HB or HCC on radiological findings, raised alpha fetoprotein (AFP) level and on needle biopsy

were included. Clinical data collected from record and was analyzed by using SPSS version 20. SIOPEL-3 protocol was followed.

**Results:** Altogether 81 patients were enrolled, 75 (92%) hepatoblastoma and 6 (7.4%) HCC. Males were dominant 57 (70%). Minimum age was 3 months in HB with mean age of presentation 18 months and HCC 132 months. Majority 26 (32%) presented with raised AFP levels >30,000 ng/ml, fifteen (18.5%) in lacs and only 7 (8.6%) with less than 1000. Histological diagnosis of HB was made in 37 (49%) without further sub typing, twelve (16%) had fetal type and 7 (9%) epithelial. Twenty six (32%) had pretext-II disease, 18 (22%) pretext IV and 15 (18%) pretext III. Sixteen (20%) with metastatic disease, 23 (28%) with vascular involvement Treatment was abandoned by 28(34%) and nine (11%) including all HCC were offered palliation. Fifty one (68%) patients with HB received neo-adjuvant chemotherapy and 25 (33%) were proceeded for surgery. Twenty one (28%) patients were cured, 20(26 %) died and 5(%) had relapse.

**Conclusions:** Majority of our study population particularly HCC had dismal prognosis attributable to advance metastatic and aggressive unresectable disease on presentation. However patients with hepatoblastoma having unifocal localized disease had fair survival after timely chemotherapy and complete surgical resection.

PO068 / #1884 | Publication Topic: AS05 SIOP Scientific Program / AS05.j Liver Tumours

#### TREATMENT RESULTS AND CHALLENGES FOR THE MANAGEMENT OF HEPATOBLASTOMA FROM A SPECIALIZED CENTER IN MEXICO

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**Background and Aims:** Hepatoblastoma (HB) accounts for 2% of all pediatric tumors at our institution which is the first pediatric oncology-devoted hospital in Mexico. Given the paucity of data on HB in pediatric patients in Mexico, the aim of the study was to describe the treatment and outcomes of children with hepatoblastoma at the Teleton Children's Oncology Hospital (HITO).

**Methods:** A retrospective review of the records of all children with HB enrolled from 2014 through 2020. Standardized treatment was given as per SIOPEL protocols, SIOPEL 3-SR protocol with six courses of cisplatin for standard-risk patients, SIOPEL-4 protocol with dose-dense

cisplatin/doxorubicin chemotherapy and radical surgery for patients with high-risk hepatoblastoma.

**Results:** A total of 10 patients with HB were identified, all male, average age was 2.29 years, and abdominal distension was the pivot symptom for consultation (100%). The histological subtype was mixed fetal and embryonal epithelial HB diagnosed in 100%. All patients had AFP levels >100 ng/mL. Initial biopsy was carried out in 77% and 23% reached microscopic negative margin resection (RO) as initial treatment. According to PRETEXT classification, 2 patients were as II, 6 as III, and 1 as IV tumors. Distant metastases were detected in 2 cases. Four patients were classified as high-risk and the rest as standard-risk. Mortality was associated with surgical complications in 1 patient. The overall survival of 33%, and a 55% mortality mainly from metastases followed by disease progression. Stratified by standard-risk group had the best outcomes, with 80% and 20%.

**Conclusions:** Although they represent a small proportion of individuals, patients with hepatoblastoma are a challenge in the treatment of this disease. They have a risk of greater morbidity and mortality in surgical treatment, despite having adequate support treatment in our center. It is necessary to improve the factors that precede the delay in diagnosis and arrival at a specialized center for comprehensive treatment.

PO069 / #1470 | Publication Topic: AS05 SIOP Scientific Program / AS05.j Liver Tumours

#### PEDMARK® REDUCED THE RISK OF CISPLATIN-INDUCED OTOTOXICITY IN PEDIATRIC PATIENTS WITH HEPATOBLASTOMA, SEEN IN A TURKISH COMPASSIONATE USE TREATMENT PROTOCOL

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**Background and Aims:** Cisplatin induced-ototoxicity (CIO), with permanent hearing loss is observed in >60% of pediatric patients in Turkey (ASCO2014; Tacyildiz). PEDMARK® (sodium thiosulfate anhydrous) reduced the risk of CIO in patients with localized solid tumors as observed in Phase 3 studies (SIOPEL 6 & COG ACCL0431). The aim was to evaluate the investigational product (PEDMARK®) provided to pediatric patients via a compassionate use treatment protocol (CUP) in Turkey.

**Methods:** Patients (1-month to <18 years) with standard-risk hepatoblastoma (HB) ( $\leq 3$  involved liver sectors, no metastases, an alpha-fetoprotein (AFP) level of  $>100$  ng per milliliter), and treatment plans including cisplatin were eligible. PEDMARK® was administered intravenously 6-hours after each cisplatin infusion. Adverse events (AEs), demography, hearing and tumor outcomes were recorded.

**Results:** The CUP enrolled 8 patients with HB over 3-years (OCT2019 – DEC2022) from 4 academic institutions in Turkey. Median age and weight were 1-yr (range: 3-months – 3-yrs) and 9.5 kg. All patients had newly diagnosed HB, with mixed ( $n = 5$ ), embryonal/fetal ( $n = 2$ ), or HB NOS ( $n = 1$ ) histology. Patients had HB PRETEXT 3 ( $n = 5$ ), 2 ( $n = 2$ ), or 1 ( $n = 1$ ), with a median baseline AFP of 54,000. All patients had Brock Grade 0 on hearing tests prior to treatment. Patients received a median of 6-cycles (range: 4–6) of cisplatin and PEDMARK®. Patients with hearing exams available post-treatment ( $n = 7$ ), all maintained Brock Grade 0. At a median of 0.8-months post-treatment, 7 patients had a complete response (CR) and 1 had progressive disease. All CRs were sustained at a median follow-up of 26.3-months. Two patients had nausea/vomiting (grade 1–2). No Grade $\geq 3$  related-AEs were reported.

**Conclusions:** PEDMARK® was well-tolerated when supplied via a Turkish CUP to reduce the risk of CIO in pediatric patients with hepatoblastoma. No hearing loss was observed post-treatment and outcomes were consistent with expected responses following cisplatin.

PO070 / #124 | Publication Topic: AS05 SIOP Scientific Program / AS05.k Germ Cell Tumours

#### OVARIAN TERATOMA WITH POORLY DIFFERENTIATED SOMATIC TYPE PNET MEDULLOBLASTOMA IN A CHILD

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**Background and Aims:** Germ cell tumors are more common in Asia. However, malignant transformation of teratomas is rare, even rarer when it is transformed into somatic type PNET reminiscent of medulloblastoma.

**Methods:** We report here our experience in an 11-year-old girl who presented with prolonged menarche of one month bleeding who underwent a left laparoscopic cystectomy with drainage of 4.5 liter of fluid and removal of the cyst for presumed benign teratoma.

**Results:** Serum tumor markers were normal. Pre-laparoscopic procedure CT scan revealed a large  $27 \times 19 \times 11$  cm right adnexal cystic lesion with several mural nodules in anterior wall, with scattered foci of calcifications. Once histopathology resulted in malignant transformation, she was referred to Pediatric Oncology five weeks later. PET-MRI scan revealed areas of FDG avid irregular soft tissue thickening in abdomen and pelvis, right para-aortic node, and a left internal mammary node. She then underwent a laparotomy, with removal of

left ovary and resection of tumors with Intraoperative findings of widespread carcinomatosis peritonei with multiple metastatic nodules including the para-aortic and right thoracic diaphragm nodules. She received treatment as per Children's Oncology Group ACNS0334 with three cycles of chemotherapy with vincristine, cyclophosphamide, etoposide followed by tandem autologous stem cell rescue with carboplatin and thiotepa and radiation therapy. She is currently at 20 months post completion of medulloblastoma based therapy and remains disease free.

**Conclusions:** Caution should be taken when considering laparoscopic removal for presumed large cystic ovarian germ cell tumors. Outcome for teratoma with malignant transformation into peripheral neuroectodermal tumor previously reported is dismal. Chemotherapy and treatment should be directed at the PNET and not germ cell tumor component.

PO071 / #1237 | Publication Topic: AS05 SIOP Scientific Program / AS05.k Germ Cell Tumours

#### MANAGEMENT OF ADVANCED TESTICULAR TUMOR IN CHILDREN WITH SEVERE ACUTE KIDNEY INJURY (AKI) UNDERGOING HEMODIALYSIS

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**Background and Aims:** Testicular germ cell tumor is the second most common pediatric testicular cancer, especially in adolescents. Chemotherapy is feasible in a dialysis patient, but there are no standard guidelines making the administration of chemotherapy in dialysis patients more challenging.

**Methods:** We present a successful treatment of patient with testicular tumor in children with severe AKI

**Results:** A fifteen-years-old boy came with a history of a mass in the right testis in the last six months. At the initial presentation, he had massive left pleural effusion and uremic encephalopathy with eGFR 4.83 ml/min/1.73m<sup>2</sup>. The serum LDH 1987 U/L, beta-HCG 9352.21 mIU/mL, AFP 19725.85 ng/mL, d-Dimer 28.500 ug/L. Thoraco-abdominal CT demonstrated a malignant-mass in the right testis approximately  $2.0 \times 3.5 \times 2.7$  cm with bilateral paraaortic lymphadenopathy, pleural effusion with heterogenous mass in left lung obliterating the left mainstream bronchus, pericardial effusion with intracardial mass at the left atrium, hypodense lesion in segment V of the liver and grade II hydronephrosis and bilateral hydronephrosis. He underwent a biopsy and immunohistochemistry in the cervical lymph nodes, showed embryonal carcinoma. He was given 15 Gy in five

fractions for superior vena cava syndrome. Hemodialysis was commenced before chemotherapy was given with dose reduction. He responded well, and completed six cycles of chemotherapy regimens. Hemodialysis was discontinued after cycle 2 despite no surgical urinary diversion being done. The last laboratory result was within the normal range. The right orchidectomy surgery was performed and showed a tumor with large necrotic area with chronic xanthogranulomatous inflammation. The PET-Scan evaluation showed no residual mass in the tumor bed. He is under follow-up for cancer remission.

**Conclusions:** Chemotherapy as the mainstay treatment for advanced testicular embryonal carcinoma can be given in a child with severe AKI who underwent hemodialysis. Thorough adjustment of chemotherapy dosage and side effects should be done during treatment, and further follow-up is needed.

PO072 / #31 | Publication Topic: AS05 SIOP Scientific Program / AS05.k Germ Cell Tumours

#### THE ROLE OF P53 GENE SUPPRESSOR AND BCL-2 ONCOPROTEIN IN GERM-CELL OVARIAN TUMOR PROGNOSIS DETERMINATION AMONG CHILD AND ADOLESCENT PATIENTS

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**Background and Aims:** To determine the p53 gene suppressor and bcl-2 oncoprotein forecast role in germ-cell ovarian tumor prognosis among child and adolescent patients

**Methods:** Our search is based on immunohistochemical method results of 35 patients with germ-cell ovarian tumors at I-IV stages, which were diagnosed and treated in oncogynecology and children oncology departments

**Results:** The analysis of immunohistochemical method results shows 7(20%) patients among which had been marked high expression bcl-2 oncoprotein, 11(31,4%) moderate express, 16(45,7%) low express. Analysis of p53 gene suppressor results shows 9(25,7%) patients among which had been marked high expression, 11(31,4%) moderate express, 15(42,8%) low express. The high correlation between bcl-2 expression level increases and fast tumor growth, and therefore incurability of oncologic process among of patients had been revealed. Also the high probability of tumor recurrence was noticed. In the high-positive p53 gene suppressor rate group took place aggressive current of tumor process and these patients had early recurrence and metastases, which demanded recurrent aggressive chemotherapy

**Conclusions:** p53 gene suppressor and bcl-2 oncoprotein expression in germ-cell ovarian tumors among the child and adolescent patients is characterized with high and low rates, which enables to use this rate determination for given pathology currency prognosis identification.

PO073 / #1601 | Publication Topic: AS05 SIOP Scientific Program / AS05.l Rare Tumours and Histiocytosis

#### THE OUTCOME OF PEDIATRIC NASOPHARYNGEAL CARCINOMA IN A LOW-MIDDLE-INCOME LMIC

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**Background and Aims:** Nasopharyngeal carcinoma is rare in the pediatric population. The aim of this study is to explore the outcomes among these children in resource-limited settings presenting with advanced stages of the disease.

**Methods:** A retrospective cohort study was done in the Paediatric Haematology/Oncology department of the University of Child Health Sciences and children's Hospital Lahore Pakistan from January 2015 to December 2020. The statistical analysis was done using SPSS26

**Results:** A total of 41 children were included in this study with a mean age of 11.9 years and the median age of 12 years with M: F ratio of 1.98:1. Among these 73% of cases were residents of rural areas and 27% from Urban. 22/41 (54%) had stage III and 46% stage IV. 73% of them presented with neck swellings followed by epistaxis, headache, and breathing difficulty. 23/41 (56%) completed treatment and are well, 7% abandoned treatment and 15/41 (37%) expired. Electrolyte imbalance, febrile neutropenia with background malnutrition, and advanced-stage disease was the leading cause of death among these patients. Chemotherapy and radiotherapy were given in 70% of cases and chemotherapy alone in 30%.

**Conclusions:** Overall survival of 56% can be improved by early diagnosis and better monitoring and supportive care of these children in resource-limited settings in LMIC. This also needs increased public and healthcare providers' awareness of the low threshold to suspect nasopharyngeal carcinoma. This is possible by capacity building and training programs for primary and secondary health care providers for childhood cancer warning signs and symptoms.

PO074 / #1421 | Publication Topic: AS05 SIOP Scientific Program / AS05.l Rare Tumours and Histiocytosis

#### MANAGEMENT OF ADVANCED PEDIATRIC UNDIFFERENTIATED NASOPHARYNGEAL CARCINOMA: A SINGLE VOLUME CENTER'S EXPERIENCE, MEDITERRANEAN COUNTRY

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**Background and Aims:** Pediatric nasopharyngeal carcinomas (NPCs) are very rare tumors worldwide. It is the predominant malignancy arising in the nasopharynx in this age group. Although NPC is a chemoradiosensitive disease, the standardized guidelines for diagnosis and management of pediatric NPC are still unavailable. The present study was conducted to ascertain the outcomes of children with locally advanced and metastatic at our center.

**Methods:** We retrospectively analyzed the outcomes of 21 patients newly diagnosed NPC patients with American Joint Committee on Cancer III to IV, younger than 20 years old, from 2017 to 2022. Overall survival (OS) rate estimates and Kaplan–Meier survival curves were calculated.

**Results:** Overall, the median age of the patients was 11 years (range 7.4–17 years), with a sex ratio M/F 13:7. There were 5 patients with stage III, 14 with stage IVA and 2 with stage IVB. Neck mass (38%), nasal obstruction (33.4%), headache (23.8%) were the most common chief complaints. All patients received neoadjuvant chemotherapy with 5FU-cisplatin (3 cycles for stage III and IVA, and 6 cycles for stage IVB), followed by concurrent chemo-radiotherapy with cisplatin. 17 (81%) patients were treated with Intensity-modulated radiotherapy (IMRT). The overall response for stage III and IVA was: 8 patients with complete response (CR), 4 partial response (PR), 3 stability disease (SD), and 2 patients with stage IVA had progressive disease (PD). The 2 patients with stage IVB had PD. With a median follow-up time of 45.5 months, the median overall survival (OS) was 44.47 months (ranged 11–66 months). Radiodermatitis and radio mucositis were the main toxicity, grade I (47.6%) and grade II (23.8%).

**Conclusions:** Metastatic disease at presentation was identified as the adverse prognostic factor. Reducing distant metastasis with new strategies, and late toxicities with intensity-modulated radiotherapy, are the future directions for the treatment of pediatric nasopharyngeal carcinoma.

