2021 ASPHO Conference Paper and Poster Index

Papers

Posters

Plenary Paper # 2001

IMPACT OF ALTERED COHESIN FUNCTION ON PROLIFERATION OF CORE BINDING FACTOR ACUTE MYELOID LEUKEMIA

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Background: Core binding factor acute myeloid leukemia (AML) is a common type of pediatric AML characterized by inv(16) or t(8;21) lesions that inhibit the function of the core binding factor complex. Although these rearrangements are considered favorable risk in AML, nearly 30% of children with core binding factor AML will relapse, indicating a continued need for improved understanding of AML biology and new therapeutic targets. Mutations in cohesin complex genes occur commonly in t(8;21) AML but are never found in inv(16) AML, suggesting a unique role of cohesin in the pathophysiology of each core binding factor AML subtype.

Objectives: The goal of this project is to define how cohesin mutations alter the biology of core binding factor AML. We hypothesized that loss of normal cohesin function enhances proliferation of cells expressing the RUNX1-CBFA2T1 (RC) fusion protein characteristic of t(8;21) AML and inhibits the proliferative capacity of cells expressing the CBFß-SMMHC (CS) fusion characteristic of inv(16) AML.

Design/Method: Bone marrow cells were harvested from mice with normal cohesin (*Smc3*$^{+/+}$) or cohesin haploinsufficiency (*Smc3*$^{+/-}$). We used retroviral transduction to express either empty vector control, RC fusion, or CS fusion proteins. Transduced cells were then plated in methylcellulose with stem and myeloid-promoting cytokines for serial plating assays or transplanted into lethally irradiated recipient mice to assess effects on leukemic transformation.

Results: Serial plating assays demonstrated that cohesin haploinsufficiency increased colony forming capacity of cells expressing RC protein and decreased colony forming capacity of cells expressing CS protein. Expression of several critical hematopoietic regulator genes was altered by cohesin haploinsufficiency, though these effects were dependent on which fusion protein was present. In murine RC models, an undifferentiated leukemia developed regardless of cohesin function. However, secondary transplant models demonstrated shortened survival and increased infiltration into bone marrow of leukemia with decreased cohesin function.

Conclusion: Loss of normal cohesin function differentially impacts proliferation of cells expressing the fusion proteins of core binding factor AML. In cells expressing the RC fusion associated with t(8;21) AML, decreased cohesin function provides a growth advantage prior to leukemic transformation and more infiltrative and aggressive leukemic phenotype. Alternatively, decreased cohesin function leads to a growth disadvantage in cells expressing the CS fusion of inv(16) AML with significant changes in expression of hematopoietic genes. Future experiments will focus on elucidating the underlying cellular mechanisms altered by decreased cohesin function in core binding factor AML.

Plenary Paper # 2002

UPDATED RESULTS FROM THE HGB-206 GROUP C STUDY OF LENTIGLOBIN FOR SICKLE CELL DISEASE GENE THERAPY

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Background: The ongoing Phase 1/2 HGB-206 Study (NCT02140554) evaluating efficacy and safety of LentiGlobin for SCD (bb1111) gene therapy (GT) uses a modified human β-globin gene that produces GT-derived anti-sickling hemoglobin (HbA^{T87Q}).

Objectives: Assess the efficacy and safety of LentiGlobin for SCD in HGB-206 Group C patients, with up to 2 years of follow up.

Design/Method: Patients (≥12–≤50 years) with SCD and recurrent severe vaso-occlusive events, including acute episodes of pain and acute chest syndrome (ACS), were enrolled. CD34+ cells collected by plerixafor mobilization/apheresis were transduced with BB305 lentiviral vector. LentiGlobin was infused following myeloablative busulfan conditioning. Patients were monitored for Hb levels, hemolysis markers, SCD-related outcomes, and adverse events (AEs). Data are median (min–max) unless otherwise stated.

Results: As of 3 March 2020, 40 Group C patients (23.5 [12–38] years), including 9 adolescents, initiated cell collection; 25/40 were treated with LentiGlobin and followed for 12.1 (2.8–24.8) months. All patients stopped red blood cell transfusions by 90 days post-treatment. In 16 evaluable patients with ≥6 months of follow-up, total Hb at last visit was 11.5 (9.6–16.2) g/dL, with HbA^{T87Q} contribution of 5.2 (2.7–9.4) g/dL, HbS of 6.1 (4.9–7.8) g/dL, and median HbS ≤ 60% of total Hb. At last visit, hemolysis markers were trending toward normalization (n=25). In 14 patients with ≥6 months of follow-up and history of vaso-occlusive crisis (VOC) or ACS, the annualized VOC+ACS rate was 4.0 (2.0–14.0) in the 2 years prior to treatment. Post-treatment, no ACS or serious VOCs were observed in these patients. One non-serious Grade 2 VOC occurred ~3.5 months after LentiGlobin infusion, resulting in a 99.5% (95% confidence interval, 92.4%–100%) mean reduction in the annualized VOC+ACS rate post-treatment.

The most common non-hematologic Grade ≥3 AEs post-treatment were stomatitis (n=15) and febrile neutropenia (n=11). Serious AEs reported in ≥2 patients post-treatment included nausea, opioid withdrawal syndrome, and vomiting (all n=2); 3 patients had LentiGlobin-related non-serious Grade ≤2 AEs. One death, unlikely related to LentiGlobin, occurred >18 months post-treatment in a patient with significant baseline SCD-related burden. No events of graft failure, vector-mediated replication-competent lentivirus, or clonal dominance occurred.

Conclusion: LentiGlobin for SCD results in reduced HbS expression and increased total Hb. Complete resolution of VOC/ACS was observed in almost all patients. The safety profile post-LentiGlobin remains generally consistent with myeloablative single-agent busulfan conditioning and underlying SCD. Additional patient data will be included in the presentation.

This study was a bluebird bio sponsored study.

Paper # 2003/Young Investigator Award Recipient

USE OF MRNA CAR T CELLS FOR MALIGNANT PEDIATRIC BRAIN TUMORS

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Background: Brain tumors are the leading cause of pediatric cancer death. Advances in immunotherapy such as chimeric antigen receptor (CAR) T cell therapy serve as a potential therapeutic avenue for these devasting tumors. However, their location in the brain brings the possibility of significant neurotoxicity and fatality and thus innovative strategies need to be developed to circumvent these potential toxicities.

Objectives: Building upon our prior work optimizing mRNA for use in CAR T cells (Foster et al. Hum Gen Ther 2019), we hypothesized transient mRNA CAR T cells could be successfully employed for safe and effective targeting of pediatric brain tumors including: (1) novel CAR T cell development against glypican 2 (GPC2) in medulloblastomas (MB) and high-grade glioma (HGG), and (2) GD2-directed CAR T cells in diffuse midline glioma (DMG).

Design/Method: GPC2- and GD2-directed CAR T cells were created using specific single chain variable fragments paired with 41BB and CD3-zeta co-stimulatory domains and mRNA was transfected into human T cells. GPC2-directed CAR T cells were tested *in vitro* against MB and HGG cells lines, and *in vivo* using two patient-derived MB models: Rcmb28 (group 3) and 7316-4509 (group 4). GD2-directed CAR T cells were tested against DMG cell lines and xenografts: SU-DIPG13P* and 7316-6349. mRNA CAR T cells were delivered locoregionally using an indwelling infusion catheter.

Results: GPC2- and GD2-directed mRNA CAR T cells induced significant tumor-directed cell death with concomitant T cell degranulation compared to CD19-directed mRNA CAR T cell controls in MB/HGG and DMG cellular models, respectively. *In vivo* GPC2-directed CAR T cells induced significant decrease in tumor burden in MB xenografts measured by bioluminescence after four to six repeated doses of 4×10^6 CAR T cells given intratumorally ($p<0.0001$ for Rcmb28, $p<0.05$ for 7316-4509). GD2-directed mRNA CAR T cells prolonged survival of mice harboring the aggressive DMG model SU-DIPG 13P* by 61% (mean survival 29 days versus 18 days, $p<0.01$) after four intratumoral doses of 4×10^6 CAR T cells. In addition, four intratumoral doses of 5×10^6 GD2-directed CAR T cells also significantly decreased 7316-6349 *in vivo* tumor burden ($P<0.0001$). No GPC2- or GD2-directed CAR T cell related deaths

were observed.

Conclusion: mRNA CAR T cell therapy with repeated locoregional delivery is a safe and effective method for treating pediatric brain tumors. These data highlight the utility of using mRNA to titrate CAR T cell therapy in the brain, and will serve as a basis for upcoming clinical trials.

Paper # 2004/Young Investigator Award Recipient

COMMUNICATION BREAKDOWNS IN PEDIATRIC ONCOLOGY: CONTRIBUTORS, CONSEQUENCES, AND RESPONSES

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Background: When a child is diagnosed with cancer, parents rely on communication with the clinical team. Communication efforts can fail, however, leading to negative consequences for families. Previously, we identified 8 core functions of communication in pediatric oncology: building relationships, exchanging information, making decisions, enabling self-management, responding to emotions, managing uncertainty, supporting hope, and providing validation. We also developed a multilevel framework of communication barriers from clinicians' perspectives. Prior work, however, has not characterized the parental perspective on contributing factors, negative consequences, or recovery attempts after communication breakdowns in pediatric oncology.

Objectives: To identify parental perspectives on contributing factors, negative consequences, and recovery attempts after negative communication experiences.

Design/Method: Semi-structured interviews with 80 parents of children with cancer across 3 academic medical centers at 1 of 3 time points: treatment, survivorship, or bereavement. As part of longer interviews about communication, we asked parents about "bad communication." We asked for specific negative communication experiences, and we asked, "What made this experience particularly bad," and "What could have made this better?" We used semantic content analysis to analyze transcripts from interviews, using inductive coding strategies.

Results: Parents described negative communication experiences in 76/80 (95%) of interviews involving a wide array of healthcare professionals across multiple specialties. We identified 4 categories of contributors to negative experiences: individual (n=68), team (n=26), organization (n=46), and greater healthcare system (n=16). Parents indicated 12 types of negative consequences resulting from failures to fulfill communication functions: emotional distress and decreased emotional support (responding to emotions), insufficient understanding (exchanging information), decreased trust or confidence (building relationships), decreased self-confidence and decreased engagement (providing validation), false hope and decreased hope (supporting hope), inconvenience, financial insult, decreased access to resources (enabling family self-

management), and medical harm. Parents also indicated 5 categories of supportive responses by clinicians: exploring, acknowledging, informing, adapting, and advocating. When clinicians did not respond sufficiently, parents often increased their own advocacy for the child. Parents also emphasized that clinicians should engage them in finding solutions and resolving conflicts. Lastly, one parent suggested that clinicians should assume communication will fail and develop contingency plans ahead of time.

Conclusion: Communication breakdowns are common and negatively affect parents and children in pediatric oncology. Clinicians should plan for communication breakdowns, and respond by exploring, acknowledging, informing, adapting, advocating, and engaging parents in finding solutions.