PO075 / #15 | Publication Topic: AS05 SIOP Scientific Program / AS05.I Rare Tumours and Histiocytosis

#### LANGERHANS CELL HISTIOCYTOSIS IN CHILDREN. CLINICAL PROFILE AND OUTCOME

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**Background and Aims:** Background Langerhans cell histiocytosis LCH in children is a rare entity that involves many organ systems with particular clinical features but serious long-term consequences. **Objectives** This study aims to describe clinical course of LCH and outcome in children, especially in terms of neuro-endocrinal sequel.

**Methods:** A retrospective study including all patients aged less 16 years old initially diagnosed with LCH was performed from January 2005 to December 2022. Patients were staged and treated according

to LCH protocol regimens. Survival rate was studied by Kaplan-Meier method.

**Results:** A total of 27 patients are identified, 13 boys and 14 girls with a median age of 40 months ranging from 8 to 114 ms. Involved sites were skeleton 81.4%, skull especially (82%), liver, spleen, lymph nodes 26%, skin 29.6%. Exophthalmos was present in 26%. Pneumothorax was revealed in one patient while 22% of patients presented with diabetes insipidus. Overall survival is 92.5%, two patients died, the first from progressive disease and the second from a secondary acute lymphoblastic leukemia. Among the remaining patients, 28% developed complications including secondary Haemophagocytic lymphohistiocytosis sHLH (n = 2), learning difficulties and cerebellar ataxia (n = 1), psychiatric disorders (n = 1), epilepsy (n = 1), mandibular fracture (n = 1).

**Conclusions:** Conclusion Langerhans cell histiocytosis is a rare pathology, initial manifestations are classic, but their ignorance remains at the origin of a consequent diagnostic and therapeutic delay.

PO076 / #1711 | Publication Topic: AS05 SIOP Scientific Program / AS05.I Rare Tumours and Histiocytosis

#### MANAGEMENT OF SCROTAL TUMORS IN A LOW INCOME COUNTRY

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**Background and Aims:** Testicular and paratesticular tumors are usually revealed by a scrotal mass. Testicular tumors in prepubertal boys are often benign (60–75%), allowing fertility sparing surgery. Paratesticular tumors in boys are dominated by rhabdomyosarcoma (RMS). Despite their clinical similarity they require different managements and have divergent prognosis. This study aims to underline the benefit of fertility sparing surgery in the treatment of testicular and paratesticular tumors only when evidence of its safety is made.

**Methods:** This is a retrospective, descriptive study, grouping 11 patients managed in our department of pediatric surgery over 10 years, in collaboration with the department of pediatric oncology of our institution.

**Results:** We had managed 11 prepubertal boys. The main symptom was painless scrotal mass with no inflammatory signs. There was no general state impairment nor early pubertal symptoms. Only one patient was operated without ultrasound examination, as he was initially misdiagnosed as cord hydrocele. The average size of the tumor was about 4.2cm [3cm; 6cm]. The alpha fetoprotein (AFP) rate was high in 4 cases: 2 yolk sac tumor (YST), 1 unclassified tumor, and one combined germinal tumor (choriocarcinoma, YST and teratoma). In this last case, we noticed a high rate of chorionic gonadotropin hormone. Tumorectomy was performed in 3 cases. Two of them had

a complementary orchiectomy. There were at final 4 cases of mature teratoma, one case of splenogonadal fusion, 2 cases of YST, one combined germinal tumor and 3 cases of RMS. Two patients with RMS have had a relapse and required intensified chemotherapy, second surgery and autologous stem cell transplantation for one of them. All of our patients are actually in remission.

**Conclusions:** We performed orchiectomy for all our patients but one. organ sparing treatment should have been performed for benign tumors.

PO077 / #1873 | **Publication Topic: AS05 SIOP Scientific Program / AS05.I Rare Tumours and Histiocytosis**

**HISTIOCYTOSIS: A REVIEW OF THE LAST FIVE YEARS IN A TERTIARY REFERRAL HOSPITAL**

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**Background and Aims:** Diagnosing Langerhans cell histiocytosis (LCH) is challenging as it is crucial to have a diagnostic suspicion. They can present at any age despite having a peak incidence between 1 and 4 years. Clinical presentation may present as a mild and auto-limited or a severe form involving many systems and progressing very quickly.

**Methods:** We retrospectively reviewed the pediatric cases with histiocytosis diagnosed between 2018 and 2023 and evaluated them according to age, symptoms, anatomical location, and chemotherapy protocol.

**Results:** We recorded three patients with the diagnosis by histopathology of LCH. They all had a time gap of at least three weeks between the first inpatient consult and the diagnosis. Two patients were three years old and had a unique lesion, one bone skull lesion, and the other one had nodal involvement. Meanwhile, the youngest patient had multiple skin lesions as the initial symptom. Even though the clinical presentations were the most common types, the patients had at least three weeks of delay in the diagnosis. At least three physicians evaluated the patients before getting to the diagnosis. It is important to remark that the youngest patient had the most prolonged delay in diagnosis, with at least five different physicians evaluating him before the diagnosis. The two patients with a single site affected in a single system received treatment with standard chemotherapy protocol, but the youngest patient died after not responding to different chemotherapy lines.

**Conclusions:** As we know, LCH may be a challenging disease to diagnose. However, it is vital to establish protocols for patients with persistent symptomatology, particularly those younger than two years presenting, as they may progress rapidly to high-risk multisystem disease. It is essential to review the approach given to these patients to avoid delays in the diagnosis and treatment.

PO078 / #230 | **Publication Topic: AS05 SIOP Scientific Program / AS05.I Rare Tumours and Histiocytosis**

**PEDIATRIC CLIVAL CHORDOMA: A CASE REPORT**

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**Background and Aims:** Chordoma are very rare bone tumors of the axial skeleton that arise from notochordal remnants. They exhibit locally aggressive behavior and treatment is a challenge because a complete resection is very rare, and response to radiotherapy or chemotherapy is unpredictable.

**Methods:** The authors describe the diagnosis, treatment, and outcome of a pediatric chordoma.

**Results:** A 11-year-old male presented with 6 months of insidious evolution characterized by abdominal pain and reflux, headache, cervical pain, gaze movements impairment, right eye loss of vision and photophobia. A craniospinal MRI was done reporting a non-osteolytic bone tumor located in the anterior portion of the base skull, measured 150.3 × 130.3 mm, with an heterogeneous signal intensity, surrounding both carotids, loss of interface with the pituitary gland, and extension to the lymphoid tissue. No metastatic disease was detected. He underwent an endoscopic transnasal approach with subtotal resection, pathology confirmed a chordoma. Because of the bulk of remnant a second resection was done, leaving a residual tumor around 20 mm. Intensity Modulated Radiotherapy (IMRT) with a total dose of 54Gy was indicated after 60 days post-surgery. As the disease was non metastatic with good local control we decided not give him any chemotherapy. During follow-up of 13 months, he has shown normalization of ocular movements, normal visual evoked potentials, and stable disease on MRI.

**Conclusions:** We highlight the importance of local control for clival chordoma, resection should be attempted even in various steps in order to have the maximal safe resection. Post operative radiotherapy was effective as demonstrated by follow-up MRI scans in this case, although a longer period of follow up should be done.

PO079 / #1029 | **Publication Topic: AS05 SIOP Scientific Program / AS05.I Rare Tumours and Histiocytosis**

**ASSOCIATION OF INFANTILE HAEMANGIOMAS OF CHILDHOOD WITH THE SYNDROME: PHACE SYNDROME**

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**Background and Aims:** PHACE syndrome (posterior fossa anomalies, haemangioma, arterial lesions, cardiac abnormalities/aortic coarctation, ocular anomalies) is a neurocutaneous syndrome characterised by large segmental haemangiomas of the face, neck and/or scalp.

**Methods:** A three-month-old female patient was presented with a haemangiomatic lesion on the right eye margin extending to the eyelid following the detection of a 7.8 × 7.6 mm arcuate aortic aneurysm during prenatal follow-up, after being operated for aortic aneurysm at 1 week postnatally. On physical examination, the patient appeared mildly hypotonic. There was a haemangioma localised on the upper lid and external canthus of the right eye and esotropia and an operation scar on the sternum due to aortic aneurysm. Laboratory tests revealed haemoglobin 9.2g/dL, Hct 28, MCV 80fL, MNS 2220, platelet 696000, Ddimer 535, B12 746.

Superficial tissue USG performed for the lesion area revealed a lesion extending from the right periorbital area to the eyelid level and laterally, reaching 13.1 mm in the widest part of the subcutaneous tissues, accompanied by internal vascularity in Doppler. Cranial MRI revealed developmental volume asymmetry in the posterior fossa, inferior cerebellar hemisphere dysplasia and hypoplasia, filling from the right vertebra, right ICA, right hemisphere and left carotid system. Aneurysmal enlarged structure and arteriovenous malformation were detected, left transverse sinus was hypoplastic.

**Results:** Propranolol was started at a dose of 0.5 mg/kg/day and increased to 1.2 mg/kg/day. No side effects were observed during the follow-up, marked regression of the lesion was observed at the end of the first month and almost complete resolution was found at the end of the fifth month.

**Conclusions:** PHACE syndrome should be considered in patients with large facial segmental infantile haemangiomas (>5 cm in diameter); however, sometimes patients may present with a picture dominated by findings other than haemangioma. Awareness of the components of the syndrome is important. It requires regular multidisciplinary approach due to the involvement of many organs.

PO080 / #1852 | Publication Topic: AS05 SIOP Scientific Program / AS05.m Brain Tumours

#### IMPACT OF THE CREATION OF A MULTIDISCIPLINARY CLINIC ON THE EVOLUTION OF PATIENTS WITH CNS TUMORS IN A DEVELOPING COUNTRY

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**Background and Aims:** As well as the results on epidemiology that were collected from the data obtained from the year 1995 to the year 2020, in the National Medical Center 20 de Noviembre in a total of 236 patients, which were found that the most common brain tumors are low-grade astrocytomas, medulloblastomas and germ cell tumors; the age at which brain tumors occur most frequently in pediatric patients is 6 to 10 years with a total of 80 cases out of the 236 in the study.

**Methods:** A retrospective observational analytical study was conducted and descriptive statistics were used for data analysis.

**Results:** A total of 236 pediatric patients at the National Medical Center were diagnosed with brain tumors of different histologies from 1995 to 2020. According to the distribution by gender, 60.59% (143 cases) of the tumors occurred in men and 39.41% (93) in women. The predominant histologies were low-grade astrocytomas 36.86%, followed by medulloblastomas 25.85%, germline tumors 11.86%, ependymomas 10.16%. The distribution by age group was found as follows: < 1 year: 4 cases, 1 to 5 years: 68 cases, 6 to 10 years: 80 cases, 11 to 15 years: 74 cases, more than 16 years: 10 cases. The distribution by topography was reported according to the affected anatomical site, finding the following: cerebellum 70 cases, cerebral stem 37 cases, optic nerve 4 cases, suprasellar region 37 cases, and others.

**Conclusions:** The creation of a multidisciplinary group that cares for patients with brain tumors in an integral way, has achieved earlier treatment and joint decision-making to seek a better evolution of patients.

It is necessary that patients with brain tumors receive comprehensive and personalized care by the specialties involved, since this improves the quality of treatment and therefore the quality of life.

PO081 / #1650 | Publication Topic: AS05 SIOP Scientific Program / AS05.m Brain Tumours

#### INI1 PROTEIN EXPRESSION DISTINGUISHES DESMOPLASTIC INFANTILE GANGLIOGLIOMA FROM ATYPICAL TERATOID/RHABDOID TUMOR : A CASE REPORT

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**Background and Aims:** Atypical teratoid/rhabdoid tumor (AT/RT) is a rare tumor of the central nervous system (CNS) mostly seen in infants and is often associated with a dismal outcome. Its diagnosis nowadays relies on the negative INI-1 nuclear immunostain in tumor cells which has been suggested as useful marker to distinguish AT/RT from other malignant pediatric CNS tumors.

**Methods:** We present a 5-year-old girl who had desmoplastic infantile ganglioglioma (DIG) misdiagnosed as AT/RT with transformation into glioblastoma, treated in the department of oncological radiotherapy of the Farhat Hached Hospital, Sousse, Tunisia.

**Results:** A 5-year-old female, presented with headaches and strabismus evolving for the last 3 months. The family history was unremarkable. Physical examination revealed no abnormality, with a normal neurological examination and a bilateral grade 3 papilledema. Magnetic resonance imaging (MRI) of the brain revealed a solid/cystic mass measuring 60 × 58 × 47mm with heterogeneous enhancement and severe surrounding brain edema. She underwent a complete resection of the tumor. Histopathology supported the diagnosis of AT/RT, tumor cells were GFAP (+), Desmine (+) and EMA (+). Craniospinal MRI and cerebrospinal fluid (CSF) cytology were negatifs. She underwent chemotherapy alternating Cisplatin-VP16 with cyclophosphamide-vincristin and craniospinal radiotherapy (RT) in a 1.8 Gy fractioning up to a total dose of 36 Gy with a posterior fossa boost of 23.4Gy, using three-dimensional conformal RT. Two months after the end of treatment, craniospinal MRI demonstrated evidence of tumor recurrence. She had a repeat debulking of tumor. Histopathology revealed definite histologic progression of a DIG to high-grade glioma consistent with Glioblastoma. Immunohistochemistry (IHC) was performed showing no loss of INI1 expression. The patient was initiated on temozolomide with tumor progression.

**Conclusions:** This case highlights the pitfalls in diagnosing DIG and the importance of INI1 protein analysis that should be routinely performed in all malignant pediatric embryonal CNS tumors.

PO082 / #1129 | Publication Topic: AS05 SIOP Scientific Program / AS05.m Brain Tumours

#### EVALUATION OF TEMOZOLOMIDE TREATMENT IN CENTRAL NERVOUS SYSTEM TUMORS

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**Background and Aims:** We planned to evaluate the treatment results of our patients with CNS tumors who needed new drugs with Temozolomide (TMZ), an alkylating agent.

**Methods:** In our center, the diagnosis date, age, gender, pathology result, and life expectancy of patients with CNS tumors were recorded. Treatment responses and mean survival times of 27 patients who underwent TMZ were evaluated.

**Results:** Of the 27 patients included in the study, 14 (52%) were male and 13 (48%) were female, with a mean age of 7.8 ± 4 years. High grade glial tumors were detected in 19 (70%) patients who underwent RT+TMZ. Of the 14 patients who received TMZ as adjuvant therapy, 11 died of recurrence after a mean follow-up of 17.4 months (3-40 months), and 3 of them are still under follow-up for the disease for an average of 50 months. TMZ was used in 12 patients (3 medulloblastoma, 1 pinealoblastoma, 1 low-grade glial tumor (DDGT),

7 high-grade glial tumor) with other recurrent CNS tumors. Of the 7 lost patients, 2 received TMZ treatment for relapse, 5 for adjuvant treatment and for relapse. Four patients are disease-free and one patient with DDGT is being followed up with disease. The mean follow-up period of all patients was 27 months (3-85 months), and 17/27 (63%) of the patients died due to progression. Overall survival (OS) was 28.9% and event-free survival (EFS) was 20.6% in all patients.

**Conclusions:** Mortality rates are still very high in high-grade glial tumors and other recurrent brain tumors in patients with CNS tumors. TMZ has not been shown to be effective in improving this poor prognosis.

PO083 / #1148 | Publication Topic: AS05 SIOP Scientific Program / AS05.m Brain Tumours

#### RECLASSIFICATION OF OUR PATIENTS WITH MEDULLOBLASTOMA ACCORDING TO MOLECULAR EVALUATION AND TREATMENT RESPONSES

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**Background and Aims:** Medulloblastoma (MB) has been typified at the molecular level and its prognostic signs have begun to emerge. We reclassified the MB patients we followed in our center and evaluated their response to treatment.

**Methods:** Gender, age, surgery dates, pathology results, risk groups, treatment characteristics, recurrence and death times of medulloblastoma patients were recorded. Patients with missing immunohistochemical staining according to the new pathological classification were reevaluated by pathology.

**Results:** Of 21 patients, 10 (47.6%) were girls and 11 (52.3%) were boys, aged 1-15 years (mean: 6.95). According to Chang's classification, 7 (33%) patients were standard risk and 14 (67%) patients were high risk. The median time to start radiotherapy after surgery was 41 (22-90) days. Recurrence was observed in six (28.5%) patients. 2 patients were in the SHH group without WNT, one patient relapsed at 17 months and the other at 30 months. Three of the four patients died after relapse, and one patient died due to sepsis after radiotherapy without receiving chemotherapy. One of the deceased patients was Neurofibromatosis type 1 and relapsed 41 months after diagnosis. She died 5 months after recurrence. Diagnosed at the age of one, the patient in the non WNT non SHH group has been followed in remission for 3 years with autologous transplantation without receiving radiotherapy treatment. The 5-year overall survival rate (OS) of our patients was 73.4%, while the event-free survival rate (EFS) was 67.9%. OS was 74% and EFS was 63.5% in patients with molecularly non-WNT non-SHH.

**Conclusions:** The results we found in patients with molecular typing are consistent with the literature. More molecular studies and

consolidation in terms of treatment are needed to reclassify the non WNT non SHH group within itself. The search for a biological agent in MB continues.

PO084 / #588 | Publication Topic: AS05 SIOP Scientific Program / AS05.m Brain Tumours

#### MANAGEMENT OF GLIOMAS OF THE OPTIC PATHWAYS IN CHILDREN: EXPERIENCE OF THE PEDIATRIC ONCOLOGY CENTER OF CASABLANCA

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**Background and Aims:** Optic pathway gliomas (OPTs) are generally very low-grade tumors and represent up to 5% of all pediatric CNS tumors.

Despite the high survival rate, treatment and management of these tumors are complex and challenging.

The objective of this work is to evaluate the management of gliomas in children in our institution

**Methods:** This is an observational and retrospective study on OPGs cases diagnosed in patients under 18 years old, from January 2017 to December 2021.

Their diagnosis was retained by imaging +/- anatomopathological study, treated by surgery, chemotherapy, and radiotherapy.

Evaluation was done by brain +/- orbital MRI.

**Results:** We retained 10/30 cases of OPGs, i.e., 34% of the overall series. Sex ratio (M/F) was 2.3 and median age was 8 years [3-14 years]. One patient had neurofibromatosis type 1; the rest had no pathological history. The most frequent mode of revelation was visual disorders (60%), then seizure, hemiplegia or HTIC syndrome in other cases. Median evolution before first consultation was 6 months [1-24 months].

Clinical examination revealed: diplopia in 4 patients, exophthalmos in 3 patients, café au lait spots in 2 patients and ptosis associated with nystagmus in 1 patient.

The diagnosis was retained on cerebral MRI in all patients. Extension to optic nerve was found in 4 patients (40%) and to pituitary gland in 1 patient (10%). The presence of unidentified white objects (UBO) was observed in 1 patient. One patient underwent a partial exeresis with anatomopathological study.

Nine patients received chemotherapy according to the SIOP LGG 2004 protocol, and 1 patient died at the time of diagnosis. Two patients received radiotherapy.

Two patients, are in complete remission, 3 patients were in progression, 3 patients died and 1 patient was lost to follow-up during his therapeutic sessions.

**Conclusions:** Delayed diagnosis and advanced stages make OPGs in children a pathology with relatively poor survival.

PO085 / #589 | Publication Topic: AS05 SIOP Scientific Program / AS05.m Brain Tumours

#### THERAPEUTIC EVALUATION OF MEDULLOBLASTOMA CASES IN PEDIATRIC ONCOLOGY AT THE 20TH AUGUST 1953 HOSPITAL

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**Background and Aims:** Medulloblastoma is the second most common type of CNS tumors in children, accounting for 20% of total population. Children with medulloblastoma can experience a wide range of functional problems due to clinical stigma and complications of its treatment.

**Methods:** This is a retrospective observational study that included patients under 18 years old, over a period from January 2017 to December 2021.

Their diagnosis was made by imaging and/or anatomopathological study, treated with chemotherapy and radiotherapy. The evaluation was clinical and radiological by brain MRI.

**Results:** We retained 10 cases of medulloblastoma, i.e. 34% of the total series. Males were the most affected with a sex ratio (M/F) of 4. The median age was 8 years [2-10]. The median duration of evolution was 7 months [1-23 months]. The most frequent mode of onset was intracranial hypertension syndrome with a rate of 80%. Five patients had normal clinical examination; cerebellar syndrome was present in 3 patients, tetraplegia and central facial paralysis in 1 patient respectively.

40% of the tumors were located in PCF, and 60% on the sub tentorial level.

Medulloblastoma was associated with active hydrocephalus in 80%. One patient had occipital involvement. The leptomeningeal contrast was observed in 4 patients and extension to suprasternal level in 1 patient classifying them in high grade category. The CSF study was performed in 5 patients, returned positive in 1 patient and negative in 4 patients.

Three patients had a total removal of the tumor and 2 patients a surgical biopsy.

All patients received chemotherapy except for 1 patient who dropped out of follow-up. Seven patients received radiotherapy.

78% are in complete remission and 22% had progressed under chemotherapy and consequently under palliative treatment.

**Conclusions:** Medulloblastomas are heterogeneous tumors in their clinico-radiological characteristics. Their prognosis is conditioned by local and metastatic extension and its degree of surgical resection.

PO086 / #475 | Publication Topic: AS05 SIOP Scientific Program / AS05.m Brain Tumours

#### EPIDEMIOLOGICAL, CLINICAL, HISTOLOGICAL AND RADIOLOGICAL PROFILE OF PEDIATRIC CNS TUMORS

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**Background and Aims:** Up to 25% of solid tumors in pediatrics are CNS neoplasms, which are also leading cause of cancer mortality in children.

The objective of this study is to evaluate epidemiological, clinical, anatomopathological and radiological characteristics of pediatric brain tumors in pediatric oncology unit of Casablanca

**Methods:** This is an observational and retrospective study that included all cases of malignant central nervous system tumors detected in pediatric patients, from January 2017 to December 2021. they were confirmed by CT, MRI or biopsy with anatomopathological study.

**Results:** We identified 30 cases of malignant brain tumors, with a sex ratio (M/F): 2 and a median age of 7 years [2-15 years];. We found 1 case of neurofibromatosis type 1 and 1 case of neoplasia in ancestry. The most frequent mode of revelation was the HTIC syndrome (47%), followed by visual disorders (34%), seizures (20%), endocrine disorders (6%), hemiplegia (6%) and cranial pair involvement in 1 patient (4%). The median evolution before the first consultation was 6 months [1-60 months].

Clinically, diplopia was found in 7 patients, exophthalmos in 3 patients, cerebellar syndrome in 6 patients, café au lait spot in 3 patients, 2 patients with ptosis, aphasia in 2 patients; neurological signs such as pyramidal syndrome, tetraplegia, hyperpiloisity, facial paralysis and hemiplegia were detected.

The tumors located in the subtentorial level were 70%, in the supratentorial stage 14 % and 16% in chiasma and optic tract. Five patients were diagnosed by surgical biopsy with anatomopathological study.

we found : medulloblastoma (34%), optic tract glioma (34%), ependymoma (10%), germinoma (7%), glial tumor (3%), xantho-astrocytoma

(3%), medullo-epithelium (3%), atypical rhabdoid teratoid tumor (3%), astrocytoma (3%)

**Conclusions:** On a practical level, the results obtained do not reflect the reality of the overall incidence in the region, due to delay in diagnosis or the rapid worsening.

PO087 / #292 | Publication Topic: AS05 SIOP Scientific Program / AS05.m Brain Tumours

#### OUTCOMES AND ABANDONMENT RATES OF DIFFUSE INTRINSIC PONTINE GLIOMA IN A SUPER-SPECIALITY SETUP IN NORTHERN INDIA

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**Background and Aims:** Diffuse intrinsic pontine glioma (DIPG) presents as cranial neuropathies, long tract signs and ataxia, with a median survival of less than 1 year in most of the cases. We describe our outcomes and abandonment analysis of DIPGs at our institution.

**Methods:** We retrospectively analysed data from the last decade from 2010 to 2020, and patients suffering from diffuse intrinsic pontine glioma were evaluated.

**Results:** A total of 15 patients were analysed. Patients belonged to age group of 5.1 to 10 years and 10.1-15 years which constituted 33.33% (5/15) of cases. Male:Female ratio was 0.66:1. Country of origin was India in 73.33% (11/15). Patients presented with increased ICP and Cranial nerve deficits in 33.33% (5/15). Biopsy could be performed in 1 patient which resulted in grade III. None of them had metastasized. Only 1 patient underwent gross total resection and VP shunt could be placed in 20 % (3/15) of patients. Three patients abandoned treatment before starting radiotherapy 20% (3/15). Number of patients who completed radiotherapy were 11/15 (73.33%) and one abandoned during the course of radiotherapy. Among the patients who continued treatment-Temozolamide (TMZ) and Radiotherapy regimen was given in 33.33% (4/12) of cases. The radiotherapy alone was used in 13.33% (2/12) of cases. The other regimen used were Adjuvant Temozolamide (TMZ) Post Radiotherapy (RT), Concurrent TMZ+ RT, Adjuvant TMZ and TMZ only with each constituting 8.33% (1/12) of cases. Most common response after radiotherapy was progressive disease 40% (6/15) followed by stable response 20% (3/15) followed by minimal response 13.33% (2/15) and partial response in one. Number of patients that relapsed or had a progressive disease among those who did not abandon treatment was 83.33% (10/12). Loss to follow-up after completion of treatment due to relapse was (1/12) 8.33%. Median survival of all patients who completed treatment was 0.750 (95% CI- 0.665-0.835) years. Overall median survival of the entire cohort was 0.750 years (0.598-0.902).

**Conclusions:** Treatment abandonment combined with poor outcomes is a major hurdle to improving survival in diffuse intrinsic pontine glioma in the developing world.

PO088 / #308 | Publication Topic: *AS05 SIOP Scientific Program / AS05.m Brain Tumours*

### OUTCOMES AND ABANDONMENT RATES OF MEDULLOBLASTOMA IN A SUPER- SPECIALITY SETUP IN NORTHERN INDIA

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**Background and Aims:** Medulloblastoma is most common malignant brain tumor in children, and has a tendency to disseminate via the cerebrospinal fluid (CSF). We describe our outcomes and abandonment analysis of medulloblastoma at our institution.

**Methods:** A retrospective review of the patients electronic health record suffering from medulloblastoma was compiled from last decade (2010-2020) and was analyzed.

**Results:** A total of 26 patients were analysed. Most of the patients belonged to age group of 5.1 to 10 years 53.8%(14/26). Male:Female ratio was 5.5:1. Country of origin was India in 76.9%(21/26). Patients presented with increased intracranial pressure in 80.76%(21/26). Patients who underwent surgery were 96.15%(25/26). One patient abandoned prior to the surgery (3.8%). Gross total resection was feasible in 64%(16/25), near total in 24%(6/25). VP shunting was done in (7/25) 28% of patients. Patients who abandoned treatment prior to radiotherapy 57.69%(14/26) . One patient abandoned during the course of radiotherapy 4%(1/25). Number of patients who underwent surgery and completed full course of radiotherapy were 44%(11/25) Patient lost to follow-up who completed full course of radiotherapy was 18.18%(2/11). Patients who received packer regimen was 63.63%(7/11) and 18.18%(18.18%) of patients received SJMB protocol. Patients who completed treatment was 34.61%(9/26). Incidence of relapse in the patients who completed treatment was 77.77%(7/9). Number of patients that completed treatment and died of relapse was 11.11%(1/9). The median survival of the patients who completed treatment was 4.66 years until the last follow-up. The mean survival of the patients who completed treatment until the last follow-up was 3.360 years (95%CI-1.946-4.774).

**Conclusions:** Treatment abandonment combined with poor outcomes is a major hurdle to improving survival of medulloblastoma in the developing world.

PO089 / #345 | Publication Topic: *AS05 SIOP Scientific Program / AS05.m Brain Tumours*

### CHILDHOOD ASTROCYTOMAS - OUTCOMES AND ABANDONMENT ANALYSIS FROM A SUPER- SPECIALITY SETUP IN NORTHERN INDIA

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**Background and Aims:** Astrocytomas are a form of glioma; can be indolent or aggressive, depending on tumor grade, which drives prognosis and clinical decision making. We describe our outcomes and abandonment analysis of astrocytoma at our institution.

**Methods:** A retrospective analysis of the electronic health records of patients from 2010 to 2020 was done and patients suffering from astrocytoma were analysed.

**Results:** A total of 30 patients were analysed. Most of the patients belonged to age group of 5.1 to 10 years and constituted 40%(12/30) of the patients . Male:Female ratio was 3.28:1. Country of origin was India in 70%(21/30). Patients presented with increased intracranial pressure in 46.66%(14/30). Most commonly the location was infratentorial 50%(15/30). Metastasis occurred in 3.33%(1/30). All patients underwent surgical resection. Grade I tumor was most common and constituted 53.33%(16/30) and grade IV tumors were 10%(3/30). Gross total resection was feasible in 50%(15/30) of patients. A total of 96% (29/30) of the patients received radiation. Overall 33.33%(10/30) completed radiotherapy. One patient abandoned during the course of radiation 3.33%(1/30). Patients who had complete response to radiation and surgery was 23.33%(7/30) . Stable response occurred in 20%(6/30) and progressive disease occurred in 13.33% (4/30). Total number of patients suffering from astrocytoma that abandoned treatment were 30%(9/30). The median survival of the all patients until the last followup 5.6 years (95%CI- 0–11.703).

**Conclusions:** Treatment abandonment combined with poor outcomes is a major hurdle to improving survival in astrocytoma in the developing world.

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### THE CLINICAL FEATURES REMAIN THE MOST IMPORTANT PART: POLYGLLOBULIA AS THE LEADING SYMPTOM OF PITUITARY ADENOMA

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**Background and Aims:** Cushing syndrome is rarely seen in children and adolescents (only 10–15% of cases in the pediatric age). When caused by an endogenous glucocorticoid overproduction, it is most frequently secondary to an ACTH-producing pituitary microadenoma (Cushing disease). In children, Cushing disease usually presents as a decrease in growth rate due to the steroids direct effect on bone epiphyses. Other symptoms are weight gain, hydric retention and osteopenia. Hematologic alterations are not usually the main complaint in pediatric consultation. Moreover, some hematologic aberrations may indicate underlying endocrine disorders. Polyglobulia is associated with Cushing syndrome secondary to decreased erythrophagocytosis caused by glucocorticoid excess and stimulation of erythropoietin synthesis or positive regulation of erythropoiesis. It occurs more frequently among women due to the less important role of testosterone in the erythropoiesis regulation.

**Methods:** A literature review based on a case study.

**Results:** An 11-year-old girl was referred for polyglobulia as an incidental finding during an endocrinological follow-up for growth stagnation. She referred to occasional headaches, and presented stop ingrowth rate, facial plethora, overweight (+4 kg in one month), hirsutism, and abdominal and upper limb striae. Based on clinical symptoms and in the context of polyglobulia differential diagnosis, a complete endocrinological study was performed with growth factors, hormones including ACTH, celiac screening, SHOX gene study, 24-hour urine cortisol and abdominal ultrasound, within normal limits. The first cranial magnetic resonance imaging (MRI) and abdominal MRI in September 2022 were normal; no pituitary ACTH-producing tumors or adrenal adenomas were found. However, Cushing disease justifying the symptoms was confirmed by a dexamethasone suppression study so, although the MRI was negative, we did not abandon the etiologic search and repeated the cranial MRI three months later where a microadenoma was finally visualized.

**Conclusions:** Complementary tests should support the clinical diagnosis, being signs and symptoms the guide and basis of any medical diagnosis.