Paper # 2005

A NOVEL, BIOENGINEERED, HUMAN, ORGANS-ON-A-CHIP MODEL OF PRIMARY AND METASTATIC OSTEOSARCOMA

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Background: Established preclinical models of solid bone tumors like osteosarcoma (OS) are unable to faithfully recapitulate the diseased human physiology. Monolayers and mouse models have been used extensively to unravel the mechanisms and pathways governing OS pathogenesis. Unfortunately, the existing paradigm has clear limitations, as is evident by the plateauing of progress in OS treatment, particularly evident in patients with metastasis at diagnosis.

Objectives: Bioengineered human OS models and organs-on-a-chip (OOC) systems have since been developed to more accurately mimic native human tumor tissues and improve the inefficient drug development process. Previously we succeeded in developing a biomimetic, human tissue model of Ewing sarcoma, and a multi-tissue, microfluidic OOC platform. Here, we employed both approaches towards bioengineering novel human 3D tumor models of primary bone and secondary lung OS, and then integrated both into our OOC platform to enable drug testing.

Design/Method: Briefly, OS cell lines were used to generate 3D, tumor-like aggregates, which were subsequently introduced into and cultured within engineered functional bone tissue scaffolds as our model of the primary bone tumor. In parallel, we engineered a model of OS lung metastasis by growing metastatic OS cell lines with matured bronchial epithelial and endothelial cells on an air-liquid-interface transwell. Both primary and secondary OS models were then co-cultured in our OOC platform, enabling us to simultaneously administer anti-cancer drug treatments to both OS tissues.

Results: The bioengineered primary OS bone model was able to recapitulate several phenotypes

of native tumors and their microenvironment missing in monolayer cultures. Both intra- and inter-tumor heterogeneity were reproduced, hypoxia-mediated angiogenesis was re-activated, and vasculogenic mimicry was induced. Notably, unlike monolayers, our bioengineered OS model could be cultured stably for several weeks, allowing for the application of clinical drug treatment regimens. The secondary OS lung model allowed us to capture features of the metastastic tumor microenvironment and increased resistance to chemotherapeutics. Both primary and secondary OS tissues could be successfully co-cultured in our OOC platform. Integration also allowed us to recreate lung tissue metastasis *ex vivo*, and to screen canonical and experimental drugs against both tissues using more physiologically relevant drug distribution to achieve more clinically relevant results.

Conclusion: Overall, we successfully generated, and then co-cultured within our integrated OOC platform, new, more native-like 3D bioengineered models of primary and secondary OS. These have significant advantages over established preclinical models, and have the potential to explore novel questions regarding tumor microenvironments and translational applications.

Paper # 2006

ROLE OF CYCLIN DEPENDENT KINASE 8 IN FUSION-POSITIVE RHABDOMYOSARCOMA

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Background: Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma of childhood. Patients with RMS tumors classified as fusion-positive (FP) most commonly express the PAX3-FOXO1 fusion protein and survival for this group of patients is less than 30%. Since PAX3-FOXO1 is not currently druggable we sought to identify proteins that interact with PAX3-FOXO1 and might serve as mechanisms of indirect inhibition of PAX3-FOXO1. Cyclin dependent kinase 8 (CDK8) emerged as such a vulnerability. CDK8 is a transcription-associated kinase and acts as an oncogene in adult colorectal cancer and AML. A CDK8 inhibitor is being evaluated in phase 1 clinical trials in AML and breast cancer. Recent genomic studies nominate CDK8 as an RMS cell-line dependency. We **hypothesize** that CDK8 is broadly expressed in FP-RMS, that CDK8 supports PAX3-FOXO1-driven transcription, and thus is a rational therapeutic target for this cancer.

Objectives: To understand how CDK8 contributes to FP-RMS tumorigenesis in vitro, investigate the value of CDK8 as a therapeutic target in vitro, and finally assess the pre-clinical efficacy of CDK8 inhibition in vivo.

Design/Method: To understand how CDK8 contributes to FP RMS tumorigenesis, we will assess the impact of CDK8 loss of function (LOF) on FP-RMS cellular phenotypes including proliferation, apoptosis, differentiation, and stemness. To investigate the value of CDK8 as a therapeutic target in vitro, we will examine CDK8 expression in human RMS tissue microarrays and perform in vitro drug studies of CDK8 small molecule inhibitors senexin A and B, cortistatin

A, and SEL120-34A. To assess the pre-clinical efficacy of CDK8 LOF in vivo, we will test the impact of genetic or pharmacologic CDK8 inhibition in FP-RMS xenografts in immunodeficient mice. Resulting tumors will be analyzed for target validation and mechanisms of tumor inhibition.

Results: Thus far, we have found that LOF of CDK8 via RNAi inhibits growth of human FP-RMS cells in vitro, in part due to induction of apoptosis and more modestly, myogenic differentiation. Pharmacologic inhibition of CDK8 in FP-RMS cell lines via senexin A induces cytotoxicity with an IC50 in the 100-150nM range. In vivo pharmacologic studies testing SEL120-34A are ongoing in mouse xenograft studies.

Conclusion: This work introduces the importance of CDK8 in FP-RMS and provides rationale for continuing biochemical and in vivo work illuminating the biology and targetability of CDK8 in FP-RMS.

Paper # 2007

OBESITY ATTENUTATES T-CELL FUNCTION WHICH IMPACTS T-CELL IMMUNOTHERAPIES IN LYMPHOBLASTIC LEUKEMIA

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Background: Acute lymphoblastic leukemia is the most common malignancy in childhood. Despite vast improvements in treatment, studies have shown that children who are obese at diagnosis have poorer survival outcomes. The mechanisms of decreased therapeutic responses in obese individuals are not well understood. Changes in pharmacokinetics are partially responsible; however, there is growing interest in understanding how obesity-associated alterations in immune surveillance affects disease progression and therapeutic responses. This is of particular interest given the increasing use of immunotherapy in hematologic malignancies including chimeric antigen receptor T-cell therapy (CAR-T) and bi-specific T-cell engagers (Blinatumomab), which require functional T-cells to target and eliminate leukemia cells. The impact of obesity on the efficacy of these classes of immunotherapies is currently unknown.

Objectives:

1. Determine how adipocyte-secreted factors impact the function of endogenous T-cells
2. Determine if obesity-induced immune dysfunction reduces the efficacy of T-cell based immunotherapies

Design/Method: We developed an *in vitro* model of obesity utilizing a protocol that differentiates murine bone marrow stromal cells into adipocytes. Primary mouse T-cells were stimulated for 72 hours in either unconditioned media or conditioned media (stromal cell-conditioned media or adipocyte-conditioned media) followed by flow cytometry to determine the expression of activating (CD44) and inhibitory (PD-1) surface proteins, intracellular cytokine

production (IFN-γ and TNF-α), and levels of cytolytic machinery (Perforin and Granzyme B). Similar experiments were conducted on *ex vivo* T-cells isolated from healthy patients and patients with leukemia (samples obtained from Emory Biorepository). Cytolytic experiments were conducted utilizing engineered CD19 CAR T-cells or Blinatumomab targeted against human B-ALL cell lines *in vitro*.

Results: Compared to murine T-cells activated in control media, T-cells activated in the presence of adipocyte-secreted factors exhibited an exhausted phenotype highlighted by the failure to produce the effector mediators IFN-γ, TNF-α, Perforin, and Granzyme B. Similar compromised responses were observed in T-cells isolated from obese patients with and without leukemia. Furthermore, we found that the *in vitro* cytolytic efficacy of both CAR T-cells (4 hour and 24 hour) and naïve T-cells with Blinatumomab (72 hour) was significantly reduced in the presence of adipocyte-secreted factors.

Conclusion: Adipocyte-secreted factors compromise the function of endogenous T-cells (in the presence and absence of Blinatumomab) and CAR T-cells. Given results demonstrating compromised T-cell function from obese pediatric patients with leukemia, our findings suggest that clinical assessments are necessary to determine if obesity reduces the efficacy of Blinatumomab and CAR T-cells in pediatric patients receiving treatment for lymphoblastic leukemia.

Paper # 2008

AZACITIDINE AS EPIGENETIC PRIMING FOR CHEMOTHERAPY IS SAFE IN INFANTS WITH KMT2A-REARRANGED ALL

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Background: Acute lymphoblastic leukemia (ALL) with *KMT2A* rearrangement (*KMT2A*-r) in infants <1 year is an aggressive leukemia subtype, associated with early relapse and poor survival. Infant *KMT2A*-r ALL blasts are characterized by DNA hypermethylation, which contributes to chemoresistance and has been associated with poor prognosis. Epigenetic priming with DNA methyltransferase inhibitors reverses methylation and improves the chemotherapy *in vitro* blast cytotoxicity. Azacitidine, a pyrimidine nucleoside analog of cytidine and hypomethylating agent, is effective in adult myelodysplastic syndrome and has been safely used in combination with chemotherapy in children with leukemia.

Objectives: To determine the safety and tolerability of adding azacitidine to the Interfant-06 standard chemotherapy backbone in infants with newly diagnosed *KMT2A*-r ALL.

Design/Method: The Children's Oncology Group (COG) trial AALL15P1 (NCT02828358) was

a single arm, open label, groupwide pilot trial. Eligibility criteria included B-ALL or acute leukemia of ambiguous lineage with ≥50% B-lymphoblasts, <366 days of age at diagnosis, and >36 weeks gestational age at enrollment. Exclusions included Down syndrome, secondary ALL, and prior cytotoxic therapy (except intrathecal chemotherapy or corticosteroids). Following standard Interfant induction, infants with *KMT2A*-r received 4 courses of azacitidine, 2.5 mg/kg/dose intravenously over 10-40 minutes daily for 5 consecutive days, immediately preceding the start of a chemotherapy course on day 6. Dose limiting toxicity (DLT) was defined as any grade 5 toxicity or any grade 3-4 toxicity that led to significant delays or therapy omissions within the first 3 courses of azacitidine plus chemotherapy. Infants without *KMT2A*-r were removed from protocol following induction and did not receive azacitidine.

Results: The study accrued from March 2017 to December 2019. Of the 78 infants enrolled, 56 (72%) had *KMT2A*-r, 31 completed at least 3 courses of azacitidine and were evaluable for DLT, and 25 were inevaluable (due primarily to early events). Two infants (6%) experienced a DLT. The reported DLTs were both grade 4 neutropenia associated with a greater than 4 week delay in therapy, during Consolidation and Delayed Intensification. At no time did the DLT rate meet or exceed the pre-defined continuous stopping boundary. Other observed toxicities were within the expected range for infants receiving intensive ALL therapy.

Conclusion: Azacitidine is safe and well tolerated in infants receiving standard chemotherapy for ALL. Future studies are necessary to test the efficacy of this treatment strategy.

Paper # 2009

HORMONE-RELATED THROMBOSIS IN ADOLESCENT GIRLS: RISK FACTORS AND MANAGEMENT CHALLENGES

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Background: Hormonal therapy is prescribed to adolescent girls for a variety of indications, including contraception, heavy menstrual bleeding and dysmenorrhea. Venous thromboembolism (VTE) is a serious complication of hormonal therapy, with higher risk associated with estrogen-containing medications. Because of low incidence in the pediatric population, the contribution of additional risk factors and adverse effects of treatment are not well studied.