PO091 / #221 | Publication Topic: *AS05 SIOP Scientific Program / AS05.m Brain Tumours*

#### CLINICAL FEATURES AND LONG-TERM OUTCOMES OF PEDIATRIC MENINGIOMAS AT A SINGLE CENTER IN MEXICO

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**Background and Aims:** Meningiomas are rare in children, accounting for 1–2% of pediatric CNS tumors. In addition, they exhibit a somewhat different clinical spectrum and pathological findings compared with adult cases. Pediatric meningiomas usually have larger sizes and unusual localizations

**Methods:** A retrospective study was done in order to identify the demographics, clinical characteristics, treatment and survival of pediatric cases diagnosed with meningioma from 2006 to 2021 at Hospital Civil Juan I. Menchaca, Guadalajara, Mexico

**Results:** Six cases were identified: 4 girls and 2 boys with a mean age of 9.5 years. Symptoms had an insidious onset around one-year before diagnosis in all cases. The most common symptoms were seizures, headache, and ocular manifestations. One case with a tumor at the pterygopalatine fossa presented with dysphonia. Three had raised intracranial pressure at diagnosis. Brain MRI revealed extensive extra-axial masses, range from 3.1 × 4.7 cm to 7.5 × 5.5 cm. Tumor location was intracranial in 5 cases (4 left parietal, 1 occipital) and 1 intra and extracranial located at petroclival region and pterygopalatine fossa. The histopathological features were three transitional, one atypical, one fibrous and one rhabdoid. Treatment consisted in complete resection in 4 cases, and 2 cases with incomplete resection received radiotherapy doses of 50 and 54 Gy. One case recurred after 3 years from the diagnosis and received a 2nd surgery, this case was not completely resected in the first line of treatment. None had clinical evidence of neurofibromatosis type 2. The mean follow-up period was 43 months, overall survival was 100% and event-free survival was 83.3%.

**Conclusions:** Although our series is small, we can conclude that prognosis was excellent after complete resection and no need of radiotherapy, but the clinical course must be carefully observed specially in partial resected tumors for possible long-term tumor recurrence.

PO092 / #269 | Publication Topic: *AS05 SIOP Scientific Program / AS05.m Brain Tumours*

#### NEUROCYSTICERCOSIS MIMICKING A PEDIATRIC HIGH-GRADE GLIOMA: A CASE REPORT

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**Background and Aims:** Cysticercosis is currently considered the most common helminthic infection of the nervous system and a cause of acquired epilepsy in many low- and middle-income countries.

Neuroimaging findings of neurocysticercosis can be nonspecific and may be seen in other diseases of the nervous system.

**Methods:** Report case

**Results:** A previously healthy 9-year-old Hispanic male presented with decreases strength of the left leg and a month later had a seizure. The MRI showed a single intra-axial heterogeneous mass in the right parietal lobe, measuring  $3.5 \times 3 \times 2.8$  cm. The lesion showed restricted diffusion, annular enhancing to gadolinium, and peripheral tumor edema. The main suspicion was a high-grade glioma. Physical exam was consistent with left hemiparesis. He received a complete resection of the mass. The histopathologic analysis surprisingly demonstrated giant cells, larvae and inflammatory component establishing the diagnosis of neurocysticercosis. He received anti-helminthic treatment and at follow up of 20 months he is seizure free.

**Conclusions:** Neurocysticercosis must be considered in the differential diagnosis of brain tumors in endemic regions and we must be aware of its imaging appearance.

PO093 / #716 | Publication Topic: AS05 SIOP Scientific Program / AS05.m Brain Tumours

#### TREATMENT OF DIFFUSE INTRINSIC PONTINE GLIOMA AT A SINGLE INSTITUTION IN MEXICO

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**Background and Aims:** Patients with diffuse intrinsic pontine glioma (DIPG) have dismal prognosis and palliation is essential.

**Methods:** Clinical features, treatment, and outcomes of DIPG at "Hospital Civil de Guadalajara Dr Juan I. Menchaca" were described. The cohort was divided in two time intervals: 1999–2010 and 2011–2021 based on the establishment of a multidisciplinary neuro-oncology team in 2011

**Results:** From 1999–2010, 26 patients were identified (median age of 5 years). The median duration of symptoms was 67.5 days prior to diagnosis. Initial imaging was CT in 5 and MRI in 23 cases. Biopsy was performed in 3 cases. Twenty three patients received radiotherapy (RT: 54 to 60 Gy) at mean of 40.5 days from diagnosis. Five patients didn't received RT due to premature death or refusal. Chemotherapy before RT was used in 11 patients, during RT in 9 patients, after RT in 23 patients. ICE chemotherapy was the most frequent regimen. The median survival was 7.5 months. Four patients died of treatment-related infections. Palliative care at diagnosis was offered in 29% of patients. From 2011–2021, 26 cases were identified (median age of 7.2

years). The onset of symptoms had a median of 69.26 days. Diagnostic imaging was MRI in all cases. Biopsy was performed in 3 cases. 23 patients received RT (46 to 56 Gy) at mean of 41 days from diagnosis. Chemotherapy before RT was used in 16, during RT in 13, and after RT in 18 patients. Bevacizumab/irinotecan/TMZ was the most common regimen. Median survival was 10 months, with no deaths from toxicity. In this cohort 90% of cases had palliative care from diagnosis

**Conclusions:** With the establishment of a multidisciplinary team, treatment for patients with DIPG was de-escalated leading to less treatment-related deaths and palliative care involvement was more prevalent.

PO094 / #633 | Publication Topic: AS05 SIOP Scientific Program / AS05.m Brain Tumours

#### DIAGNOSIS AND TREATMENT OF INTRACRANIAL GERM CELL TUMORS AT CHILDREN'S HOSPITAL 2

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**Background and Aims: Objective:** Intracranial germ cell tumors (IGCTs) are a rare type of tumor that commonly affects children and young adults. IGCTs are classified into germinomas, non-germinomatous germ cell tumors (NGGCTs), and mixed germ cell tumors. The objective of this study is to describe the clinical presentation, treatment, and outcomes of pediatric IGCTs at the Children's Hospital 2 in Vietnam

**Methods:** An retrospective analysis of 14 patients diagnosed with IGCTs at the Children's Hospital 2, Vietnam, from May 2020 to May 2022.

**Results:** Of the 14 patients, the incidence is around 3.5 times higher in male than in female. The median age was 10.5 years old  $\pm$  2.6. The median time from symptom onset to first course of chemotherapy was 41 days  $\pm$  3.2 days. The predominant presenting symptom was headache (50%), followed by early precocious puberty (14%) and diabetes insipidus (14%). IGCTs were most commonly found in the pineal gland (43%), followed by the pituitary region (36%). The two main common pathologies were Non-germinomas (57.1%) and Germinomas (42.9%). Eight patients underwent partial (5/14) or total (3/14) resection, and all patients received the modified chemotherapy protocol of Société Internationale d'Oncologie Pédiatrique Central Nervous System Germ Cell Tumor II (SIOP CNS GCT II). Eight patients received radiation therapy. The progression-free survival rate was 57%.

**Conclusions:** This study provides insight into the clinical presentation, treatment, and outcomes of pediatric IGCTs at the Children's Hospital 2, Vietnam. The diagnosis of IGCTs can be challenging due to their rarity and the variability of clinical symptoms. IGCTs require multimodal treatment coordination of many departments, including chemotherapy, surgery, and radiation therapy. Further studies are needed to explore the long-term outcomes of pediatric IGCTs in low-income countries

PO095 / #1226 | Publication Topic: AS05 SIOP Scientific Program / AS05.m Brain Tumours

#### OVERALL SURVIVAL ANALYSIS OF MEDULLOBLASTOMA PATIENTS TREATED BY POST-OPERATIVE CRANIOSPINAL IRRADIATION: RETROSPECTIVE STUDY

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**Background and Aims:** Long term disease free survival after surgery and radiotherapy has been reported around 60–70% in medulloblastoma patients. Aim of the study is survival analysis of medulloblastoma patients treated with post-operative craniospinal irradiation (CSI) with or without concurrent chemotherapy.

**Methods:** Out of fifty six evaluable patients (between 2015–2020), thirty nine patients were eligible for the study. All 39 patients completed treatment according to standard protocol. Radiotherapy prescription dose was according to standard or high risk stratification. Statistical analysis was done using Statistical Package for Social Science software version 21 and survival curves were constructed using the Kaplan meier method.

**Results:** Out of 39 patients [26 pediatric (<= 16 years), 13 adults (> 16 years)], 11 patients were female and 28 patients were male. Median age of presentation was 9 years (range 3–16 yrs) in pediatric and 25 years (range 17–44 years) in adult population. In pediatric group, 20 (52.6%) and 6 (15.7%) patients were in standard and high risk category respectively. In adult group, 7 (18.4%) and 5 (13.1%) patients were in standard and high risk category respectively. 6 patients and 1 patient died in pediatric and adult age group respectively. With the median follow up of 10 months in pediatric group (range 0–58 months), overall survival was 76.9% (20/26). With the median follow up of 29 months in adult group (range 3–78 months), overall survival was 92.3% (12/13). With the median follow up of 17 months, overall survival was 85.2% [(16/20 (80%) pediatric), 7/7 (100%) adult] and 72.7% [(4/6 (66.7%) pediatric), 4/5 (80%) adult] in standard and high risk groups respectively in combined group. The difference in overall survival was not statistically significant in view of risk category (p-value = 0.432).

**Conclusions:** Our follow up is very short but results are convincing. For pediatric population, more stringent counselling of parents and follow-up is necessary.

PO096 / #352 | Publication Topic: AS05 SIOP Scientific Program / AS05.m Brain Tumours

#### POSSIBILITIES OF EMBRYONAL BRAIN TUMORS VISUALIZATION IN CHILDREN AND COMPARISON WITH MOLECULAR CLASSIFICATION

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**Background and Aims:** Our aim is to identify specific signs of embryonal tumors (ET) in accordance with the molecular classification using standard and advanced magnetic resonance imaging (MRI).

**Methods:** We analyzed MRI results in 304 children with ET. All tumors were evaluated by the following criteria: localization, clarity of contours, structure, presence of perifocal edema, volume of contrast enhancement in the tumor, metastases, and MR-spectroscopy for specific metabolite search.

**Results:** Medulloblastoma were diagnosed in 228 (75.0%) patients. The majority of cases were characterized by a solid tumor with cysts, some of them with calcifications and hemorrhages. The contrast pattern varied from 25% to 75% of the tumor volume. In 45 cases (19.7%), metastases were detected in the substance and along the membranes of the brain and spinal cord. An atypical teratoid-rhabdoid tumor was determined in 46 (15.1%) patients like heterogeneous tumor, with calcifications, hemorrhages, necrosis, and cysts, and 50–70% of the tumor volume was contrasted. In 8 cases (17.4%), craniospinal leptomeningeal metastasis was determined. ET with multilayer rosettes was detected in 23 (7.6%) cases. A large solid tumor was determined supratentorially, with single calcifications in some cases. In 3 cases (13.0%), a multicystic structure was observed, and less than 25% of the tumor volume was contrasted. CNS neuroblastoma was detected in 6 (1.9%) patients, presenting as a cystic-solid tumor. The solid component had areas of necrosis. After contrast, a non-uniform increase in the MR signal was observed, ranging from 25% to 75% of the tumor volume. All tumors had clear contours, mild and moderate perifocal edema and diffusion restriction. On MR spectroscopy, a high peak of Choline and the ratio of Choline/Aspartate were detected, while the presence of specific metabolite (Taurine) was observed only for medulloblastoma.

**Conclusions:** ET CNS has characteristic features of MR morphology? so studies towards a narrower differential diagnosis of the ET using radiogenetics can help oncologists.



PO097 / #1326 | Publication Topic: AS05 SIOP Scientific Program / AS05.n New Drugs/Experimental Therapeutics

### KAPOSIFORM HEMANGIOENDOTHELIOMA AND REFRACTORY KASABACH-MERRITT PHENOMENON TREATED WITH SIROLIMUS

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**Background and Aims:** Kaposiform haemangioendothelioma (KHE) is a rare benign vascular tumor, that infiltrates soft tissues aggressively. Kasabach-Merritt phenomenon (KMP) occurs in 42–71% of KHE cases. It is a life threatening disseminated intravascular coagulation (DIC) with thrombocytopenia, hypofibrinogenemia and high risk of bleeding. We present a case of neonatal KHE treated successfully with sirolimus who failed to respond to propranolol, steroid and vincristine.

**Methods:** A female newborn presented with a reddish-purplish swelling on her left axillary and upper chest area. Her hemoglobin level was 6,5 g/dL, platelet count 38 10<sup>3</sup>/ml, fibrinogen level 65 mg/DI and very high free fibrin products consistent with DIC. Ultrasound examination revealed a mass on the left abdominal wall which was rich in blood flow, suggesting a vascular tumor. The patient had the diagnosis of KHE with KMP.

**Results:** Various combination therapies including prednisolone, propranolol and vincristine were administered without any response and had to be transfused several times with fresh frozen plasma, cryoprecipitate, and platelets. Eight weeks later, sirolimus therapy with off-label use was started. After 30 days of sirolimus administration, the coagulation profile improved. At the end of 15 months, thoracic mass regressed significantly. Treatment was stopped at 18 months of time and no toxicity was experienced.

**Conclusions:** Sirolimus is a safe and effective treatment option in refractory KMP that can prevent life-threatening complications.

PO098 / #638 | Publication Topic: AS05 SIOP Scientific Program / AS05.n New Drugs/Experimental Therapeutics

### USE OF ALPELISIB IN PIK3CA-RELATED DISORDERS IN CHILDREN

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**Background and Aims:** PIK3CA-related disorders are rare, benign but often morbid conditions managed by oncologists in a multidisciplinary setting involving interventional radiologists, surgeons and dermatologists. Previously, medical therapeutic options are limited. With the identification of the causative PI3K/AKT/mTOR pathway, the use of pharmacological inhibitors of the pathway has been a game changer in the management of these complex patients. Alpelisib is an inhibitor of PI3K and has been used successfully on PIK3CA-mutated breast cancer. We describe the use of alpelisib in paediatric PIK3CA-related non-oncologic disorders in our centre.

**Methods:** Three children, aged 2 to 8 years old, were given alpelisib on a compassionate managed access program for proven PIK3CA-mutated CLOVES (Congenital Lipomatous Overgrowth, Vascular anomalies, Epidermal nevi, Skeletal anomalies), giant VLM (Venolymphatic Malformation) and KTS (Klippel-Trenaunay Syndrome). All children were treated previously with multiple therapies including sclerotherapy, surgery and oral sirolimus, an mTOR inhibitor, with variable success.

**Results:** Mean duration of treatment was 12.3 months, ranging from 1 to 30 months. Response is demonstrated in the significant reduction of rectal bleeding episodes for the child with KTS and the reduction in size of the lipomatous tumours in the child with CLOVES. For the child with VLM, duration of treatment is too short to assess effect. Adverse effects include mucositis and diarrhoea, necessitating a reduction in dose or temporary cessation of the medication. No hyperglycaemia was demonstrated. Therapy is still ongoing.

**Conclusions:** Alpelisib is tolerable and is showing promise in the management of PIK3CA-related disorders in children in our centre. Oncologists are well-placed to use familiar oncological principles of molecular diagnosis and targeted therapy to treat this group of non-oncologic but no less morbid conditions with a shared molecular pathogenesis.