Objectives: Our objectives were to describe: (1) risk factors in adolescent girls presenting with VTE while on hormonal therapy, (2) incidence of bleeding symptoms while on anticoagulation and (3) rates of pregnancy associated with changes in hormonal therapy.

Design/Method: Clinical and laboratory data was obtained retrospectively from electronic medical records for patients age 13-19 years who presented to the University of Michigan Health System between 2013 and 2020 with a diagnosis of VTE while taking any estrogen or progestin containing medication. Data obtained included personal and family history, medications, results of laboratory testing, duration and type of therapy, bleeding symptoms and pregnancies.

Results: Forty-one patients were included. Thirty-eight were taking a combined oral contraceptive at the time of presentation, two were taking progestin-only medications and one had a contraceptive patch. Median age at presentation was 17.5 years and median duration of hormonal therapy at the time of VTE diagnosis was 5.5 months. At least one additional risk factor for thrombosis was present in 93% of patients, and 73% had two or more. Most common risk factors were obesity, recent immobility, significant family history, infection, central venous catheter placement, and autoimmune/inflammatory condition. Management included anticoagulation in 98% of patients, with 55% of these switching their anticoagulant at least once. Patients on anticoagulation were asked about menstrual bleeding at follow up 67% of the time, and 41% of those reported heavy menstrual bleeding. Hormonal therapy was stopped at diagnosis in 90% of patients, and in 32% of these patients there was no re-initiation. Of those who remained off hormonal therapy, 33% became pregnant within a year.

Conclusion: In this study, the majority of adolescent girls with VTE while on hormonal therapy had multiple additional risk factors for thrombosis. There was a substantial rate of heavy menstrual bleeding reported by patients on anticoagulation and a considerable risk of pregnancy if hormonal therapy was discontinued at diagnosis and not replaced with an alternative. This patient population clearly stands to benefit from multidisciplinary care with early involvement of specialists from adolescent gynecology or adolescent medicine.

Paper # 2010

IMPLEMENTATION OF NEAR-UNIVERSAL HYDROXYUREA UPTAKE AMONG CHILDREN WITH SICKLE CELL ANEMIA

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Background: Without early initiation of disease modifying therapy, the acute and chronic complications of sickle cell anemia (SCA) begin early in childhood and progress throughout life. Hydroxyurea is a safe and effective medication that reduces or prevents most SCA-related complications. Despite recommendations to prescribe hydroxyurea for all children with SCA as young as nine months of age regardless of clinical severity, utilization remains low.

Objectives: To 1) review the hydroxyurea prescribing practices within the Cincinnati Children's Hospital Medical Center (CCHMC) Comprehensive Sickle Cell Center over the period 2010-2019 comparing the periods before and after the release of the 2014 NHLBI guidelines, and 2) analyze the impact of this shift in treatment strategy upon clinical events.

Design/Method: We completed a retrospective review of hydroxyurea prescribing practices and associated clinical outcomes at our institution over a 10-year period before and after the 2014 NHLBI recommendations to use hydroxyurea for all children with SCA.

Results: We identified 439 patients with sickle cell disease followed at CCHMC from 2010-2019 (47% female, age range: 0-22 years); 275 had SCA (HbSS, HbS^0-thalassemia). Hydroxyurea use more than doubled within our pediatric SCA population from 43% in 2010 to 95% in 2019. The age of hydroxyurea initiation was significantly younger during 2014-19 compared to 2010-13 (median 2 y vs 6 y, p =< 0.001). Of 36 patients with SCA not on hydroxyurea in 2019, 28 received chronic transfusions and the remaining 8 received no disease-modifying therapy. With this change in clinical practice, nearly all (69/71= 97%) children born after 2013 received disease-modifying therapy by the end of 2019, primarily hydroxyurea (93%). Concurrently, the number of SCA-related admissions significantly decreased from 67/100 patient-years in 2010 to 39/100 patient-years in 2019 (p < 0.001). Further, of the 66 patients born from 2013 and on hydroxyurea, 49 (74%) have had no SCA-related complications, while 10 (15%) have had one SCA-related event.

Conclusion: The early and universal prescription of hydroxyurea for children with SCA is the recommended standard-of-care. Here, we demonstrate that a careful and deliberate approach to follow this guideline in clinical practice via a commitment from the entire clinical team is feasible and results in measurable improvements in patient outcomes. Our approach and improved outcomes may provide a model to expand hydroxyurea use for more children with SCA in order to optimize their clinical course and quality of life.

Paper # 2011

FOOD INSECURITY, HEALTHCARE UTILIZATION, AND QUALITY OF LIFE IN PATIENTS WITH SICKLE CELL DISEASE

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Background: Pediatric patients with sickle cell disease (SCD) are more likely than their peers to live in a food insecure household. In other pediatric populations, food insecurity (FI) has been associated with poorer physical and mental health. Little is known about the relationship between FI and health among pediatric patients with SCD.

Objectives: Describe rates of household FI, self reported healthcare utilization and quality of life (QOL) among patients with SCD. Test the hypothesis that FI is associated with higher rates of healthcare utilization and lower QOL compared to children with SCD living in food secure households.

Design/Method: Observational study of 99 patients with SCD ages 5- 24 years recruited July 2015 - July 2019 during a routine SCD clinic visit. A baseline survey was administered to a caregiver of patients <18 years as well as the patient, and directly obtained from the patients >18 years. Baseline survey assessed FI (USDA Food Security Short Form), healthcare utilization (Stanford Healthcare Utilization Scale), and QOL ($PedsQL_{TM}$ Sickle). Scoring and transformation was done via established methods: USDA FS (range 0-6; ≥1 indicating some

level of FI, 1 = marginal FI, 2-4 = moderate FI, 5-6 = high FI), and PedsQL$_{TM}$ (range 0-100; ≤60 indicating low QOL). One way ANOVAs, correlations, and chi-squared tests were used for analyzing differences in FI, healthcare utilization, and QOL scores.

Results: Among participants, 52 (52%) were female and 75 (76%) had Hgb SS genotype. The age distribution was: 17% ages 5-7 years, 30% ages 8-12 years, 27% ages 13-17 years, 25% ages ≥18 years. More than a third (35%) of patients screened positive for FI, with a distribution of 37% marginal FI, 40% moderate FI, and 23% high FI. More than half (52%) of all patients received SNAP benefits in the last 12 months. Receiving SNAP benefits was associated with higher rates of FI (p=0.02). While FI scores were not significantly associated with rates of healthcare utilization, a higher FI score was associated with lower overall QOL score (p=0.03). QOL was also inversely related to ER visits (p=0.003), hospital stays (p=0.002), and hospital nights (p=0.001).

Conclusion: More than one in 3 children and young adults with SCD, including those receiving SNAP benefits, were food insecure and FI was associated with lower overall QOL. Given the high rate of FI seen among children and young adult patients with SCD, interventions for FI will be important for improvement in QOL and other clinical outcomes.

Paper # 2012

DIAGNOSTIC UTILITY OF TARGETED NEXT GENERATION SEQUENCING IN VASCULAR ANOMALIES

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Background: Vascular anomalies are diverse entities and can range in severity from self-limiting to life-threatening. Diagnosis and care of these patients is challenging due to overlapping clinical and histologic features. The mTOR inhibitor sirolimus has been used to treat a variety of vascular anomalies, but not all patients respond to this treatment. Recently, it has been established that many vascular anomalies arise from somatic mutations in cancer genes (*PIK3CA, AKT, NRAS*). Use of cancer genomics in patients with vascular anomalies may establish a genetic diagnosis and expand use of targeted medical therapies. We evaluated the utility of targeted next generation sequencing for vascular anomalies patients at a single pediatric center.

Objectives: To explore the use of a targeted next generation sequencing test designed for cancer in establishing genetically informed diagnoses for patients with vascular anomalies.

Design/Method: Using OncoPanel, a hybrid-capture and massively parallel sequencing assay that surveys DNA sequences of 447 genes implicated in cancer, we analyzed genetic variants in lesional tissue from vascular anomalies patients evaluated at Boston Children’s Hospital between 5/2/2017 and 3/23/2020.

Results: Lesional tissue from 137 patients was successfully sequenced and analyzed under the Dana Farber Cancer Institute Profile protocols DFCI 11-104 and DFCI 17-000. Clinical diagnoses prior to testing were diverse and 11 patients (7%) had an unknown diagnosis. Mutations in PIK3CA were common (61/137). Most mutations in PIK3CA (44/61) occurred in 1 of 5 hotspots (C420R, E542K, E545K, H1047L, and H1047R). To date, 18 patients in our cohort have been treated with targeted medical therapy informed by their genetic diagnosis, including 10 patients treated with alpelisib, 5 patients treated with miransertib, and 3 patients treated with trametinib. Several more await enrollment on clinical trials. For patients with diagnoses previously categorized as unknown (n=11), sequencing led to identification of a genetic variant in 6 patients (54%). Additionally, 8/138 patients had variants requiring further evaluation for potential germline involvement (*BRCA2, PTEN, RASA1*).

Conclusion: Use of next generation sequencing in vascular anomalies patients identified actionable variants in a large proportion (80/137) of the patients in our cohort. Targeted therapies based on specific genotypes hold promise as clinical trials in vascular anomalies are emerging. Additionally, sequencing in this cohort identified several variants suggesting a germline cancer predisposition requiring follow-up. Use of next generation sequencing has clinical utility and increased use of this testing may improve diagnosis, prognosis, and treatment for patients with vascular anomalies.

Paper # 2013

FACTORS ASSOCIATED WITH GENOMIC TESTING IN PATIENTS WITH PEDIATRIC LEUKEMIA

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Background: Leukemia is the most common type of cancer in children with significant disparities in survival. Genomic testing impacts treatment decisions and may be one arena in which there are disparities in access. While previous research has highlighted disparities in testing access in adult oncology populations, there has been little research in genomic testing access in a pediatric oncology population.

Objectives: Our aim was to identify patient and disease characteristics associated with genomic testing in a pediatric population with leukemia at UCSF. We hypothesized that minority race/ethnicity, patients with public insurance, and patients from low socioeconomic status (SES) areas are tested less frequently, and that patients with high risk disease are tested more frequently.

Design/Method: A cohort of patients with a diagnosis of leukemia during the study period (2016-2019) who received at least one course of chemotherapy at UCSF was identified and reviewed from the UCSF cancer registry. Patient and disease characteristics were collected via structured review of the electronic health record. UCSF500 testing status was documented in the

institutional Molecular Oncology Initiative Registry. Baseline characteristics were tabulated by testing status. Logistic regression analyses were used to estimate the unadjusted odds ratio and corresponding 95% confidence intervals for UCSF500 testing. Characteristics that were hypothesized to affect testing *a priori* or those found to be associated with testing (p-value < 0.05) were included in the multivariable model to obtain adjusted odds ratios.