PO099 / #1145 | Publication Topic: AS05 SIOP Scientific Program / AS05.n New Drugs/Experimental Therapeutics

### TRAMETINIB THERAPY FOR CHILDREN WITH NEUROFIBROMATOSIS TYPE 1 AND PLEXIFORM NEUROFIBROMA

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**Background and Aims:** Plexiform neurofibromas (PNF) are benign nerve sheath tumors occurring in patients with neurofibromatosis type 1 (NF-1). These lesions may cause refractory pain, organ dysfunction due to compression, neurological deficits, cosmetic issues or deformity, and mortality. Treatment with mitogen-activated protein kinase (MEK) inhibitors, such as selumetinib and trametinib, has demonstrated benefit for these tumors, resulting in an alternative to repeated debulking surgery and another ineffective medical treatment. The aim is to report

a single Pediatric Oncology Unit experience in the use of trametinib as monotherapy, in patients (p) with PNF and NF-1

**Methods:** retrospective review of clinical records of p with PNF/NF-1 treated with trametinib at Hospital de Niños Ricardo Gutierrez, from January 2017 to December 2022. Trametinib Dose: 0.025 mg/kg/day

**Results:** Six patients with PNF/NF-1 receive trametinib (5 head and neck - 1 paraspinal-, 1 paraspinal and retroperitoneal). Median age at the start of treatment was 12 yrs. old. Two females. Median of previous medical treatment lines: 1 (0-3)-conventional chemotherapy, imatinib. Four partial resection surgery was attempted in three patients. Median time of treatment with trametinib :12 mo. (Range 4 - 24). All patients achieved clinical response, with partial remission by RECIST ( $\geq 30\%$ ), measured by MRI Three patients underwent partial resection post treatment and improve the quality of life. The patient treated due to refractory pain resolved it with a sustained response. One patient progressed and began treatment with selumetinib Toxicities: dermatological Grade1- : 6p, CPK increased with normal troponin: 1pp

**Conclusions:** Trametinib is a useful alternative in patients with PNF/NF-1 with deformities where initial surgery cannot be performed, or with refractory pain. Toxicity was acceptable. Defining the duration of treatment is a future challenge. Selumetinib, currently not available in Argentina, will be soon approved and could improve the results in this population based on published evidence.

PO100 / #637 | Publication Topic: AS05 SIOP Scientific Program / AS05.n New Drugs/Experimental Therapeutics

### MEK INHIBITION FOR CHILDREN WITH INOPERABLE PLEXIFORM NEUROFIBROMAS IN NEUROFIBROMATOSIS TYPE 1 - REAL-WORLD EXPERIENCE FROM HONG KONG

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**Background and Aims:** Plexiform neurofibromas (PNs) are infiltrative and debilitating neoplasms that occur in up to half of patients with Neurofibromatosis Type 1 (NF1). For lesions that are inoperable, MEK inhibition has been shown to be an effective strategy for achieving disease control. As real-world data is scarce, here we present our experience in treating NF1-associated PNs using MEK inhibitors in Hong Kong.

**Methods:** Retrospective review on pediatric NF1 patients with symptomatic, inoperable PNs treated with MEK inhibitors in Hong Kong. Since 2021, treatment was based on either selumetinib (compassionate-access program) or trametinib (off-label use) in two Institutions. Clinical, genetic and radiological data were collected.

**Results:** Thirteen patients with genetically confirmed NF1 (including 1 with mosaic disease) were started on MEK inhibitors (5 males, 8 females) at the median age of 7.5 years (range: 3.5-18.5). Selumetinib was used in 11 patients and trametinib in 2. The index lesions were located in the trunk/paraspinal region for 10 patients, head and neck area in 2, and limb in 1. Primary symptoms that led to treatment initiation included disfigurement (n = 8), pain (n = 7), motor impairment (n = 2), neuropathy (n = 1) and interference with mastication (n = 1). After a median treatment duration of 12 months, tumor size reduction was noted in 5 patients (38%; by imaging in 4, by clinical examination in 1), whereas the remaining patients had stable disease. Drug-related toxicities included cutaneous eruption in 6 (46%, 2 required dose reduction), alopecia in 2, and asymptomatic increase in creatine kinase in 2 (dose reduction in 1).

**Conclusions:** MEK inhibitors are effective in treating NF1-associated PNs, and side effects are manageable. Questions that remain to be addressed include the optimal duration of therapy, the role of treatment in pre-symptomatic lesions, and strategies to facilitate drug access.

PO101 / #1739 | Publication Topic: AS05 SIOP Scientific Program / AS05.o Tumor Biology, Immunology and Immunotherapy

### IDENTIFYING CANCER PREDISPOSITION SYNDROME IN CHILDREN. THE ROLE OF THE PEDIATRIC ONCOLOGIST

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**Background and Aims:** Childhood malignancies are rare, with environmental exposures and lifestyle habits playing minor roles on their development. The evolution of next-generation sequencing and the discovery of new variants have increased awareness of the heritable genetic factors involved in childhood cancers. Up to 10% of childhood tumors, according to different studies, are caused by germline mutations, in the context of cancer predisposition syndromes (CPS). The early detection of these syndromes by pediatric oncologists may be beneficial in order to determine optimal treatments, and follow-up, to

manage conditions specific to the syndrome (not related to the oncological process) and to provide appropriate genetic counseling to the family.

**Methods:** In this single-center study, we provide our experience in the last years to detect cancer predisposition syndromes in a pediatric oncology unit. We select aleatory oncologic patients that have already finished their treatment. We performed in those who met any clinical or familiar criteria, a whole exome sequencing panel that included 110 genes that are frequently mutated in CPS.

**Results:** Fifty post-treatment patients were randomly selected for a specific appointment to study familial cancer. Of these, 44 patients were determined to be eligible for genetic testing. We have detected in 20% of these, a genetic cause that may justify the clinical picture they present.

**Conclusions:** We highlight the importance of dedicating a specific appointment with families to detect patients who may have a cancer predisposition syndrome.

PO102 / #119 | Publication Topic: AS05 SIOP Scientific Program / AS05.p Supportive Care and Palliative Care

#### CHALLENGES IN A CASE OF HEPATO-SPLENIC CANDIDIASIS - AN OVERLOOKED CAUSE OF PROLONGED FEVER IN PEDIATRIC IMMUNOCOMPROMISED HOST

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**Background and Aims:** Hepatosplenic candidiasis (HSC) is a rare complication occurring after a prolonged period of neutropenia, mainly in the context of hematological malignancies. The diagnosis may be challenging and relies on clinical, biological and radiological considerations.

**Methods:** A 5-year-old female presented with one month duration of pancytopenia. Bone marrow Aspirate showed ALL pre-B phenotype. On Day 7 chemotherapy, the patient was febrile neutropenic. The fever pattern did not improve after couple of days. On Day 5 fever neutropenia, Initiated Empiric Liposomal amphotericin-B (3mg/kg/day), fungal screening imaging was free. The patient developed right hypochondrial tenderness. Serial galactomannan and peripheral blood culture was negative. CT abdomen and pelvis with contrast revealed: Hepatomegaly with hypo dense focal lesions. Liposomal amphotericin B (Duration: 13 days) was shifted to Caspofungin. Candida mannan was done positive: 90 pc/ml (Normal Reference < 62 pc/ml), No available b D-glucan, fungal PCR and fungal cultures were negative. Candida-mannan level rose then started to decline, Fine needle Aspiration Ultrasonography > necrotic. Echocardiography and Fundus examination had no findings. The patient received 65 days-duration Caspofungin, then discharged on oral Voriconazole. Intensive methotrexate was omitted and the patient started on interim low dose chemotherapy. The patient continued consolidation phase without complications and the first radiological regression after 5 month of antifungal therapy PET-

CT scan repeated (10 months after the start of Anti-Fungal): still residual lesion but regressive. Oral Voriconazole was discontinued after PET results (post reinduction Maintenance chemotherapy).

**Results:** It is challenging in treatment of invasive Candidiasis in immunocompromised children to quietly address the role of steroids in persistent systemic manifestation as well as the proper duration of therapy in case of persistent radiological lesions.

**Conclusions:** Almost 20% only of Hepato-splenic candidiasis have positive blood cultures, PCR was more superior to blood cultures, and it can identify undiagnosed cases and expand the understanding of the disease spectrum.

PO103 / #1001 | Publication Topic: AS05 SIOP Scientific Program / AS05.p Supportive Care and Palliative Care

#### EFFECT OF NUTRITIONAL SUPPLEMENTATION ON TREATMENT-RELATED MORTALITY AND OVERALL SURVIVAL OF CHILDREN WITH CANCER IN GUATEMALA

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**Background and Aims:** Malnutrition is prevalent in many resource-limited countries and has been shown to influence treatment-related morbidity and mortality of children and adolescents with cancer. We sought to identify whether early targeted nutritional interventions could improve treatment-related mortality and survival of children with cancer in Guatemala.

**Methods:** We conducted a retrospective review of 428 patients aged 1 year to 18 years with newly diagnosed acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), Wilms tumor, Hodgkin lymphoma, or Burkitt lymphoma (BL) who were treated between January 1, 2004, and December 31, 2007 at Unidad Nacional de Oncología Pediátrica (UNOP) in Guatemala City, Guatemala. Nutritional interventions, treatment-related mortality, toxicities using the CTCAE 3.0 were extracted, and outcome data were collected, and both summary data and time-to-event data were analyzed. Statistical analysis examined the relationships among nutritional status, interventions, and cancer types.

**Results:** One-hundred-fifty-three (36%) patients were either moderately or severely malnourished at diagnosis. Malnutrition was highest among patients with Hodgkin Lymphoma (80%), and AML (53%). Nutritional interventions were started in 234 (55%) of patients. Those that received nutritional intervention were more likely to improve nutritional status (21%) than those without intervention (16%). Overall

Survival was lowest in patients with AML (39%) and highest in patients with BL (85%). Patients with severe malnutrition had highest mortality (60%), death from infection (16%), treatment-related mortality (32%), progressive disease (12%), and relapse (40%). Baseline nutritional status was associated with overall survival, which was lowest in those with severe malnourishment (40%). Nutritional intervention does not appear to significantly improve overall survival.

**Conclusions:** Nutritional status at diagnosis remains an important prognostic factor for children with cancer, despite nutritional intervention. Patients with malnourishment at diagnosis have higher rates of treatment-related mortality and inferior overall survival. Identifying those more likely to benefit from nutritional supplementation remains elusive and needs to be further investigated.

PO104 / #1536 | Publication Topic: AS05 SIOP Scientific Program / AS05.p Supportive Care and Palliative Care

### SERIOUS EVENTS OF CLINICAL DETERIORATION IN ONCOLOGICAL PATIENTS AT A THIRD-LEVEL PEDIATRIC HOSPITAL IN SOUTHEAST MEXICO

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**Background and Aims:** Patients admitted to pediatric hematology services are especially susceptible to developing life-threatening clinical deterioration. The aim of this study was to assess the incidence of serious medical complications defined as need for vasopressors, invasive/non-invasive ventilation, CPR, unplanned transfer to PICU, and non-palliative death while hospitalized.

**Methods:** In 2022, we started a prospective registry of clinical deterioration events that occurred in patients hospitalized in the pediatric hematology unit; the present study describes events identified from January 2022 to January 2023. Clinical data was extracted from the chart and documented on case report forms. Data were analyzed using descriptive statistics.

**Results:** During the study period, 60 clinical deterioration events were detected, corresponding to 9.88 events for every 1,000 days of hospitalization, deterioration events due to hospital admission was 8.88%, vasopressors 34 (56.6%), ventilation 22 (36.6%), transfer to PICU 3

(5%) and RCP 1 (1.6%), the evolution between the patients who were transferred to the PICU and those who remained on the Oncology floor was 18 (30%) were transferred to the PICU and 42 (70%) remained on the Oncology floor, with a mortality of 8 (44.4%) in the PICU and 10 (23%) in the Oncology floor, overall mortality of 30%, the average hospital stay in the PICU was 8.22 days per patient.

**Conclusions:** Treatment toxicity is an important cause of death in children with cancer in our setting, due to limited access to intensive care and late identification of deterioration. To address this issue, the Early Warning Assessment Scale (EVAT) pilot was initiated in January 2023 to reduce treatment-related complications and increase overall survival for patients at a tertiary pediatric hospital in the southeast of Mexico.

PO105 / #734 | Publication Topic: AS05 SIOP Scientific Program / AS05.p Supportive Care and Palliative Care

### IMPROVED USE OF FOLINIC ACID AS A RESCUE MEDICATION FOR HIGH-DOSE METHOTREXATE

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**Background and Aims:** Folinic acid (FA) is used to minimize the adverse effects of high-dose methotrexate (HDMTX). Insufficient or delayed administration of FA poses the risk of irreversible toxicities from prolonged methotrexate exposure whereas the potential for FA over-rescue has been reported in children with acute lymphocytic leukemia. FA rescue protocols differ based on the HDMTX regimens used and institutional/regional practices. A multidisciplinary panel of experts met to coalesce the best published evidence on the pharmacology of FA in relation to HDMTX and to provide guidance for improved FA rescue.

**Methods:** The panel (3 hematologists, 2 oncologists, 2 pharmacologists, 1 pharmacist) convened to discuss the following: 1) pharmacology of FA; 2) FA administration in HDMTX regimens of specific cancers; 3) risk of FA over-rescue; 4) additional measures used in cases of delayed methotrexate clearance.

**Results:** The main action of FA is to restart the intracellular folate cycle that was inhibited by methotrexate. The intracellular storage capacity of FA potentially protects cancer cells from the subsequent dose

of HDMTX and can result in over-rescue if given too soon. FA rescue should never begin  $\leq 24$  hours following the start of HDMTX infusion regardless of cancer type. The initial dose of FA depends on the serum methotrexate level identified around 24 hours following HDMTX infusion. Hydration and urine alkalinization are paramount; glucarpidase, oral cholestyramine, and laxatives may be added in cases of delayed methotrexate clearance to enhance elimination and reduce toxicities.

**Conclusions:** Uniform guidelines should be established for FA rescue with respect to dose, timing, and duration for specific cancers and their respective HDMTX regimens, and should also include patient-specific guidance. Future investigations should focus on elucidating the time required for depletion of intracellular methotrexate and FA, which would allow for more appropriate timing of FA rescue as well as ensure maximum efficacy of HDMTX in subsequent courses.

PO106 / #1078 | Publication Topic: AS05 SIOP Scientific Program / AS05.p Supportive Care and Palliative Care

#### ARTIFICIAL INTELLIGENCE(AI) AIDS IN PRIOR-AUTHORIZATION FOR FINANCIAL ASSISTANCE TO CANCER PATIENTS – A VALIDATION STUDY BY NAVYA-AI AND INDIAN CANCER SOCIETY–CANCER CURE FUND (ICS-CCF)

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**Background and Aims:** Since 2011, ICS-CCF has funded USD 23 Million for 9800 underprivileged patients with Cancer. We have previously reported on the functioning and outcomes of the project. We also reported pilot findings of use of Artificial Intelligence (AI) in vetting the screening applications, demonstrating 99% concordance with cancer experts and potential time-save of up to 5-fold expert-time. Now we report the findings of the validation cohort.

**Methods:** The Due Diligence Team (DDT) formed the first tier of concordance evaluation and General Advisory Council (GAC) was the second tier of authorizing body used for concordance. Clinical data of beneficiaries were input in AI and if the output treatment options matched the planned treatment, the application was authorized and sent directly to GAC, otherwise rejected, and deferred to DDT. Concordance between prior-authorization by NavyaAI, DDT and GAC, with potential time-saving was evaluated.

**Results:** The validation cohort consisted of 919 pediatric patient application to ICS-CCF from February 2021 to March 2023 (Pilot study n = 411). The diagnosis was hematolymphoid malignancy in 696 (75.7%) and rest were solid tumors. NavyaAI recommended 800/919(87%) for

approval, rejected 3/919(0.3%) and 116/919(12.6%) were deferred to DDT for decision. Upon final decision after DDT and GAC reviews, the concordance between NavyaAI and GAC was 99.75% (798/800) for approvals and 100% (3/3) for rejections. The pilot study of 411 pediatric patients presented in SIOP 2021 reported concordance between NavyaAI and approvals of 99.7%.

**Conclusions:** This validation study confirms the confidence in utilizing AI for prior-authorizations for financial assistance to cancer patients, on a scale with scope. The model can serve as a useful health-economy model for National Health Insurance.

PO107 / #1809 | Publication Topic: AS05 SIOP Scientific Program / AS05.p Supportive Care and Palliative Care

#### CHEMOTHERAPY INDUCED THROMBOCYTOPENIA AT LUBUMBASHI GFAOP PEDIATRIC ONCOLOGY UNIT

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**Background and Aims:** Hematologic toxicity is one of the most frequent side effects of chemotherapy. It can reduce treatment adherence, chemotherapy dose and survival. Few studies have described the burden of chemotherapy induced thrombocytopenia (CIT) in pediatric oncology especially in low-income country of Africa. The aim of this study is to describe the frequency and consequences of CIT in a GFAOP pediatric oncology unit at Lubumbashi in Democratic Republic of the Congo(DRC).

**Methods:** A cross-sectional descriptive study was performed. Data were collected from hospital records of patients admitted for cancer treatment in this pediatric oncology unit from 2012,January to 2022,January.We have considered 4 grades of thrombocytopenia: grade 1:platelet count 75–99 G/L grade 2:platelet count 50–75 G/L grade 3:platelet count 25–50 G/L grade 4:platelet count <25 G/L According to GFAOP guidelines, transfusion was indicated from grade 3 or in case of regarding clinic conditions.

**Results:** Out of 420 children admitted with cancer during this period,we have noticed 39 cases of thrombocytopenia(9,3%).Among them, 36 children were diagnosed with one of the five pediatric cancers whom chemotherapy is supported by GFAOP according to adapted protocols: Five acute lymphoblastic leukemia (ALL) One Burkitt lymphoma Four Hodgkin Lymphomas Eight nephroblastoma Eighteen retinoblastomas Epistaxia was the most frequent sign in 11 cases(28,2%),followed by petechia (15,4%). Seventeen cases of thrombocytopenia(43,6%) were grade 1, 15 grade 2(38,5%),5 grade 3(5,1%) and 2 grade 4 (5,1%) Twenty six patients(66,7%) had got transfusion;total blood with or not reduced plasma. Packed platelet was not available. We have noticed 4 deceases caused by thrombocytopenia and we had no treatment abandonment caused by thrombopenia.

**Conclusions:** In resource limited conditions, it is possible to take care of the most of pediatric cancer and manage hematologic toxicity.

Transfusion conditions must be improved for adequate management of thrombocytopenia.

PO108 / #1140 | Publication Topic: *AS05 SIOP Scientific Program / AS05.p Supportive Care and Palliative Care*

### WHEN A CURE IS NOT POSSIBLE: THE IMPACT OF METRONOMIC CHEMOTHERAPY IN CHILDREN WITH ANTICANCER TREATMENT FAILURE AT HOSPITAL CIVIL DE GUADALAJARA, IN MEXICO

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**Background and Aims:** **Background:** The prognosis of childhood cancer has increased over the years, nevertheless, there are patients resistant to treatment who will not heal.

**Methods:** **Method:** We analyzed medical records of patients who received MC from 2020 to 2022 at HCGJIM. We excluded patients that only received one cycle of MC or abandonment.

**Results:** **Results:** We analyzed 29 of 50 patients that received MC (cyclophosphamide, ibuprofen, MTX, VP-16) during the study period. The average age was 11 years (1-18) and the majority were male (76%). Patients received 5–14 cycles (220–588 days) of MC: 19/29, 2–5 cycles and 10/29 6–14 cycles. Fourteen patients died, ten are still in treatment (palliative performance scale 97%) and five are under surveillance (minimum 8 months, maximum 6 years; 1 ALL, 1 AML, 1 astrocytoma, 1 osteosarcoma, 1 hepatoblastoma).

**Conclusions:** **Conclusions:** It is important to integrate Metronomic Chemotherapy into palliative care to improve quality of life in children. MC helps to reintegrate children to their usual activities (going to school and park, decreased hospitalizations and decreased blood transfusions) and also helps their family to enhance the perception of the phase of the disease that their children are in, managing to resignify the death process.

PO109 / #609 | Publication Topic: *AS05 SIOP Scientific Program / AS05.p Supportive Care and Palliative Care*

### DECREASE IN THE INCIDENCE OF FEBRILE NEUTROPENIA AMONGST CHILDREN WITH CANCER DURING THE COVID-19 PANDEMIC

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**Background and Aims:** Febrile Neutropenia (FN) is a common, serious, and expensive complication experienced by many children with cancer. Approximately 34% of FN in oncology patients is caused by viral respiratory tract infections. Respiratory viruses became a worldwide focus during the COVID-19 pandemic, and the Alberta Government implemented several Non-Pharmaceutical Interventions (NPI's) including mandatory school and business closure, mask wearing, and isolation in an attempt to stop the spread of COVID-19. Our study seeks to improve the understanding of the effects of these NPI's on the incidence, severity, and causative etiology of FN admissions at the Stollery Childrens Hospital in Edmonton, AB, Canada.

**Methods:** We designed a retrospective cohort study composed of a pre-pandemic control cohort that included FN admissions from the three years prior (03/2017-03/2020) to the pandemic with a pandemic cohort that included admissions during one calendar year (03/2020-03/2021) where mandatory NPI's were in place. The number of admissions per year, etiology of fever, hospital length of stay, duration of antibiotics and severity of presentation were compared.

**Results:** In total there were 269 admissions with a diagnosis of FN to the pediatric oncology service in the pre-pandemic cohort of which 174 met inclusion criteria for an average of 58 admissions per year. There were 67 admissions with a diagnosis of FN of which 38 met criteria in the pandemic cohort, a 35% decrease in FN admissions compared to the pre-pandemic incidence. Of the pre-pandemic admissions, 58 (33%) were positive for respiratory viruses, compared to only 4 (11%) of the pandemic cohort admissions, a 79% decrease (P = 0.005).

**Conclusions:** Our study concludes that the both the incidence of FN and the number of episodes of FN caused by a respiratory virus decreased amongst children with cancer presenting to the Stollery Childrens Hospital during the COVID-19 pandemic.

PO110 / #1083 | Publication Topic: *AS05 SIOP Scientific Program / AS05.p Supportive Care and Palliative Care*

### PEDIATRIC PALLIATIVE CARE UNIT FOR CANCER PATIENTS IN LATIN AMERICA: A TEN-YEAR EXPERIENCE

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**Background and Aims:** Pediatric palliative care (PPC) is a field that has been a growing need in the last few years in Latin America. The main goal of PPC is to provide medical, psychosocial, and spiritual care to children with life-threatening conditions and their families. We present the results of our PPC program at a pediatric cancer center in Latin America aimed at advanced cancer patients.

**Methods:** A retrospective cohort study of 26 patients was conducted between 01 February 2013 and 01 February 2023. Patients treated at Centro Oncológico Pediátrico de Baja California in Mexico were enrolled. The patients included were ages 0 to 18 with advanced cancer who failed to respond to conventional treatment and received end-of-life care.

**Results:** The median age of the sample was 11.7 years old. The most common cancer diagnosis was sarcomas, representing 62% of the total. Eighteen of the patients received metronomic chemotherapy and only one alternative cancer treatment. The median duration of palliative care to death (PCTD) was 157 days. A patient with Ewing sarcoma had the longest PCTD with 601 days. The most common cause of death was progression in 92% of the cases. Home care visits were given to 23 patients; the remaining were treated in the hospital. All patients received pain management therapy and psychosocial support. Seventy-three percent of primary caregivers received bereavement follow-up after the patient's death.

**Conclusions:** The management and approach of palliative pediatric cancer patients must be made in a multidisciplinary fashion. It has been proved that doing so positively impacts the patient's quality of life. It is essential to comprehend family-related issues to improve end-of-life care.

PO111 / #1604 | Publication Topic: AS05 SIOP Scientific Program / AS05.p Supportive Care and Palliative Care

#### DEXAMETHASONE MOBILISED GRANULOCYTE TRANSFUSION AS AN EFFECTIVE TOOL TO MANAGE FEBRILE NEUTROPENIA

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**Background and Aims:** Neutropenia-related bacterial and fungal infections are a major cause of morbidity and mortality in patients on chemotherapy/ myeloablative regimens. In the setting of antimicrobial resistance, managing prolonged neutropenia is extremely difficult in resource-constrained settings.

**Methods:** The data of all children (0-18 years) who received granulocyte transfusions at our centre were prospectively collected between 16 March 2022 to 15 March 2023. The dose, number of transfusions, duration of neutropenia, and outcome were recorded.

**Results:** During the study period, 23 children received a total of 65 granulocyte transfusions. All children received irradiated granulocytes after premedication. The median transfusion received was 1 (range 1-15). 4 children received >5 granulocyte transfusions for one episode of febrile neutropenia. All patients received standard of care constitut-

ing antibiotics, antifungals and supportive medicines. The underlying diagnoses included AML (11), ALL(8), aplastic anaemia (3) and BMT (3). The median neutropenic period was 16 days (12-122 days). The longest duration of neutropenia was observed in a child which aplastic anaemia who underwent a second BMT due to primary rejection the first time. All patients had febrile neutropenia; positive blood culture was reported in 15. This constituted GNB (Klebsiella/Pseudomonas) in 11, Staph aureus in 1, Candida tropicalis in 2 and Moraxella in 1. 80% GNB infections were AmpC+/Colistin resistant. 52% were hemodynamically unstable. 4 received supplemental oxygen and 6 received inotrope support. 2 received mechanical ventilation. 2 children died; the rest recovered from sepsis with the recovery of neutropenia. The average dose received was  $4.9 \times 10^9$  cells per unit. All donors were mobilised with only 1-2 doses of dexamethasone. None of the donors received GCSF. There were no serious adverse reactions to granulocyte transfusions.

**Conclusions:** With the emergence of antimicrobial resistance, providing intensive treatment is difficult. Granulocytes are effective as a tool to control infection and ensuing multiorgan dysfunction without having to escalate antibiotic treatment.

PO112 / #1427 | Publication Topic: AS05 SIOP Scientific Program / AS05.p Supportive Care and Palliative Care

#### MANAGEMENT OF SEVERE ACUTE KIDNEY INJURY (AKI) UNDERGOING HEMODIALYSIS IN ADOLESCENTS WITH ADVANCED TESTICULAR TUMOR

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**Background and Aims:** **Background:** Testicular germ cell tumor is the second most common pediatric testicular cancer, especially in adolescents. Chemotherapy is feasible in a dialysis patient, but there are no standard guidelines making the administration of chemotherapy in dialysis patients more challenging.

**Methods:** This case report describes the management of advanced testicular tumor in children with severe AKI undergoing hemodialysis.

**Results:** A fifteen-year-old boy came with a history of a mass in the right testis in the last six months. At the initial presentation, he had massive left pleural effusion and uremic encephalopathy with eGFR 4.83 ml/min/1.73m<sup>2</sup>. The serum LDH 1987 U/L, beta-HCG 9352.21 mIU/mL, AFP 19725.85 ng/mL, d-Dimer 28.500 ug/L. Thoraco-abdominal CT demonstrated a malignant mass in the right testis, approximately 2.0 × 3.5 × 2.7 cm, with bilateral paraaortic lymphadenopathy, pleural effusion with heterogenous mass in the left lung obliterating the left mainstream bronchus, pericardial effusion with intracardial mass at the left atrium, hypodense lesion in segment V

of the liver and grade II hydronephrosis and bilateral hydronephrosis. He underwent a biopsy and immunohistochemistry in the cervical lymph nodes, showed embryonal carcinoma. He was given 15 Gy in five fractions for superior vena cava syndrome. Hemodialysis was commenced before chemotherapy was given with dose reduction. He responded well and completed six cycles of chemotherapy regimens. Hemodialysis was discontinued after cycle two of chemotherapy due to clinical improvement. The last laboratory result was within the normal range. The right orchidectomy surgery was performed and showed a tumor with a large necrotic area with chronic xanthogranulomatous inflammation. The PET-Scan evaluation showed no residual mass in the tumor bed. He is under follow-up for cancer remission.

**Conclusions:** Chemotherapy for advanced cancer can be given to a child with severe AKI undergoing hemodialysis. Close observations and chemotherapy adjustments should be made during treatment, and further follow-up is needed for optimal results.

PO113 / #783 | Publication Topic: *AS05 SIOP Scientific Program / AS05.p Supportive Care and Palliative Care*

#### SEPSIS DEVELOPMENT IN ONCOLOGICAL PATIENTS AFTER IMPLEMENTATION OF THE “GOLDEN HOUR” STRATEGY IN A THIRD LEVEL HOSPITAL IN A LOW-MIDDLE INCOME COUNTRY

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**Background and Aims:** Fever and neutropenia (FN) is a common complication of cancer treatment. A first clinical practice guideline focused on the management of FN in children with cancer and HSCT was published in 2012, updated in 2023.<sup>(1)</sup> The “Golden hour” is a multimodal improvement strategy that combined system change, FN guideline development, education, auditing and monitoring, mentoring, and dissemination to decrease Time to antibiotic administration in inpatient and ambulatory areas and was initiated in Mexico back in 2014 with the support of the MAS alliance.<sup>(2)</sup> The aim of this study is to measure the impact of this strategy implementation to prevent sepsis development at the emergency room and inpatient care.

**Methods:** This is a prospective observational study where all patients with an onco-hematological diagnosis aged from 1 month to 17 years old that presented fever were included. As members of Mexico in Alliance with St Jude cooperative group and the second collaborative of the “Golden Hour” strategy we have resources of metrics given by Simple Qi platform since January 2022 to January 2023.

**Results:** All patients registered since January 2022 to January 2023 were measured having a total of 24 of which 5 of them were reported at the data base to develop sepsis and needed support at the Pediatric Intensive Care Unit, from this 3 of them died due to several complications.

**Conclusions:** We can observe how an efficient approach decreases the development of complications and death in this vulnerable group of patients. Quality improvement projects are needed in order to update process, management and attention to all kind of patients. Due to the entrance of this hospital to the 2<sup>nd</sup> collaborative of the “Golden Hour” by the MAS alliance we are now able to demonstrate its efficacy in our area giving us the necessary elements to continue with its implementation in an institutional way.

PO114 / #470 | Publication Topic: *AS05 SIOP Scientific Program / AS05.p Supportive Care and Palliative Care*

#### WALKING INABILITY IN CHILDREN DURING INDUCTION/CONSOLIDATION-I THERAPY FOR ACUTE LYMPHOBLASTIC LEUKEMIA

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**Background and Aims:** Newly diagnosed children with acute lymphoblastic leukemia (ALL) are at risk of physical impairments due to e.g. pain, fatigue and muscle weakness. The aim of this study was to examine the occurrence of temporarily independent walking inability prior to diagnosis and during induction/consolidation-I, as well as to explore potential determinants.

**Methods:** Children with ALL treated according to the ALL-11 protocol (including high-dose prednisone and vincristine) at the Princess Máxima Center for Pediatric Oncology in 2019, who had learned to walk independently prior to onset of ALL, were eligible. The number of children who lost walking ability prior to diagnosis or during induction/consolidation-I (79 days), as well as the time since start of treatment until walking inability occurred and the duration of walking inability were retrospectively retrieved from electronic patient records. Sex, age and reported pain in the lower extremities at diagnosis, changes in weight and the number of blood transfusions (as proxy for hemoglobin level  $\leq 4.3$  mmol/L) during induction/consolidation-I were explored as potential determinants for walking inability using logistic regression analyses.

**Results:** Eighty-one children were included, with median age of 6.0 years (interquartile range [IQR]: 3.6-12.5) at diagnosis and 59.3% boys. Prior to diagnosis, 12.3% of the children lost walking ability. During induction/consolidation-I, another 22.2% of the children lost their ability to walk. Median time until walking inability occurred in these latter children was 30.5 days (IQR: 19.3-45.5) following start of treatment. Median duration of walking inability was 17.0 days (IQR: 6.5-59.5). Blood transfusions were more frequently administered in children who temporarily lost walking ability compared to children who kept their walking ability (Odds Ratio: 1.6, 95%CI: 1.2-2.4). No other potential determinants were identified.

**Conclusions:** More than one third (34.5%) of newly diagnosed children with ALL temporarily lose their independent walking ability at



ALL onset or during induction/consolidation-I. Anemia seems to be associated with walking inability during induction/consolidation-I.

PO115 / #38 | Publication Topic: *AS05 SIOP Scientific Program / AS05.p Supportive Care and Palliative Care*

### HYPERGLYCEMIA AMONG CHILDREN BELOW 18YEARS WITH ACUTE LMPHOBLASTIC LEUKEMIA/LYMPHOMA ON CHEMOTHERAPY IN UGANDA; INCIDENCE, FACTORS ASSOCIATED AND IMMEDIATE OUTCOMES

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**Background and Aims:** Leukemia is among the six targeted cancers in the 2018 WHO Global Initiatives for Childhood Cancers (GICC) to improve overall survival to 60% by 2030. Chemotherapy of acute lymphoblastic leukemia/lymphoma (ALL/LBL) involves the use of steroids and L-asparaginase among others, both of which are known to induce hyperglycemia which is associated with increased morbidity and mortality. In Sub-shaharan africa, where Uganda lies, the burden of hyperglycemia among children with ALL/LBL on chemotherapy is unknown.