Results: A total of 126 patients were included. Most patients were Hispanic (47%), publicly insured (63%), had negative measurable residual disease (MRD) (74%), and had high risk disease (58%). A total of 39 patients underwent UCSF500 testing. MRD(+) (OR 6.64, 95% CI 2.85, 16.15) and high risk disease (OR 2.73, 95% CI 1.10, 7.51) were significantly associated with UCSF500 testing. In the multivariable model, non-white race (aOR 0.30, 95% CI 0.08, 0.99) and low SES (aOR 0.23, 95% CI 0.06, 0.77) were significantly associated with decreased access, while MRD(+) (aOR 10.28, 95% CI 2.98, 42.59) and English as primary language (aOR 4.82, 95% CI 1.11, 25.21) were significantly associated with increased access.

Conclusion: High risk, MRD(+) leukemia, and White race were major predictors of UCSF500 testing. Our findings suggest that there may be disparities in genomic testing access in pediatric leukemia. Expansion of this study to other cancer types and medical centers would increase the generalizability. Approaches to ensuring equitable access to genomic testing may help to address observed disparities in outcomes.

Paper # 2014

TEXAS-MEXICO BORDER RESIDENCE AND CHILDHOOD LEUKEMIA SURVIVAL: A POPULATION-BASED ANALYSIS

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Background: Rural areas are more likely to lack access to comprehensive cancer centers compared to urban areas, and disparities in survival of adults with different cancers living in rural areas have been documented. Further, adults with cancers living along the Texas-Mexico border have survival disparities. The impact of survival in children with leukemia that live in rural/urban and Texas-Mexico border areas has not been studied.

Objectives: The objective of our study was to evaluate the impact of border and rural residence on the survival of childhood acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML). Our hypothesis is that children with leukemia living along the Texas-Mexico border and in rural areas experience poorer survival compared to those living in non-border and urban areas.

Design/Method: We conducted a retrospective survival analysis leveraging data from the Texas Cancer Registry (TCR). The study included patients of 0-19 years of age diagnosed with ALL or AML from 1995 to 2017. Cox proportional hazards models evaluated factors associated with risk of death. Five-year overall survival estimates were calculated using Kaplan-Meier methods.

Results: There were 6002 patients with ALL and 1279 patients with AML. Among patients with ALL, 855 lived in border counties, and 660 lived in rural census tracts; among patients with AML, 185 lived in border counties, and 161 lived in rural census tracts. Five-year overall survival rate for patients with ALL living in non-border counties was 86% (95% confidence interval [CI]: 84% - 87%) versus 78% (95% CI: 74% - 80%) for those living in border counties ($p<0.001$). No survival difference was found among patients with AML living in non-border versus border counties. In multivariable analyses, border residence was associated with a higher hazard ratio (HR) for death in patients with ALL (HR: 1.41 [1.19 - 1.66], $p<0.001$), the risk of death in patients with AML living in border areas was similar as those living in non-border areas (HR: 1.18 (0.92 - 1.52). In stratified analyses, patients with ALL of Hispanic ethnicity and those living in urban border areas had poorer survival compared to Non-Hispanic children and those living in urban and non-border areas; patients with AML from rural and border areas experienced higher mortality (HR: 2.08 (1.11 - 3.91), $p=0.02$) compared to those that lived in rural and non-border areas.

Conclusion: Children with leukemia living along the Texas-Mexico border experience poorer survival, underscoring the need to understand the geographic factors impacting survival in children with hematologic malignancies.

Paper # 2015

PRESCRIPTION OPIOID USE AND MISUSE IN PEDIATRIC CANCER SURVIVORS: A NATIONWIDE CLAIMS-BASED ANALYSIS

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Background: Survivors of pediatric cancer are at high risk of experiencing pain. Opioid analgesics are often prescribed to control cancer-related pain. However, little is known about patterns of prescription opioid use and misuse among pediatric cancer survivors.

Objectives: This study examined the prevalence of prescription opioid use and indicators for potential opioid misuse in pediatric cancer survivors during the early post-therapy period, as compared to peers without cancer.

Design/Method: Using the IBM MarketScan Commercial Database, we identified 6 422 survivors, who completed therapy for leukemia, lymphoma, central nervous system, bone, or gonadal cancers (age ≤21 years at diagnosis) during 2009-2017 and remained continuously insured for ≥1 year post-therapy. We also identified 7 713 349 individuals who matched eligibility criteria but had no cancer diagnosis (with a randomly assigned, fictitious date of therapy completion) as a comparison group. Outcomes assessed: (1) any (≥1) opioid prescription filled, (2) number of opioid prescriptions received, and (3) total days of supply in the first-year post-therapy. Outcomes also included indicators of potential misuse in the first-year post-

therapy: (4) high opioid dosage (prescribed daily doses of ≥100 morphine milligram equivalents) and (5) opioid overlap (multiple opioid prescriptions overlapping for ≥7 days). Outcomes were compared between pediatric cancer survivors and comparisons in unadjusted and adjusted analyses controlling for sociodemographic factors.

Results: Among eligible subjects, a *higher* proportion of survivors than comparisons received an opioid prescription post-therapy (21.7% versus 6.9%). Among opioid recipients, survivors received *longer* duration of supply (mean: 24.0 versus 12.0 days) and filled *more* prescriptions (mean: 2.5 versus 1.6 prescriptions) post-therapy than comparisons. Moreover, a *higher* proportion of survivor recipients than comparisons were classified as having high daily doses of opioids (9.1% versus 5.1%) and overlapping opioid prescriptions (7.7% versus 2.0%). In adjusted analyses, these survivor-comparison differences persisted (p-values<0.001). For example, adjusted models showed that survivor recipients were 94% (marginal effects: 4.8 percentage points, p<0.001) and 335% (marginal effects: 6.7 percentage points, p<0.001) *more* likely than comparisons to experience high daily doses and overlapping opioids, respectively. Among survivors, older age and a bone cancer diagnosis were strongly associated with increased likelihoods of prescription opioid use, high daily doses, and overlapping opioids (p-values<0.05).

Conclusion: This study showed an elevated rate of prescription opioid use in pediatric cancer survivors. Importantly, rates of prescription opioid misuse were generally low but substantially higher in survivors than peers without cancer. Oncologists regularly seeing survivors should explore non-opioid options for pain management to prevent opioid misuse.

Paper # 2016

ASSESSMENT OF A BEREAVED PARENT MENTOR PROGRAM FOR PARENTS WHOSE CHILD DIED OF CANCER

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Background: The death of a child is devastating and results in life-long grief in surviving parents. Bereavement after the death of a child has been associated with worse parental physical and psychosocial well-being compared to non-bereaved parents. Evidence suggests that parents desire and benefit from support provided by other bereaved parents. This support allows bereaved parents the ability to talk openly, express their feelings without judgment, and feel less lonely and isolated. To foster this peer support, St. Jude Children's Research Hospital established a peer-to-peer mentorship program for bereaved parents in which trained bereaved parent mentors offer support to newly bereaved parents.

Objectives: This study aims to describe the Bereaved Parent Mentor Program's mentor and mentee characteristics and qualitatively analyze the content of their documented encounters.

Design/Method: We used a retrospective cohort design and qualitative analysis for the study. Trained bereaved parent mentors documented encounters with newly bereaved parent mentees using a secure web platform. Mentors provided a summary of the encounter including any identified concerns or need for professional psychosocial support. Descriptive statistics were used to describe mentor and mentee characteristics. Semantic content analysis methodology was utilized to qualitatively analyze the encounters.

Results: A total of 1,368 encounters occurred between 44 mentors and 152 mentees from January 1, 2014 through February 29, 2020. Most mentors and mentees were mothers (66% and 80%, respectively). There were only 7 encounters (0.5%) flagged as serious concern for professional psychosocial support. Common themes included mentors: providing suggestions and guidance; offering encouragement and praise; and normalizing the mentee's experience. Additionally, mentors shared their own bereavement experience as a way of supporting the mentee. The mentors and mentees discussed aspects of life that may exacerbate grief including the variation of the grief experience between spouses, the grief of surviving siblings, and important dates that may trigger strong emotions such as the anniversary of the child's death, birthdays, and holidays. Parents pairs also discussed coping and self-care strategies such as the use of spirituality and religion, support from partner/spouse and family members, and meaning making through sharing stories and philanthropic efforts. Finally, many bereaved parent mentees expressed gratitude and verbalized the therapeutic benefit of having a peer mentor during their bereavement.

Conclusion: This structured bereaved parent mentor support program fostered powerful and rich interactions. Future research should evaluate the overall assessment and impact of this program has on bereaved parent's psychosocial and physical well-being.

Paper # 2024/Early Career Award Recipient

MEK INHIBITION OVERCOMES STROMAL CELL-MEDIATED RESISTANCE TO MRX-2843, A DUAL MERTK/FLT3 INHIBITOR

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Background: MERTK tyrosine kinase is aberrantly expressed in 80% of pediatric acute myeloid leukemia (AML) samples, and inhibition of MERTK with the small molecule tyrosine kinase inhibitor (TKI) MRX-2843 prolongs survival in AML xenograft models. While treatment with MRX-2843 reduces leukemia in peripheral blood, it is less effective in the bone marrow, suggesting a role for the bone marrow microenvironment in therapeutic resistance. The MEK/ERK pathway has been implicated as a mediator of resistance to TKIs in the bone marrow niche and MEK inhibitors have been approved for clinical use.

Objectives: To determine the role of MEK/ERK signaling in stromal cell-mediated resistance to MRX-2843.

Design/Method: AML cell lines (Kasumi-1, OCI-AML5, C1498) were cultured alone or with the Hs27 or OP9 stromal cell lines and treated for 72 hours with vehicle, MRX-2843, a MEK inhibitor (MEKi, PD0325901 or pimasertib), or MRX-2843 and MEKi combined. After treatment, leukemia cells were collected, stained with Po-PRO-1 iodide (PoPro) and propidium iodide (PI), and analyzed by flow cytometry to identify apoptotic ($PoPro^{+}$, PI^{neg}) and dead (PI^{+}) cells. Alternatively, cell lysates were prepared and analyzed for phosphorylated and total ERK proteins by immunoblot or phospho-kinase array. C57bl/6 mice (n=5) were treated once daily with 65 mg/kg MRX-2843 and 5 mg/kg PD0325901 administered by oral gavage and were weighed and visually evaluated for toxicity.

Results: Co-culture with stromal cells provided significant protection from cell death induced by MRX-2843 treatment (no co-culture vs. co-culture: Kasumi-1: 61.2% vs. 31.9% dead, OCI-AML5: 79.1% vs. 25.8%, C1498: 66.0% vs. 42.3%). ERK phosphorylation was induced in stromal cell co-cultures and was refractory to inhibition in response to treatment with MRX-2843 in the presence of stromal cells. Moreover, treatment with MRX-2843 in combination with PD0325901 or pimasertib restored induction of cell death in stromal cell co-cultures to levels observed in the absence of co-culture and provided significantly enhanced anti-leukemia activity relative to vehicle or single agents. Mice treated with both MRX-2843 and PD0325901 exhibited no significant weight loss or overt toxicity.

Conclusion: Induction of MEK/ERK signaling by stromal co-culture protects leukemia cells from MRX-2843-induced cell death. Treatment with MEKi overcame stromal cell-mediated resistance to MRX-2843 *in vitro* and the combination therapy was well-tolerated in mice, implicating this approach as a promising treatment for AML in children.

Paper # 2025

SEX-BASED DISPARITIES IN OUTCOME IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA: A COG REPORT

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Background: Males with acute lymphoblastic leukemia (ALL) have historically experienced inferior survival compared to females.

Objectives: To determine whether sex-based disparities persist with contemporary therapy when adjusted for other prognosticators, and whether patterns of toxicity and treatment failure vary by sex.

Design/Method: We analyzed a cohort of 9764 patients age 1-30.99 years enrolled on frontline

COG B-ALL (8202, 54.4% male) and T-ALL (1562, 74.3% male) trials between 2004-2014. Duration of treatment was sex-dependent, with males receiving an additional year of Maintenance therapy. We explored sex-based differences in the distribution of various prognosticators [age, initial white blood cell (WBC) count, central nervous system (CNS) status, cytogenetics, minimal residual disease (MRD)], event-free and overall survival (EFS, OS), toxicity rates, and the cumulative incidence of causes of treatment failure, including treatment-related mortality (TRM) and subcategories of relapse by site.

Results: Among B-ALL patients, males were older than females and non-significantly more likely to have unfavorable cytogenetics. There was no difference in CNS status. Among T-ALL patients, prognostic factors did not differ by sex. While absolute differences were small, B-ALL males were less likely to have end induction marrow MRD <0.01% (76.1% vs. 78.1%; p=0.04) while T-ALL males were more likely to achieve end induction MRD <0.01% (59.0% vs. 56.8%; p=0.01). Males with B-ALL experienced inferior EFS [hazard ratio (HR) 1.19, 95% confidence interval (1.06-1.33); p=0.004] and OS (HR 1.17, 95CI 1.00-1.37; p=0.046), even after adjustment for other prognostic factors. The inferior B-ALL outcomes were attributable to a higher rate of relapse in males than females (11.2%±0.5% vs. 9.6%±0.5%; p=0.001), particularly relapses involving the CNS (4.2%±0.3% vs. 2.5%±0.3%; p<0.0001). CNS relapses among males occurred somewhat later than among females (median 2.5 years vs. 2.1 years; p=0.049), but most occurred during therapy. There was no difference in the cumulative incidence of isolated bone marrow relapse (5.4%±0.4% vs. 6.2%±0.4%; p=0.49). There were no sex-based differences in EFS or OS in T-ALL. Among all patients, osteonecrosis rates were lower among males (5.3% vs. 6.8%; p=0.002). TRM did not differ by sex.

Conclusion: Small sex-based disparities in ALL survival and relapse rates persist despite overall outcome improvements and extended treatment duration with additional intrathecal therapy in males. This is mainly attributable to a higher risk of CNS relapse in males with B-ALL, despite no sex-based differences in initial CNS status. Future studies determining mechanisms underlying this disparity, including potential sex-based differences in metabolism of corticosteroids, are warranted.

Paper # 2026

CIRCULATING ENDOTHELIAL CELLS AND ENDOTHELIAL INJURY MECHANISMS IN HEMATOPOIETIC CELL TRANSPLANT

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Background: Endothelial injury after hematopoietic cell transplant (HCT) is multifactorial and perhaps universal. Thrombotic microangiopathy (TMA) and hepatic veno-occlusive disease (VOD) are known causes of endothelial damage, but little is known about the timing of initial endothelial injury related to these diseases. Damaged endothelial cells are ejected into circulation

and appropriately termed circulating endothelial cells (CECs). CECs are a direct product of vascular injury and a tractable tool to study mechanisms of endothelial injury by direct examination of the injured tissue.

Objectives: Our goal was to characterize endothelial damage after HCT using CEC analysis.

Design/Method: We prospectively measured CEC kinetics in pediatric HCT recipients. CECs were extracted from fresh blood using immunomagnetic isolation with a CD146 antibody. CECs were measured as an absolute value (CECs/mL) or relative to each patient's baseline value (Δ CEC). CEC kinetics were compared with patient demographics and HCT complications.

Results: Fifty-three HCT patients underwent CEC analysis. A total of 637 CEC samples were collected starting from before transplant and up to day 168. Fourteen patients (26%) were diagnosed with moderate or high-risk TMA. Seven were high-risk and 6 required complement-blocking therapy with eculizumab. All patients treated with eculizumab (p=0.03) and those with high risk TMA (p=0.02) more than doubled their baseline CEC count. Four patients treated with eculizumab had over a 5-fold elevation in CECs from baseline. CEC elevations were closely associated with sC5b-9 in high-risk TMA patients and those treated with eculizumab. All patients with VOD requiring defibrotide (n=3) more than doubled their baseline CEC count. The highest CEC count recorded (164 CECs/mL, Δ CEC=13.4) occurred in a patient with BK polyomavirus (BKPyV) viremia. Plasma BKPyV copy number was temporally associated with CEC elevations and immunofluorescence microscopy of CECs confirmed intracellular BKPyV in 5 patients with BKPyV viremia. Electron microscopy of CECs showed evidence of mitochondrial damage.

Conclusion: CECs are an informative, real-time assessment of injured endothelial tissue. Our data show a robust relationship between CECs and endothelial injury after HCT. This is most pronounced in high risk TMA, TMA requiring eculizumab and VOD requiring defibrotide. CEC elevations closely align with sC5b9 levels, a marker of severe TMA, emphasizing the role of terminal complement in vascular damage. CEC elevations were also related to rising BKPyV viremia and further investigation identified direct infection of CECs with BKPyV. Future CEC studies will investigate the consequences of endothelial injury at the RNA, molecular, proteomic and functional levels.

Paper # 2027

RISK OF ACUTE KIDNEY INJURY DURING VASO-OCCLUSIVE PAIN EPISODES MANAGED WITH KETOROLAC

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Background: Vaso-occlusive pain episodes (VOEs) account for over 90% of hospital admissions for patients with sickle cell disease (SCD). Ketorolac, an IV non-steroidal anti-inflammatory drug (NSAID), is often used in combination with opioids to manage pain crises.

The exact relationship between ketorolac use and kidney injury in pediatric patients with SCD remains incompletely understood.

Objectives:

1. Determine the prevalence of acute kidney injury (AKI) among patients with SCD treated with ketorolac for VOE.
2. Assess the impact of ketorolac on the development of AKI in this patient population.

Design/Method: A retrospective chart review and case control analysis were performed. We included data from all hospitalizations with VOE treated with ketorolac between January 2014 and December 2019. Encounters were excluded if the patient had previous AKI, chronic kidney disease or surgery during the admission. AKI was defined as a serum creatinine increase by ≥0.3 mg/dL or 50% from pre-admission baseline.

We used optimal match methodology to find control admissions (2:1 ratio) to those in which patients developed AKI, matching for age, gender, fetal hemoglobin percent, baseline hemoglobin, Blood Urea Nitrogen (BUN)-to-creatinine ratio, SCD-related admission reason, and comorbidities. We used non-parametric tests to compare the dose of ketorolac between cases and controls.

Results: A total of 903 encounters of 210 patients (50.5% females) were included in this study. Median age at admission was 15.4 years (IQR=10.5-18.7), and median length of stay was 3.4 days (IQR=2.2-5.0). There were a median of 2 admissions per patient (IQR 1-4). AKI was noted in 12 encounters (1.3%).

There was no significant difference between cases (n=12) and controls (n=24) in total daily dose of ketorolac, daily weight-based dose (1.3, IQR=0.9-1.6 vs. 1.2, IQR=0.8-1.5 mg/kg; p-value=0.814), or number of doses administered (10.0, IQR=6.0-12.0 vs. 9.5, IQR=7.0-12.3, p=0.839). Median length of stay did not differ significantly between groups. At admission, cases had higher creatinine (0.56, IQR=0.4-0.8 vs. 0.32 mg/dL IQR=0.3-0.4, p=0.002) and higher BUN (9.5 IQR=7.8-21 vs. 6.0, IQR=4.8-8.3, p=0.015).

Conclusion: We found a 1.3% prevalence of AKI in patients with SCD admitted for VOE who received ketorolac, lower than the 17% prevalence previously reported. There was no significant difference in the amount of ketorolac administered between groups to explain the development of AKI. Higher BUN and creatinine on admission suggest that cases often present with AKI. These findings highlight the ketorolac dose-independent risk of AKI among children with SCD and the need for more research focused on underlying mechanisms.

Paper # 2028

EFFECT OF ALLOIMMUNIZATION ON CLINICAL AND ECONOMIC OUTCOMES IN SICKLE CELL DISEASE

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Background: Alloimmunization to minor red blood cell (RBC) antigens diminishes the identification of compatible RBCs for transfusion, complicates pregnancy and stem cell transplantation, and is associated with negative overall health outcomes. The burden of alloimmunization falls disproportionately on sickle cell disease (SCD) patients. While procurement cost and donor recruitment are challenges, transfusion-associated alloimmunization may be greatly diminished in the SCD population through prophylactic phenotypic or genetic matching, where appropriate. Due to the significant incremental cost of prophylactic antigen matching (generally about $100 per antigen), there is controversy as to whether additional efforts to prevent alloimmunization are cost-effective.

Objectives: To quantify the incremental impact of alloimmunization on hospitalization length, intensive care utilization, inpatient mortality, and total hospital cost among patients with SCD.

Design/Method: A cross-sectional study of alloimmunized and non-alloimmunized SCD patients was performed using the Premier Hospital dataset (January 2015–June 2019). Alloimmunization was defined by the presence of blood bank test codes for antiglobulin crossmatch and RBC antibody identification in a patient's record. SCD was defined using ICD-10 codes. Overall, alloimmunized SCD patients and non-alloimmunized SCD patients were matched based on: sex, age, month and year of admission and type of visit (outpatient/inpatient). Demographic, clinical and billing characteristics were retrieved and used to calculate: hospital and intensive care unit (ICU) length of stay, inpatient mortality, and total cost per discharge. Simple bivariate comparisons were performed. All tests were conducted assuming a two-tailed test of significance and an alpha level of 0.05. Multivariable regression models adjusting for diagnosis related groups with an incidence ≥1% were performed.

Results: Overall, 599,934 alloimmunized patients were matched to 13,144,836 healthy controls, resulting in 11,846 alloimmunized SCD patients and 10,563 non-alloimmunized SCD controls. The groups had similar median ages (29 vs 30 years for alloimmunized and non-alloimmunized, respectively), sex (59.4% vs. 63.5% female) and race (87.4% vs. 85.6% Black) distributions, and similar medical diagnosis groups. Alloimmunized SCD patients had 42% and 72% longer length of hospital and ICU stay (IRR 1.42[1.36;1.49]; p<0.0001 and IRR 1.72[1.42;2.09]; p<0.0001), 61% greater likelihood of intensive care admission (OR 1.61[1.41;1.83]; p<0.0001), and 2-fold greater risk of inpatient mortality (OR 2.04[1.44;2.90; p<0.0001] compared to non-alloimmunized SCD patients. Median cost per discharge was $3,713 ($p$<0.0001) and $1,397 ($p$<0.0001) greater for inpatient and outpatient visits for alloimmunized SCD patients.