**Methods:** This was a hospital-based prospective cohort study carried out at the 2 main paediatric cancer treatment sites in Uganda (Mulago National Referral Hospital and Uganda Cancer Institute) from March to August 2022. A total of 84 participants with ALL and LBL on either induction or re-induction chemotherapy were recruited and each followed up for one month. A random blood glucose (RBG) level was determined at pre-induction and on days 8, 15, 22, and 29. Hyperglycaemia was defined as a random blood glucose concentration of  $\geq 200$  mg/dl (11.1mmol/l) in two or more determinations. The data was analyzed using STATA 16.

**Results:** The mean age (SD) was 9.2( $\pm$ 4.2) years. Majority were males 55/84 (65.5%) and younger than 10 years of age (56.0%). Eight children in the age range of 8-16 years developed hyperglycemia (9.5%)(95% CI (3.2-18.1)) commonly in the second and third weeks of induction. Of these, 5/8 developed DKA and received insulin therapy. Only female gender was independently associated with hyperglycemia,  $P = 0.026$ . Hyperglycaemia resolved in 7/8 (87.5%) children, majority of whom achieved remission and were alive at the end of induction.

**Conclusions:** The cumulative incidence of hyperglycemia in children with ALL and LBL on induction chemotherapy using current guidelines is high at 95 per 1000. Most occur in the second and third weeks of induction and present with DKA but with no increased mortality. Female children are most at risk.

PO116 / #952 | Publication Topic: *AS05 SIOP Scientific Program / AS05.q Psychosocial (PPO)*

### THE SOCIO ECONOMIC AND PSYCHOLOGICAL IMPACT ON PARENTS WITH CHILDREN LIVING WITH CANCER IN PAEDIATRIC ONCOLOGY WARD, LAGOS, NIGERIA

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**Background and Aims:** **Background:** Cancer is a terminal disease that affects deeply and painfully not only the child who has cancer but also their parents. Through this study, we will discuss pediatric cancer and socio-economic and psychological the impact on parents. **Objective:** This study is to identify and examine the socio-economic and psychological impact on the parents with children living with cancer in paediatric oncology ward in Lagos University Teaching Hospital, Idi-araba, Lagos state.

**Methods:** **Methods:** This study employed random sampling method with the aid of semi-structured interviewer questionnaire to sample twenty (20) parents with a child diagnosed with cancer within a period of 12 months. Data derived from the questionnaire were analysed using Statistical Package for Social Sciences (SPSS) version 25.

**Results:** **Result:** A high proportions (90.0%) of the parents especially mothers' employment were exposed to disruption such as job quitting or job loss with a little or no financial support system of about 20%. Ninety percent (90%) of the associated financial constraints and burden was due to cancer-related expenses. All (100%) the parents were anxious, depressed and withdrawn with mal-adaptive coping skills, 80% were sure about getting help and more information from a psychotherapist, while the other 20% were either not sure or do not need help.

**Conclusions:** **Conclusion:** Family socio economic, psycho-social and emotional well being were negatively affected by child illness and care.

PO117 / #914 | Publication Topic: *AS05 SIOP Scientific Program / AS05.q Psychosocial (PPO)*

### EMOTIONAL AND BEHAVIORAL SYMPTOMS IN CHILDREN AS LONG-TERM PSYCHOLOGICAL EFFECTS OF CANCER TREATMENT

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**Background and Aims:** Cancer in children is associated with a number of psychogenic reactions and symptoms caused both by traumatic treatment as well as by medical, psychological and social consequences, which, reinforcing each other, lead to severe emotional and behavioral problems and social maladjustment. The purpose is to study emotional and behavioral symptoms as long-term psychological effects of cancer treatment in children with hemoblastoses, CNS and other solid tumors

**Methods:** 49 children (22 girls; 27 boys) aged 4 to 17 years (median 8.5): 18 (37%) with hemoblastoses; 17 (35%) with CNS tumor; 14 (28%) – other solid tumors; in remission from 24 up to 132 months (median 52, mode 71). Methods: analysis of verbal material and content of child's playing in the Jungian sandbox, its emotional and behavioral reactions; clinical interview with parents. Statistical processing was carried out in the MS Excel program.

**Results:** 78% of children showed anxiety-related neurotic symptoms; 32% - social maladjustment; all children developed various forms of protective behavior symptoms, including regressive - 53% and autoaggressive - 45%. Children with CNS tumors are twice as likely as those with hemoblastoses to develop autoaggression - 68% and 32%, respectively. Regressive behavior is also significantly more often detected in children with a CNS tumor than with hemoblastoses - 92 and 8%,  $p < 0.01$ . 10 (20%) experienced multiple trauma, including the loss of relationships as a result of parental divorce or the death of a loved one, 8 of them were children with CNS tumors.

**Conclusions:** Diagnosis and correction of the emotional and behavioral sphere in children is not just a clinical or psychological, but a general medical and social problem. It is extremely important to provide children with individual emotional and behavioral correction at the very first stage of cancer diagnosis and treatment. Children with CNS tumors are the most vulnerable group.

PO118 / #1108 | Publication Topic: AS05 SIOP Scientific Program / AS05.q Psychosocial (PPO)

### EMOTIONS ON STAGE: A PILOT STUDY ON THE EFFECTS OF THE USE OF THEATRICAL TECHNIQUES FOR EMOTIONAL ENHANCEMENT

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**Background and Aims:** To date, there are few studies in which structured educational interventions are presented with the use of theatrical techniques. The theater is seen as an intervention tool, as it contains both the game and the educational component (Bonato, 2016; Levy, 2005). The present study aims to investigate the effectiveness of the use of some theatrical techniques, such as empathy, in improving emotional recognition skills in children with oncohaematological dis-

eases. The methodology is both qualitative and quantitative and the research design is longitudinal.

**Methods:** The participants involved in this study, after the parental informed consent signature, were 10 children with an average age of 9 years (SD = 2.06; range: 7-13), 6 males and 4 females with various oncohaematological diseases. Nepsy-II social recognition tasks were adopted before and after the intervention, both with self and parental approval reports and mood questionnaires. Each intervention meeting was structured along four phases: vision, recognition, discussion and acting.

**Results:** A t test was run to understand the possible changes in social recognition T scores pre and post intervention. The test resulted significant ( $t(9) = -1.84$ ;  $p = 0.04$ ) with the pre-intervention scores (M = 8.40; SD = 3.7) lower than the post-intervention ones (M = 10.40; SD = 2.1). The declared delight was reported in all the total 40 intervention meetings. The children's declared a bad mood decrease before and after the meetings ( $t(9) = 3.28$ ;  $p = 0.005$ ) and an increase of good mood ( $t(9) = -2.37$ ;  $p = 0.02$ ).

**Conclusions:** The results are promising, even if more patients should be involved in the next studies on this topic and the setting should be more stable. The strengths could be identified in the usefulness of this typology of emotional enhancement in patients that could have problems in verbalizing their emotional states.

PO119 / #199 | Publication Topic: AS05 SIOP Scientific Program / AS05.r Epidemiology, Policy and Advocacy

### PRELIMINARY HISTOPATHOLOGICAL STUDY OF MALIGNANT TUMORS IN KENITRA

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**Background and Aims:** Beyond Casablanca cancer registry of 2008-2012 and Rabat cancer registry of 2009-2012, there is a lack of exhaustive national and regional epidemiological statistics. So, sufficient data are not available to use as reference and to compare against it, especially in the city of kenitra. In order to contribute in enriching these data, this preliminary study is conducted. The main aim of this investigation is to determine the frequency and the characteristics of malignant tumors in the city of Kenitra.

**Methods:** A histopathological study is realized among 461 confirmed cancers cases, collected from the Department of Pathology in the regional Hospital of Kenitra, from January 2017 to December 2021, different data were analysed.

**Results:** 49, 8 % of patients were men, and 50, 2 % were women, the average age was  $55,32 \pm 16,25$  years. Patients were aged from 6 to 93 years old. Carcinoma is the most common type of cancer with a rate of

64, 6 %. Skin and breast cancer were the most predominant locations with respectively 25% and 20%, lymphoid tissue was 9,1%, bladder 9,3%, prostate and bone 4,8%.

**Conclusions:** Our study is still ongoing to evaluate other risk factors and other parameters, nevertheless the establishment of a regional cancer registry in the city is highly recommended.

PO120 / #238 | **Publication Topic:** *AS05 SIOP Scientific Program / AS05.r Epidemiology, Policy and Advocacy*

#### EPIDEMIOLOGICAL PATTERN OF CHILDHOOD CANCER TREATED AT PRIVATE DR SULIMAN FAKEEH HOSPITAL AND THEIR OUTCOME, JEDDAH CITY, SAUDI ARABIA

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**Background and Aims:** Increasing role of private hospital at KSA supported by implementing medical insurance involvement in medical care and charity society to support treatment of children with cancer. Frequent surveillance of cancer outcome is important to improve modes of treatment Cure rate of acute lymphoblastic leukemia reach 85% and 70% for solid tumor

**Methods:** From October 2017 to December 2022 all pediatric cases diagnosed with cancer will be reviewed to assess even free survival, EFS and over all survival, OS

**Results:** Total cases 63 with male 42 and female 21. Acute lymphoblastic leukemia ALL 21, Acute myeloid leukemia AML 2, Hodgkin lymphoma HL 4, Non Hodgkin lymphoma NHL 4, Wilms tumor WT 8, Retinoblastoma RET 7, Neuroblastoma NBL 4, Brain tumor 4, bone tumor 2, and 1 for each; synovial sarcoma, LCH, HLH, ovarian teratoma, CML, hepatoblastoma HBL and abdominal inflammatory myofibroblastic tumor. Disease recurrence 13/63 with EFS 80%. 9 cases died, 1 from toxicities (infant HL) and 8 recurrent diseases (3 ALL, 2 NBL, 1 RET, 1 HBL and 1 brain stem glioma). 4 cases salvaged after disease recurrence; ALL with early combined relapse after allogeneic SCT, stage 4 HL received 2<sup>nd</sup> line chemotherapy then autologous SCT, RET received 2<sup>nd</sup> line chemotherapy and synovial sarcoma local relapse received 2<sup>nd</sup> line chemotherapy with safe margin 2<sup>nd</sup> look surgery and local radiotherapy with OS 86%. 13/63 cases indicated radiotherapy

**Conclusions:** Private hospital could support health care system in diagnosis and management of childhood cancer. Using risk directed therapy for all types of tumour would have impact on outcome

PO121 / #1081 | **Publication Topic:** *AS05 SIOP Scientific Program / AS05.r Epidemiology, Policy and Advocacy*

#### POST PANDEMIC COVID-19 REFLEX- INCREASE IN LATE DIAGNOSIS OF CHILDHOOD CANCER IN THE WEST OF PARANÁ- BRAZIL

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**Background and Aims:** Introduction: In 2020, Brazil and the world faced an outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The Program aims to help health professionals in the early recognition and referral of suspected cases was interrupted. In view of this new scenario, we evaluate the degree of tumor involvement in children and adolescents two years after the COVID-19 pandemic. Objective: To analyze the number of cases referred and the stage of children and adolescents with cancer treated in the period from 2007 to 2022.

**Methods:** Methodology: We retrospectively evaluated children under 19 years of age from January 2007 to December 2022 in hospital of childhood cancer in Cascavel, Paraná, Brazil. Low Risk (LR) (stage I and II) and High Risk (HR) (stage III and IV) for solid tumors. Leukemias of Low Risk and High Risk, according to age and leukometry at diagnosis, with HR < 12 months and > 10 years, and leukometry >50,000/mm<sup>3</sup>.

**Results:** 912 patients were treated from 2007 to 2022, of which 507 (56%) HR and 405 (44%) LR. There was a predominance of HR over LR, of 2009 to 2013. LR over HR from 2014 to 2018, period in which we developed the early diagnosis project. After 2019, predominance of HR over LR (post COVID-19 pandemic).

**Conclusions:** Comments: Children and adolescents during the COVID19 pandemic were diagnosed with advanced disease. These data allow us to say that the Covid 19 pandemic associated with the interruption of actions aimed at the guidance and training of health professionals may be related to the change in the presentation and severity of the disease in children and adolescents in the western of Paraná, Brazil.

PO122 / #1376 | **Publication Topic:** *AS05 SIOP Scientific Program / AS05.r Epidemiology, Policy and Advocacy*

#### PROFILE OF RESPIRATORY VIRAL INFECTIONS IN PEDIATRIC HAEMATO-ONCOLOGY UNIT - PROSPECTIVE STUDY FROM A TERTIARY CARE CENTER IN SOUTH INDIA

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**Background and Aims:** One-third of children with cancer have viral infection. Prompt microbiological identification in pediatric hemato-oncology cohort could help the clinician in prognostication and de-escalation of treatment at appropriate times. We aimed to study the profile of respiratory viral infections in our tertiary care unit.

**Methods:** With Institutional ethics committee approval, a prospective descriptive study was done in our tertiary care PHO unit between January-2020 & August-2021. Children <18 years presenting with

fever and/or respiratory symptoms were enrolled with informed consent. Nasal swabs for viral RT-PCR studies were done apart from standard unit protocol with bacterial cultures and antibiotics. Details of demographic data, history, physical findings and lab parameters (Complete Hemogram/cultures/viral PCR), treatment and patient outcomes were analyzed. All samples were analyzed for RT-PCR covering >10 common respiratory viruses and SARS-CoV2 was later added to the panel.

**Results:** Of the 84 events in 58 patients, 16 patients had more than 1-episode; 52.4% was noted in <5-years. Our population included 83.3% post-chemotherapy, 5.9% bone marrow transplant recipients and 10.7% with benign haematological conditions requiring immunosuppressive therapies/primary immunodeficiencies. Fever was noted in 90% patients followed by respiratory complaints in 21% cases; 53.6% were neutropenic (ANC < 1500 cells/mm<sup>3</sup>). Median duration of illness was 6.9 days (range: 1-42 days) with 88% requiring hospitalization, 10.7% requiring intensive care and 3.5% succumbing to their illness. In our study, 57.1% had viral positivity, 10.7% had bacterial infection and 7.1% had mixed infection. Rhinovirus was the most frequently detected followed by SARS-CoV-2. There was no statistically significant difference in duration or severity of illness or neutropenia status between those with or without virus PCR positivity. There was no significant difference in clinical outcomes of viral respiratory infections in children with or without neutropenia.

**Conclusions:** Identification of a respiratory viral pathogen in low risk febrile neutropenia & stable children might help in rationalised decision making on antibiotics, especially in the era of multi-drug resistant bacteria.

PO123 / #426 | Publication Topic: AS05 SIOP Scientific Program / AS05.r Epidemiology, Policy and Advocacy

#### EPIDEMIOLOGICAL PROFILE OF CHILDHOOD CANCER AT THE LUBUMBASHI UNIVERSITY CLINIC IN THE DEMOCRATIC REPUBLIC OF CONGO

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**Background and Aims:** Cancers in children under 17 years of age have specific epidemiological and management characteristics. The objective of this study was to determine the epidemiological profile of childhood cancers in Lubumbashi.

**Methods:** A cross-sectional descriptive study was conducted in the University Clinics of Lubumbashi from 2018-2019. Data col-

lection was carried using a statistical form with a number of parameters.

**Results:** In this study, 99 of the 3024 cases of children who visited the pediatric ward during the study period were diagnosed with cancer, a prevalence rate of 3.27%. Only (71.7%) of the cases had consulted a general practitioner at the first sign of illness. Retinoblastoma being the first childhood cancer with 29.3%, followed by kidney tumors (23.2%), lymphomas (13.1%) and leukemias (12.1%) all combined forms. 87.9% had easy access to chemotherapy. Among them, (28.7%) chemotherapy and surgery with a curative aim. Childhood tumors show a remission in (20.7%), 35.6% of deaths and almost (27.6%) remain under background treatment.