Conclusion: Determination of the total cost of alloimmunization in SCD should include the significant negative health outcomes associated with alloimmunization, including greater likelihood of ICU admission and inpatient mortality.

Paper # 2029

COVID-19 IN CHILDREN AND YOUNG ADULTS WITH SICKLE CELL DISEASE IN THE PROVINCE OF QUEBEC

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Background: Patients with sickle cell disease (SCD) may be at higher risk for a more severe COVID-19 disease course, given an underlying chronic inflammatory state, splenic dysfunction, vasculopathy and secondary organ dysfunction.

Objectives: We aim to describe the prevalence, clinical characteristics and outcomes of SCD patients infected with SARS-CoV-2 between March 2020 and January 2021 in the province of Quebec.

Design/Method: In March 2020, a web-based registry using a standardised questionnaire to capture SARS-CoV-2 infections among SCD patients in the province of Quebec was implemented. Nine tertiary care centres including 4 paediatric hospitals caring for an estimated 1500 SCD patients contributed to the registry. All SCD patients with a confirmed SARS-CoV-2 infection by polymerase chain reaction were included. The outcomes were hospitalization, admission to intensive care unit (ICU), or death.

Results: Forty-two SCD patients with confirmed SARS-CoV-2 infection were reported in the registry, representing approximatively 2.8% of all SCD patients in Quebec, as compared to 2.7% of positive COVID-19 cases in the general population, p=0.75. The median age (IQR] was 24 [14-30] years old; 14 (33%) patients were <18 years old; and 35 (83%) were <40 years old. SS, SC and S-beta-thalassemia genotypes were present in 22 (52%), 15 (36%) and 5 (12%) patients, respectively. Pre-existing chronic kidney disease, systemic hypertension and pulmonary hypertension were identified in 4 (10%), 4 (10%) and 3 (7%) adult patients, respectively. Twenty (48%) patients were on hydroxyurea and 10 (24%) on chronic exchange transfusion program. At presentation, 4 (9.5%) had veno-occlusive crisis, 5 (12%) acute chest syndrome, 19 (45%) fever, 5 (12%) anosmia and 8 (19%) were asymptomatic. While the majority of patients (31/42; 74%) had mild disease course, 33% of patients required hospitalization (3 children and 11 adults). Thus, the hospitalization rate was significantly higher in our SCD cohort compared to the general population (33% vs. 7%, p<0.00001). Of the 12 (28%) non-ICU hospitalizations, 4 (9.5%) received simple transfusion, 6 (14%) antibiotics, 6 (14%) L-arginine and none received antivirals. Mean hospital duration was 5.5 ±3.1 days. Two (5%) SC adult patients (23 and 66 years old) required ICU admission, mechanical ventilation and exchange transfusion. No death occurred in our cohort.

Conclusion: Children and young adults with SCD had a similar prevalence of SARS-CoV-2 infections compared to the general population in the province of Quebec. While no death

occurred, the rate of hospitalization was significantly higher in SCD patients compared to the general population.

Poster # 1

HEMATOLOGIC AND HEMOSTATIC DERANGEMENTS IN CHILDREN WITH COVID-19: THE MIAMI EXPERIENCE

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Background: Acute COVID-19 infection has shown to cause dysregulation of the hematologic and hemostatic systems. Laboratory abnormalities, particularly leukopenia, thrombocytopenia, elevated D-dimer, and prolonged prothrombin time (PT) are considered poor prognostic factors in adults. The prognostic significance of these laboratory abnormalities among pediatric patients remains underreported.

Objectives: To evaluate the prognostic implications of hematologic and hemostatic derangements in pediatric patients with acute COVID-19 infection.

Design/Method: A retrospective chart review was performed after IRB approval was obtained. Patients eligible were those younger than 22-years-of-age evaluated at the emergency room (ER) in a single tertiary care center, between March 1st and September 10th, 2020, with a laboratory confirmed COVID-19 infection by nasopharyngeal polymerase chain reaction (PCR) analysis. Children with prior history of inherited bleeding or clotting disorders were excluded. Asymptomatic patients who incidentally screened positive for COVID-19 at admission (e.g. admission for trauma, scheduled procedure) were also excluded. Abnormal laboratory parameters were set in accordance with current COVID-19 published literature. Statistical significance was evaluated at $p<0.05$.

Results: Two-hundred-and-ninety-six pediatric patients with laboratory confirmed COVID-19 infection were evaluated in the ER. Fifty-six of these patients met inclusion criteria. The most common presenting symptoms were fever (n=35; 63%) and nausea/vomiting (n=22; 39%). Fourteen patients (25%) required respiratory support and 15 patients (27%) required intensive care unit admission. Patients with leukopenia (WBC < 4.5 x 10^3/mL), compared to those without leukopenia, had longer length of hospitalization (9 days vs. 4 days; p =0.04), higher need for ICU admission (80% vs. 23%; p<0.01) and higher development of SIRS (60% vs. 21%; p=0.05). Thrombocytopenia (platelets < 150 x 10^3/mL) was associated with higher need for ICU admission (56% vs. 23%; p=0.05) and subsequent development of sepsis/SIRS (56% vs. 18%; p=0.02). Neither elevated D-dimer > 1.0 ug/mL nor prolonged PT > 14.5 seconds were associated with clinical outcome. No patients developed deep vein thrombosis, pulmonary embolism, or ischemic stroke.

Conclusion: Our study confirms that while children with COVID-19 present with hematologic and hemostatic laboratory abnormalities similar to those observed in adults, their prognostic significance differs. Leukopenia and thrombocytopenia were identified as independent prognostic factors of disease severity. Although the majority of children had elevated D-dimer or PT upon initial presentation, these markers were not associated with development of severe clinical complications.

Poster # 2

NOVEL USE OF MIDLINE CATHETERS FOR RED BLOOD CELL EXCHANGE VIA APHERESIS

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Background: Automated Red blood cell exchanges (RBCX) are vital procedures for primary and secondary stroke prevention in individuals with sickle cell disease (SCD) and require adequate vascular access to achieve optimal inlet flow rates. Central venous access devices (CVAD) require surgical placement and are associated with complications including infection, thrombosis, bleeding, device malfunction and pneumothorax. Peripheral vascular access is challenging in pediatrics due to small vessel size and mobility of the veins. Midline catheters (MC), placed in the deeper peripheral veins of the upper arms, provide an alternate vascular access for apheresis. MCs can be placed at the bedside under ultrasound guidance and have been effective in adults for apheresis procedures.

Objectives: We report the novel use of MC for RBCX in pediatric and young adult patients with SCD at our institution.

Design/Method: Retrospective chart review was performed on 8 patients with SCD who underwent RBCX using CVAD or MC, between April 2018 & July 2020. Demographic, clinical and outcome data were collected.

Results: Six SCD patients underwent a total of 48 RBCX procedures using a power-injectable MC (POWERWAND™ XL, access Scientific, LLC, San Diego, CA), 2 patients underwent 4 procedures using CVAD (8Fr Medcomp®). All apheresis procedures were performed using the Spectra Optia® apheresis system, version 11.3 (Terumo BCT, Inc., Lakewood, CO). Age range of patients using MC was 13 to 22y. Patients using CVAD were 5yrs and 22yrs of age. Inlet flow rates ranged from 33 to 65 mL/min (median=50), TBV processed ranged from 2872 to 8466 mL (m=6668), and procedure time ranged from 1.25 to 4 hours (m=2.25) for RBCX using MC. Inlet flow rates ranged from 14 to 32 mL/min (m=23), TBV ranged from 1,189 to 3687 mL (m=2438) and procedure time was 2 hours (m=2)for RBCX using CVAD. Total procedures per patient using MC ranged from 4 -17 (m=7). All patients achieved post procedure hemoglobin S levels of <10%. Improvement in ferritin levels was noted in 4 patients. No procedure related adverse

events or thrombotic events related to venous access sites or MC were recorded.

Conclusion: Reliable venous access is a major obstacle to successful performance of serial RBCX in SCD patients who are dependent on them for stroke prevention. We report the safe and successful use of MC for RBCX procedures in pediatric and young adult SCD patients, as a viable alternative to indwelling CVAD which are associated with significant complications in this vulnerable population.

Poster # 3

LONG-TERM EFFICACY AND SAFETY OF DEFERIPRONE FOR PATIENTS WITH SICKLE CELL DISEASE OR OTHER ANEMIAS

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Background: FIRST-EXT was a prospective, multicenter, single-arm, open-label extension of the FIRST study in patients with sickle cell disease (SCD) and other transfusion-dependent anemias. In FIRST, patients were randomly assigned 2:1 to receive oral deferiprone (DFP) or parenteral deferoxamine (DFO) for 12 months. The noninferiority of DFP versus DFO was previously reported. Here we report the efficacy and safety of DFP in FIRST-EXT.

Objectives: To evaluate the long-term efficacy and safety of DFP in iron-overloaded patients with SCD or other anemias.

Design/Method: Patients who completed FIRST could enter FIRST-EXT for up to 2 years. Patients previously treated with DFP continued on DFP (DFP-DFP), while those previously treated with DFO were switched to DFP (DFO-DFP). Baseline was defined as the start of FIRST for DFP-DFP patients, and the start of FIRST-EXT for DFO-DFP patients. Efficacy endpoints were yearly changes from baseline in liver iron concentration (LIC), cardiac MRI T2*, and serum ferritin (SF). We also report adverse drug reactions (ADRs), defined as adverse events at least possibly related to DFP.

Results: Patients (N=134; 89 DFP-DFP, 45 DFP-DFO) were 60.4% male, with a mean (SD) age of 16.2 (8.6) years. Most (85.8%) had SCD; 14.2% had other anemias. At baseline, all patients had elevated (≥1.8 mg/g dry weight [dw]) LIC, all but one had elevated (females >300 µg/L, males >400 µg/L) SF, and all had cardiac MRI T2* in the normal range (≥20 ms). A significant, progressive decline was seen in LIC, with mean (SD) changes from baseline to years 1, 2, and 3 of -2.64 (4.64), -3.91 (6.38), and -6.64 (7.72) mg/g dw, respectively (P<0.01 for all). A decline was also seen in SF, with mean (SD) changes from baseline to years 1, 2, and 3 of -1 (1986), -771 (2171), and -1016 (3617) µg/L, respectively (P<0.05 for years 2 and 3). Cardiac MRI T2* values changed little from baseline. The most frequent ADRs were neutropenia (9.0%), decreased neutrophil count (9.0%), and abdominal pain (7.5%); 2 patients (1.5%) experienced agranulocytosis. One patient withdrew due to ADRs of thrombocytopenia and neutropenia,

which resolved. Another patient withdrew due to generalized edema and died for reasons unknown 17 days after withdrawal from the study.

Conclusion: DFP long-term use (≤3 years) was effective in controlling body iron load in patients with SCD and other anemias. There were no new safety concerns.

ApoPharma Inc. (now Chiesi) sponsored this study. Medical writing support was provided by Oxford PharmaGenesis and funded by Chiesi.

Poster # 4

A STUDY EXAMINING THE SAFETY AND EFFICACY OF FERRIC CARBOXYMALTOSE IN A LARGE PEDIATRIC COHORT

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Background: Iron deficiency anemia (IDA) is common in the pediatric population with varying high-risk factors. Intravenous (IV) iron supplementation has become more desirable in patients with moderate to severe anemia and in patients who are either unresponsive to or have adverse side-effects secondary to oral iron. Iron sucrose and iron dextran have been traditionally used in pediatrics, while ferric carboxymaltose (FCM) has only been FDA approved in adults. One of the major advantages of FCM is the ease of dosing and efficacy. Though FCM was approved for adults in 2013 and there have been no safety concerns, it is not yet been FDA approved for pediatric patients despite a few pediatric studies demonstrating its safety and efficacy.

Objectives: To examine the utilization of different IV iron formulations in a large pediatric hospital and evaluate the safety and efficacy of FCM compared to other IV iron formulations.

Design/Method: This is a retrospective chart review study of patients who met inclusion criteria in a large pediatric hospital who received iron dextran, iron sucrose, and/or FCM between 4/1/2016 through 6/30/2020. We reviewed charts individually and collected data including patient demographics, details about each IV iron administration, and pre- and post-iron infusion lab values.

Results: The overall usage of IV iron has increased in the last 4 years and the utilization of different IV iron formulations has also changed in this time frame. In 2016, iron dextran comprised 35.7% of all IV iron administered while iron sucrose consisted of 64.3%. As the years progressed the usage of iron dextran has decreased while FCM has increased. In the first half of 2020, no patient received iron dextran and 53.4% of IV iron doses administered were FCM. Of the 164 FCM infusions analyzed, there were 7 documented adverse events. Of the 610 iron sucrose infusions analyzed, there were 10 documented adverse events. Approximately 88% of patients who received FCM required 1 to 2 doses to achieve goal hemoglobin and/or ferritin. However, 49% of patients who received iron sucrose required more than 2 doses to achieve goal hemoglobin and/or ferritin with multiple patients requiring up to 8 doses.

Conclusion: IV iron is being utilized more to treat IDA in certain patient populations. At our institution, the usage of FCM has considerably increased. Our data shows that less doses of FCM are required to treat IDA and is overall well tolerated.

Poster # 5

RETICULOCYTES COUNT: THE FORGOTTEN FACTOR IN TRANSFUSION DECISIONS IN THE NICU

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Background: Extremely low birth weight (ELBW) infants often receive packed red blood cells (PRBC) transfusions in the Neonatal Intensive Care Unit (NICU). Long-term outcomes of infants treated with liberal versus restricted criteria for PRBC transfusion have been evaluated, with conflicting results. Reticulocyte count (RC) is commonly ordered for evaluating anemia in growing premature babies. Many clinicians incorporate RC in their decision whether or not to transfuse. There is a lack of information on reference ranges for RC in growing ELBW infants and whether infant's chronologic age (CA) or adjusted gestational age (AGA) generates a specific trend in the RC.

Objectives: Our aim is to evaluate whether there is a trend in RC in ELBW based on AGA and CA.

Design/Method: A retrospective chart review of infants born 1/1/2017-12/31/2019 with birth weight (BW) 500-1000 grams was performed. We evaluated RC measured during their initial hospitalization in the NICU and performed analysis for trends in RC based on AGA and CA.

Results: A total of 142 infants were identified with BW 500-1000 grams, of which 101 survived to discharge or transfer to another institution and had RC performed. The GA (mean±SD) was 26.4±2.2 weeks. A total of 738 RCs were done with a mean of 7.3±3.1 per infant. The initial RC was done on the 4^{th} or the 5^{th} week of life in the majority of infants (73%) . As the GA increased, the week of life of the first RC decreased. Thirty-three infants (33%) never received PRBC during their hospitalization. The mean individual lowest RC was (3.7±1.6) while the mean highest RC was (11.2±3.8). We observed that the week of life and GA had a negative curvilinear relationship with the RC (beta = -1.47, $p < 0.001$ and beta = -5.21, $p < 0.001$ respectively). We observed a positive trend in RC values that reaches a peak and then experiences a downward trend.

Conclusion: There were variations in the values of the RC in this cohort. We observed a decrease over time when the mean values were evaluated for the AGA or CA. In our cohort, RCs were not done in the first week of life, a factor that may have an effect on the observed trends of RC and transfusion intervention. Our report sheds the light on a common test that is theoretically

helpful but needs guidelines on the appropriate frequency of testing and its utility in making transfusion decisions in ELBW infants.

Poster # 6

EPIDEMIOLOGY, EVOLUTION & SURVIVAL IN PATIENTS DIAGNOSED WITH NEUTROPENIC ENTECOLITIS IN COSTA RICA

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Background: Neutropenic enterocolitis (NE) is a clinical syndrome characterized by fever, neutropenia, abdominal pain, and thickening of the intestinal wall greater than 4mm. Present in children who have received intensive chemotherapy regimens, associated with malignancies such as leukemia, lymphomas and solid tumors, and non-malignant pathologies, such as aplastic anemia. The pathogenesis is related to the damage of the intestinal mucosa by cytotoxic drugs associated with neutropenia, facilitating secondary bacterial invasion. The lack of consensus in the definition and diagnosis are the main cause of variability in its incidence.

Objectives: Describe demographic, clinical evolution, management and survival of patients with a diagnosis of neutropenic enterocolitis of the Hemato-Oncology Department of the National Children's Hospital (NCH) “Dr. Carlos Sáenz Herrera” from January 1, 2010 to September 30, 2020.

Design/Method: Retrospective observational descriptive study, in the department of Hemato-Oncology of the NCH, between 2010-2020 in patients with NE. Data analysis estimated frequencies, percentages, characteristics of the patients and the events. Information was collected from laboratory and image findings, identification of compromised portions of the intestine, indicated treatment, complications, death and its association with neutropenic enterocolitis.

Results: Of thirty-seven patients, three had two events, for a total of forty events analyzed. The incidence was 2.4 per 100 cancer cases among those receiving chemotherapy. 51.4% (19/37) were male. Average age was 7.7 years with 35.1% (13/37) in the 6-10 year age range. 42.5% (17/40) were in the all induction phase, 85% (34/40) manifested abdominal pain as the main symptom, followed by fever in 45% (18/40) of the events, neutropenia was determined in 92.5% (37/40) of the events, the most frequent germs were Escherichia coli (6.5%) and Candida albicans (6.5%) . Diagnosis was made by ultrasound in 97.5% of the cases, 27.5% (11/40) reported thickness of 6mm, 15% (6/40) with a thickness greater than 10mm, 30% of the events required surgery. Complications, 12.5% (5/40) presented abdominal compartment syndrome, 10% (4/40) intestinal perforation and 10% (4/40) septic shock. The associated mortality was 7.5% (3/40) and the overall survival at 30 days of follow-up was 89% (95% ci 67.9-96.6).

Conclusion: The diagnostic triad (fever, neutropenia, abdominal pain) helps in the diagnosis, its absence does not rule it out, since there are no pathognomonic signs. In Costa Rica, the

implementation of medical management with hemodynamic support, gastric rest and broad-spectrum antibiotic therapy prevails over surgical intervention, the same reserved for severe complications.

Poster # 7

CLINICAL SPECTRUM AND TREATMENT OUTCOME OF IMMUNE CYTOPENIA AFTER PEDIATRIC CARDIAC TRANSPLANTATION

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Background: Immune cytopenias in cardiac transplant recipients pose specific challenges because of the particular importance of tacrolimus as a component of chronic immune suppressive therapy. Response to therapeutic interventions in these patients appears to differ from immune cytopenias induced by other causes.

Objectives: To report seven pediatric cases who developed autoimmune cytopenias as a complication of chronic immunosuppressive therapy after cardiac transplantation.

Design/Method: Retrospective review of patient medical records, laboratory results, therapeutic modalities, treatment response, and long-term outcomes.

Results: Seven patients developed autoimmune cytopenias post cardiac transplant, 6 were males. The median age at organ transplantation was 9.5 months. The duration between cardiac transplant and onset of autoimmune cytopenias was 3-60 months. At the time of onset of immune cytopenias all patients were on tacrolimus for post-transplant immunosuppression, and 3/6 were found to have Epstein-Barr viremia. Four of six had autoimmune hemolytic anemia (AIHA); two of which were warm IgG-mediated AIHA and two were mixed cold and warm antibody AIHA. Two had severe immune thrombocytopenia, one of these also had severe chronic immune neutropenia that required granulocyte colony stimulating factor (G-CSF). Another patient had isolated severe intermittent neutropenia, which also required G-CSF. Due to the severity of cytopenias, and limited or absent response to steroids and immunoglobulin (IVIG), Rituximab was required in all 6 patients for either severe ITP or AIHA. Two patients with AIHA had severe hemolysis causing acute kidney injury (AKI), one of which required therapeutic plasma exchange. Both of these patients were steroid refractory initially and required prompt administration of Rituximab. In all patient's tacrolimus was discontinued and changed to alternative immunosuppression regimens.

Conclusion: Pediatric cardiac transplant recipients who develop AIHA or ITP commonly have severe clinical manifestations and limited or lack of response to steroids and IVIG. Rituximab appears to be effective in most. Tacrolimus, a calcineurin inhibitor, is a likely major causative factor of immune dysregulation resulting in immune cytopenia.

Poster # 8

REPORTS OF INFECTION WITH USE OF INTRAUTERINE DEVICES IN IMMUNOCOMPROMISED WOMEN: A SCOPING REVIEW

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Background: The American College of Obstetricians and Gynecologists recommend intrauterine devices as a first line option for contraception in healthy young adult women. There are currently no clear provider practice guidelines regarding contraceptive use in adolescent and young adult (AYA) women with cancer and the data on the safety of intrauterine devices remains scarce in this immunosuppressed population.

Objectives: To investigate the quantity and quality of data available that assesses the risk of infection associated with IUD use in immunocompromised women of reproductive age.

Design/Method: We conducted a systematic scoping review of published literature following the Joanna Briggs methodology. Medline (PubMed), Embase and Cochrane Library were searched through May 4, 2020 for literature that reported on infection risk associated with IUD use in immunocompromised women of reproductive age (13-49 years old). Citation chaining of relevant results was performed to improve comprehensiveness. Sources of immunosuppression included acquired and inherited immunodeficiencies, patients currently undergoing chemotherapy or completed within the last 6 months, and patients on immunosuppressive medications. Evidence sources used for this review included both qualitative literature (case reports, reviews) as well as experimental and epidemiological study designs.

Results: The search yielded 5,016 articles, of which 73 were included in the review. The identified studies were heterogeneous in study conduct, type and length of IUD use, criteria for diagnosis of infection, and outcome reporting. Studies reporting infection risk of IUD use in AYA women with cancer were limited to six case reports and one retrospective case review; three of these cases reported associated infections, three noted no infections secondary to IUD use and the case review did not find a difference in infection risk based on type of contraceptive used. The remaining articles show trends towards safe usage of IUDs in other immunocompromised populations.