**Conclusions:** Le diagnostic statistique pathologique est une réalité qui se vit dans beaucoup de nos environnements; Le diagnostic et la prise en charge précoce restent des pronostics essentiels pour réduire le taux de mortalité chez les enfants malades.

PO124 / #976 | Publication Topic: AS05 SIOP Scientific Program / AS05.r Epidemiology, Policy and Advocacy

#### BARRIERS AND FACILITATORS TO IMPLEMENTATION OF THE SJCARES REGISTRY IN RESOURCE-LIMITED SETTINGS

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**Background and Aims:** Cancer is a leading cause of global childhood mortality, affecting 300,000 children annually. While treatable with modern therapies, children living in low- and middle-income countries (LMICs) have limited access to care and lower survival rates. Hospital-based cancer registries (HBCRs) collect detailed patient information to evaluate and evolve care. The St. Jude Global Childhood Cancer Analytics Resource and Epidemiological Surveillance System (SJCARES) is a cloud based HBCR facilitating quality data collection of pediatric cancer. Wide variation in success of implementation has warranted further research into the implementation, to create a sustainable and adaptable HBCR in LMICs. Our objective is to investigate barriers and facilitators to successful SJCARES implementation.

**Methods:** Seven of the 89 sites which have adopted the SJCARES Registry were randomly selected, stratified by global region and stage of implementation. Semi-structured interviews were conducted with key

stakeholders (clinicians, administrators, data clerks) using an interview guide developed from the Consolidation Framework for Implementation Research. Interviews were conducted via Zoom and transcribed by Landmark Associated. Transcripts were thematically coded using rapid qualitative analysis. Data was aggregated into a summary matrix.

**Results:** A total of 18 stakeholders (11 clinicians, 4 administrators, 3 data clerks) participated in the interviews. Three barrier themes were identified: 1) Lack of resources and lengthy training; 2) Incomplete prior medical records; 3) Cultural considerations and concerns for future use of data. Four facilitator themes identified included: 1) Internal support for registry; 2) Clear and extensive training courses; 3) Prior experience with research collaborations and/or other registries; 4) Single defined role responsible for uploading data into registry.

**Conclusions:** Interviewed stakeholders identified key barriers and facilitators to implementation of the SJCARES Registry across multiple phases. We plan to develop a readiness assessment and process maps to help guide more successful implementation of the SJCARES Registry and other HBCRs in LMICs.

PO125 / #780 | **Publication Topic:** *AS05 SIOP Scientific Program / AS05.r Epidemiology, Policy and Advocacy*

## EPIDEMIOLOGICAL AND DIAGNOSTIC ASPECTS OF PEDIATRIC CANCERS IN NIGER

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**Background and Aims: Introduction:** Once rare, childhood cancers are on the rise and may become a major public health problem in the coming years.

**Objective of our study:** To determine the epidemiological and diagnostic characteristics of pediatric cancers in Niger

**Methods: Methodology:** This is a descriptive study of cancer cases collected at the pediatric oncology unit of Niamey and at the Oncohaematology Department of the National Hospital of Niamey from August 1, 2021 to July 31, 2022 (12 months). Data (demographic, clinical and histological) were collected from consultation registers and patient files. Patients with a cytological and/or histological diagnosis of cancer were included.

**Results: Results:** Out of 108 patients admitted during the study period, ninety-five children (95) were included, the most affected age group was between 0 and 4 years and represented 62.10% with extremes of 2 months and 15 years. Male predominance was observed with 55.80% and a sex ratio of 1.2. The patients came from all regions of the country with a maximum of 33.7% of children coming from the Niamey

Region. Leukocoria was the most common clinical sign in 27.40% of the patients, followed by adenopathy in 25.25%, exophthalmos in 23.15% and abdominal mass. Retinoblastoma was the predominant histological form with 28.40% followed by Nephroblastoma 23.20%, lymphoma 17.90% and acute leukemia 14.70%.

**Conclusions: Conclusion:** This work shows that childhood cancers are relatively frequent in Niger and are dominated by retinoblastoma. The establishment of a pediatric cancer registry and the improvement of the technical platform for diagnosis will allow in the future to identify more cases. **Key words:** pediatric cancer- epidemiology- diagnosis- Niger

PO126 / #1062 | **Publication Topic:** *AS05 SIOP Scientific Program / AS05.r Epidemiology, Policy and Advocacy*

## THE UNMET NEEDS OF CHILDHOOD CANCER- EXPERIENCE OF A TERTIARY PEDIATRIC CENTER

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**Background and Aims:** Pediatric cancer mortality rates have declined to a low and steady percent over the past few decades. Patients with hematological malignancies such as Leukemia and Lymphoma are achieving excellent survival rates, whereas patients with solid tumors such as brain tumors and neuroblastoma are still challenged with higher rates of relapse/refractory disease. With this gap in mind, we set to find actual data of morbidity and mortality of the pediatric oncology division in a tertiary hospital.

**Methods:** A total of 981 medical charts were retrospectively reviewed from January 2013 to December 2018 at Schneider Children's Medical Center. All malignant diagnoses in patients under 20 years who were treated at our center were included.

**Results:** Over six years, 576 patients were diagnosed with cancer at our center: 274 (47.5%) with hematological malignancies, 166 with brain tumors, and 136 with extra cranial solid tumors. Median age at diagnosis was not statistically different between groups (7.4-8.4 years). Relapse rate among patients with solid tumors was 23.6%, versus 7.3% in the hematological malignancies group and 6.6% in the brain tumor group. At the time of last follow up, 88 patients (15.3%) have deceased, most of them from the solid tumor group (n = 37). The leading cause of death in the brain tumors and solid tumors groups was disease progression (100% and 97.3% respectively), as oppose to the cause in

the hematological malignancies cohort, which was almost evenly distributed between treatment related infections (42.9%) and disease progression (39.3%).

**Conclusions:** There is a growing need for better cure of pediatric solid tumor patients, since the leading cause of death in this group is disease progression. Reducing toxicity is essential mostly in the treatment of hematological malignancies, as they are as likely to demise from treatment related mortality as from disease progression.

**PO127 / #378 | Publication Topic: AS05 SIOP Scientific Program / AS05.s Survivorship**

**BILE ACID MALABSORPTION AS A LATE EFFECT IN SURVIVORS OF PAEDIATRIC CANCER: AN UNDERDIAGNOSED CONDITION?**

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**Background and Aims:** Bile acid malabsorption (BAM) has been increasingly recognised as a cause of chronic diarrhoea and urgency in adult cancer patients, particularly those who have received radiotherapy for malignancy in the pelvis. However, there is no information in the literature regarding this condition in the paediatric oncology population.

**Methods:** We describe two patients who developed severe BAM years after receiving intensive multimodal treatment for high-risk neuroblastoma.

**Results:** The two patients were diagnosed with high-risk neuroblastoma at the age of 3 and were treated as per SIOP HR-NBL1 clinical trial with chemotherapy, surgery, abdominal radiotherapy and immunotherapy. They both had primary abdominal retroperitoneal tumours and multiple metastases. During long-term follow-up they developed symptoms of abdominal pain, diarrhoea and urgency. A Selenium-Homocholic Acid Taurine (SeHCAT) scan demonstrated severe bile acid malabsorption for both cases. Treatment with bile acid sequestrants was commenced with marked improvement of symptoms and quality of life.

**Conclusions:** Bile acid malabsorption (BAM) is a common condition in adults who have undergone cancer treatment, particularly those who had treatment which can disrupt bile acid resorption such as surgery affecting distal ileum or radiotherapy in the pelvic area. There is a lack of data in the literature on the incidence and risk factors specific to the paediatric oncology population. A high index of suspicion is needed in the presence of abdominal pain, chronic diarrhoea and urgency in paediatric patients at risk of BAM. The diagnosis of BAM can be confirmed with a SeHCAT scan and treatment with dietary modifications and bile acid sequestrants is effective in controlling the symptoms and improving quality of life.

**PO128 / #1832 | Publication Topic: AS05 SIOP Scientific Program / AS05.s Survivorship**

**HORMONAL COMPLICATIONS OF CHILDREN TREATED FOR CENTRAL NERVOUS SYSTEM TUMOR: ABOUT 29 PATIENTS**

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**Background and Aims:** Endocrine complications are an important concern in the treatment of brain tumours in the childhood, The objective of our work was to study the endocrine sequelae of a series of children treated at the Salah Azaiz Institute in Tunisia, and to identify the various predictive factors.

**Methods:** We conducted an analytical cross-sectional study, involving 29 patients treated for a CNS tumor at an age of less than 18 years between 2003 and 2018 with a minimum follow-up of 3 years. A biological analysis was done in our institut of ACTH,TSH,FT4,TESTOSTERONE,ESTROGEN.

**Results:** We noted that 6 patients had delayed puberty, 14 patients had a high level of TSH, with 13 of them a normal level of FT4, 7 boys had a low level of testosterone, and 14 patients had a low level of estrogen, 7 patients had a low ACTH. An elevated level of TSH was associated with The presence of a syndrome of intracranial hypertension, high grade tumours, a surgical treatment, An low level of FT4 was correlated with a supratentorial tumor localization, a surgical treatment, and chemotherapy, a low testosterone and estrogene was found in patients with a ventriculoperitoneal shunt, and a low estrogene in supratentorial tumours specifically midline tumours, high grade and surgery or chemotherapy. Delayed puberty was associated with high grade tumours, and surgery. Dosimetric analysis has not shown a specific correlation.

**Conclusions:** The pediatric population treated for a tumor of the central nervous system is subject to developing long-term endocrine, affecting the entire hypothalamic-pituitary axis.

**PO129 / #169 | Publication Topic: AS05 SIOP Scientific Program / AS05.s Survivorship**

**AWARENESS, KNOWLEDGE, ATTITUDES AND BEHAVIORS OF PEDIATRIC ONCOLOGY SPECIALISTS ON FERTILITY PRESERVATION IN CHILDREN DIAGNOSED WITH CANCER**

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**Background and Aims:** Infertility is a common late effect of cancer treatment faced by childhood cancer survivors in adulthood. In this study, we set out to determine the knowledge, attitudes and current practices of Pediatric Oncology specialists in our country about fertility preservation (FP) methods and the barriers they encounter.

**Methods:** This cross-sectional, descriptive study was conducted between 15 January 2022 and 15 June 2022. The questionnaire developed by the researchers was sent to 152 pediatric oncologists via social media networks (e-mail, whatsapp). Twenty three responses were collected during the study period. Return rate of the responses was 15%.

**Results:** Twenty-three pediatric oncologists participated in the study. Eighteen (78.3%) of the participants were female and 5 (17.8%) were male. The physician respondents worked across the Turkiye. All physicians participating in the study reported that they routinely incorporate fertility preservation discussions into their clinical context of pediatric cancer diagnosis. Nineteen (82.6%) of the physicians reported that they always/routinely and 4 (17.4%) sometimes recommended FP. Eighteen of the physicians (81.8%) stated that they always used FP methods before the treatment started. Physicians reported that they mostly used sperm cryopreservation and oocyte cryopreservation methods in post-pubertal children. Urgency of treatment (76.2%), financial difficulties/insurance barriers of the patient (61.9%), lack of an institutional or national standard (61.9%), physicians not having sufficient knowledge about surgical methods for pre-adolescent patients (38%),<sup>1</sup> and heavy workload (23.8%) were reported as the most common barriers. All physicians in this study, recommended the preparation of an official guideline and the establishment of public oncofertility centers.

**Conclusions:** While this is among the first study in the Turkiye to examine provider discussion of FP issues, the results should be interpreted cautiously due to limitations such as the small sample size. Lack of an official guideline was considered to be a challenge for many of the physicians in our study.

PO130 / #1252 | Publication Topic: *AS05 SIOP Scientific Program / AS05.s Survivorship*

## HUMAN PAPILLOMAVIRUS VACCINATION FOR FANCONI ANEMIA PATIENTS

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**Background and Aims:** Fanconi anemia (FA) is a rare heterogeneous disorder characterized by congenital malformations and marrow failure. Patients are at risk for human papillomavirus (HPV)-associated cancers. HPV vaccination is recommended for all FA patients to reduce the occurrence of head and neck malignancies. Post-transplant vaccination has shown a similar immune response to the general population.

**Methods:** We are reporting the outcome of FA patients who received HPV vaccination post allogeneic stem cell transplantation (allo-HSCT) at the King Hussein cancer center pediatric stem cell transplant unit from Jun 2005 till Jun 2022.

**Results:** Thirty-seven patients underwent alloHSCT; the median age was 8.5 years(4.5-23.7), their median follow-up was six years(0.3-16), and the 5-years overall survival was 91.6%(95% CI: 76.1-97.2). Twenty-nine donors were match-family donors, three were unrelated cord blood, and five were haploidentical. The median time for neutrophil and platelet engraftments were 13 (range, 9-27) and 17 days (range, 12-93, respectively). Three patients(8%) developed primary graft failure, nine patients (24%) developed acute graft vs. host disease (GVHD), thirteen (35%) developed chronic GVHD, and CMV reactivation was detected in 28 patients (75%). Two patients developed metastatic squamous cell carcinoma; both died 5.5- and 12 years post alloHSCT; both had cGVHD of the mouth, and neither has received irradiation. Nine patients have received HPV vaccination according to CDC recommendation. The median age at immunization was 12.3 years(range, 9-18.4).The median time of vaccination was 1.7 years(range, 3.5-11.8)post-transplantation, with no injection site reaction or immediate side effects from the vaccination. All patients continued their scheduled oral and head and neck examinations. No head and neck tumors have been diagnosed in these patients so far, after a median time of 4(range,3-5.5)years post vaccination.

**Conclusions:** More FA patients are surviving into adulthood; therefore, prevention and early and efficient detection of malignant lesions become more critical. Immunization using the HPV vaccine may prevent HPV-related cancers.

PO131 / #1333 | Publication Topic: *AS05 SIOP Scientific Program / AS05.s Survivorship*

## IDENTIFICATION OF PLASMA BIOMARKERS OF CANCER-RELATED FATIGUE: A SYSTEMATIC REVIEW

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**Background and Aims:** Cancer-related fatigue (CRF) occurs in a significant proportion of cancer patients and has a detrimental effect on their quality of life, reintegration in daily life activities and psychosocial functioning. Previous research suggests that CRF has a multifactorial etiology involving a range of psychological, physiological and clinical factors. The exact etiology of CRF is not yet fully understood. In this review, our objective is to summarize potential plasma and serum biomarkers that could shed light on the underlying biological mechanisms associated with CRF.

**Methods:** A search was performed in Pubmed and Embase, based on the keywords fatigue, cancer, and biomarker. Articles were screened on title and abstract followed by screening on full text. Inflammation biomarkers were excluded, as this was thoroughly described in previous studies. Articles involving animal studies, markers not plasma/serum based, fatigue not related to cancer, treatment of CRF, in vitro studies, reviews and case-reports were excluded.

**Results:** 32 articles were included, of which the majority investigated patients with a diagnosis of breast cancer or a hematological malignancy. Timepoints of measurements ranged from prior to therapy up to months after treatment. Most patients received chemo- and/or radiotherapy. All studies were adult studies. Markers that

were investigated were hemoglobin (Hb), cortisol, Vascular Endothelial Growth Factor (VEGF), tryptophan-kynurenine pathway, gonadal function, neurotrophic factors, blood coagulation factors, leptin, mitochondrial DNA, platinum, Cytomegalovirus (CMV) and Epstein-Barr virus (EBV) antibody titers, Cancer Antigen 125 (CA125) and oxidative stress in generating CRF.

**Conclusions:** Markers that could potentially play a role in CRF may be involved in the stress and immune response, anemia, angiogenesis, mitochondrial dysfunction and tryptophan-kynurenine pathway. Current research has not yet provided sufficient data on biomarkers in pediatric oncology nor on their associations with physical activity measures, highlighting the crucial need for additional studies in this area.