Conclusion: Overall, use of modern IUDs in immunocompromised women of reproductive age does not appear to be greatly associated with increased risk of infection. However, the majority of quantitative data cited in the literature comes from studies in the HIV/AIDS population. There is a significant lack of data available on IUD use in women on immunosuppressive medications as well as those undergoing chemotherapy or radiation. Further study in these areas is necessary.

Poster # 9

IS THE ROUTINE USE OF PRE-MEDICATIONS BEFORE TRANSFUSIONS NECESSARY IN PEDIATRIC HEME/ONC PATIENTS?

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Background: Although the administration of packed red blood cells (pRBCs) and platelets is generally safe, transfusion reactions may occur and are potentially serious complications. Febrile non-hemolytic transfusion reactions (FNHTRs) and allergic transfusion reactions (ATRs) are the most common reactions. Recent data suggests that the rate of ATRs and FNHTRs has been dramatically reduced with the introduction of universal leukoreduction and improved washing procedures. While diphenhydramine and acetaminophen are frequently given as prophylaxis for ATRs and FNHTRs, data on their use are limited and several recent studies have challenged the utility of this practice. Additionally, diphenhydramine is sedating and is associated with a paradoxical reaction of agitation or delirium and metabolites of acetaminophen have the potential to cause significant liver injury and even hepatic failure. Based on lack of compelling evidence suggesting benefit and potential harms associated with premedication, our institution recently changed its practice to give premedications only to patients with known history of transfusion reactions.

Objectives: To compare the incidence of FNHTRs and ATRs during pRBC or platelet transfusions in patients who received pre-medication with acetaminophen and diphenhydramine versus those who did not receive premedication.

Design/Method: This is an IRB-approved retrospective chart review of pediatric patients who received a pRBC or platelet transfusion during January – December 2017 (routine use of pre-medication) and October 2019 – October 2020 (no routine use of premedication). We collected patient type, transfusion date, product transfused, pre-medication received, whether the patient developed a reaction or not, and type of reaction.

Results: 1269 transfusions were analyzed, 644 of which were premedicated, 625 were not. There was a non-statistically significant lower incidence of transfusion reactions in the premedicated group compared to the non-premedicated group (1.09% vs 2.72%, p=0.054). This was driven by a significantly lower incidence of FNHTRs in the premedicated group as compared to the non-premedicated group (0% vs 1.44%, p=0.004). There was no difference in the incidence of ATRs between the 2 groups (1.09% vs 1.44%, p=0.755).

Conclusion: The current study suggests that premedication reduces the incidence of FNHTRs but not of ATRs. This study has several limitations owing to its retrospective design, but suggests that premedication with acetaminophen to prevent FNHTRs may be of practical use, while premedication with diphenhydramine to prevent ATRs is not of benefit in this patient population. We plan to change our pre-medication policy to include acetaminophen alone for all transfusions and will then subsequently analyze the effect on the rate of FNHTRs.

Poster # 10

RATE OF RISE OF PLATELET COUNT AFTER IVIG FOR PEDIATRIC IMMUNE THROMBOCYTOPENIC PURPURA

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Background: Immune thrombocytopenia (ITP) is an autoimmune disease, causing platelet destruction and is a common cause of thrombocytopenia in children. Although cases may be asymptomatic, children often experience purpura, a petechial rash, and cutaneous bleeding. Accepted therapies for ITP include observation, corticosteroids, IV immunoglobulin (IVIG), and anti-D immunoglobulin. Despite its high cost, IVIG is commonly used in symptomatic children due to its safety profile and efficacy. Although IVIG typically raises the platelet counts of most patients within 24 to 48 hours, the actual rate of rise has never been published.

Objectives: To calculate the rate of rise of platelet counts for a large group of children with ITP after an initial dose of IVIG to determine if the rate depends on demographic or clinical characteristics. By determining the rate, we aim to give guidance as to when to draw a post-infusion platelet count in order to determine if the IVIG was effective, and thereby avoid administering a second dose.

Design/Method: We looked at the records for 116 children under 18 with presumed ITP who received IVIG. For each patient, the last platelet count prior to the IVIG dose, the start and end times of the IVIG infusion, the dose of the IVIG infusion, and the time and value of the first platelet count following the end of the infusion were recorded. From those values, the increase in platelet count from the start of the infusion to the first platelet count drawn after the end of the infusion was calculated in K/µL/hour.

Results: 97% of the patents responded with an increase in the platelet count, and 78% of patients had a rate of rise of over 0.5 K/µL/hour. Overall, the rate of rise of the platelet count ranged from - 0.1 to + 4.2 K/µL/hour (average 1.3, median 1.2). We found no statistically significant correlation between age or gender nor the season, month, or year of presentation on the rate of rise. There was statistical significance between rise of the platelet count and initial platelet count ($p=0.0197$) but this correlation may not be of clinical significance.

Conclusion: From the calculated rise in platelet count after a single dose of IVIG in a large cohort of children with ITP, we provide guidance to practitioners as to when to draw a post-infusion platelet count to determine efficacy sufficient to avoid giving a second dose.

Poster # 11

PROPHYLACTIC EMICIZUMAB-KXWH IN CHILDREN AND ADULTS WITH TYPE 3 VON WILLEBRAND DISEASE

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Background: Type 3 von Willebrand disease (type 3 VWD) is the rarest and most severe form of VWD, characterized by a total or near-total absence of Willebrand factor (VWF). This also leads to a profound deficiency of factor VIII since VWF protects FVIII from being proteolyzed and cleared from circulation. Low VWF and FVIII in type 3 VWD leads to decreased thrombin generation and has a bleeding phenotype similar to patients with hemophilia A. Current treatment of patients with type 3 VWD consists of episodic, on demand infusions of plasma derived FVIII/VWF combinations or recombinant VWF factor to achieve hemostasis. The FDA has approved emicizumab-kxwh, a subcutaneously administered, humanised, bispecific, monoclonal antibody to FIXa and FX that substitutes the function of FVIIIa for prophylaxis in patients with hemophilia A in all age groups. Since both type 3 VWD and hemophilia A have low FVIII, we report the successful novel use of emicizumab-kxwh as prophylactic therapy in 4 patients with type 3 VWD aged 2 to 44 years.

Objectives: Reports of significant improvement in symptoms in patients with type 3 VWD after institution of emicizimab-kxwh, a bispecific antibody to FIXa and X.

Design/Method: Two pediatrics patients ages 2 and 6 years old who have been hospitalized multiple times for significant bleeding with minor childhood traumas. They were treated with multiple doses of factor VIII/VWF concentrates and recombinant FVIIa. They started prophylactic therapy about 3 and 8 months ago, respectively.
Two adult patients who are sisters now 41 and 44 years old who report a lifetime of complications associated with severe hemorrhagic events requiring multiple hospitalizations, infusions of factor concentrate, and blood transfusions. Both started prophylactic emicizumab-kxwh in the spring/summer of 2019.

Results: The two pediatrics patients have had no hospitalizations or transfusions since beginning emicizumab-kxwh therapy. The two adult patients report no major bleeding events and an overall reduction in severity of spontaneous bleeding.

Conclusion: Subcutaneously administered Emicizumab-kxwh is effective prophylaxis in these severely symptomatic patients with type 3 VWD. As more substitution and rebalancing therapies in hemostasis become available, guidelines for managing rare bleeding disorders like type 3 VWD will change. Multicenter trials using patient-reported outcomes (PRO) will greatly help in formulating guidelines for the management of disorders like type 3 VWD.

Poster # 12

ULTRASOUND AND EXTRACELLULAR MATRIX (ECM) TURNOVER MARKERS FOR MONITORING PROPHYLAXIS IN HEMOPHILIA

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Background: Recurrent hemarthroses in severe hemophilia results in cartilage and bone destruction and joint arthropathy. Prophylaxis with factor and non-factor therapies can mitigate this complication. However, timing and optimal regimen is debated in the absence of tools needed for monitoring cartilage turnover.

Objectives: The main goal of this study was to assess the role of ultrasonography(US) in monitoring cartilage changes in a cohort of hemophilia A and B patients over time to determine correlation between clinical, and radiological joint scores and markers of cartilage turnover.

Design/Method: Hemophilia A and B subjects had US of knees, ankles, elbows (with / without h/o hemarthroses) performed prospectively after informed consent/ assent at study entry and again in 6- 12 months using the Hemophilia Early Arthropathy Detection US (HEAD-US) protocol [1]. Two experienced musculoskeletal radiologists opined on these findings for inter rater agreement. Blood was drawn for markers of ECM collagen synthesis (PRO-C3, PRO-C4, PRO-C5, PRO- C23) and degradation (C2M, C3M, C4M2). These were compared with clinical Hemophilia Joint Health Score (HJHS) and HEAD-US scores between subjects with < 2 hemarthroses(Group I, n=5), 2- 20 hemarthroses(Group II, n=6) and > 20 hemarthroses(Group III, n=13) with a total of 30 sets of joints assessed in 2 separate visits between Jan 2016 – Dec 2018.

Results: A total of 24 subjects (ages 8 months – 18 yrs, 30 joint sets) with severe hemophilia A(n=19) and hemophilia B(n= 5) , on prophylaxis(91%), with inhibitors (46%) were enrolled after IRB approval. Inter-reader agreement for HEAD US score was 0.796 and 0.86 for visits 1 and 2. HEAD US scores correlated with PRO-C23 (p=0.047), marker of ECM collagen synthesis in joints with and without hemarthroses (n= 60). In joints with more than 2 hemarthroses clinical HJHS (n= 22) correlated with C4M2 (0.048), marker of ECM collagen degradation. HEAD US score for Group I showed significant correlation with PRO-C3 (marker of ECM collagen synthesis) as compared to groups II and III (p= 0.003 by ANOVA).

Conclusion: Cartilage turnover in severe hemophilia revealed significant differences in markers of ECM collagen synthesis in subjects with minimal hemarthroses(less than 2) vs target joints with increased degradation of collagen which correlated with evidence of cartilage destruction on HEAD-US assessment. US can be useful for monitoring cartilage changes on prophylaxis and markers of ECM collagen turnover may be helpful to monitor efficacy of prophylaxis.

1. Martinoli C, Thromb Haemost , 2013

Funding: IIS - Bayer Pharmaceuticals

Poster # 13

ASSESSING THE SAFETY OF PROPHYLACTIC ANTICOAGULATION IN ADOLESCENTS UNDERGOING BARIATRIC SURGERY

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Background: Obesity in children and youth has almost tripled in the last three decades in Canada. Bariatric surgery, a treatment offered to severely obese adults, can result in thrombotic and bleeding complications in up to 3% and 4% of patients, respectively. Limited literature is available on the safety of prophylactic anticoagulation to prevent venous thromboembolism (VTE) in adolescents undergoing bariatric surgery.

Objectives: To evaluate the safety of a fixed-dose prophylactic anticoagulation protocol used in adolescents undergoing bariatric surgery at The Hospital for Sick Children.

Design/Method: A retrospective cohort study including patients aged 13 to 18 years submitted to bariatric surgery between October 1, 2010 and December 31, 2019 was conducted. Thromboprophylaxis consisted of a single initial dose of 30 mg of low molecular weight heparin (LMWH, enoxaparin) administered subcutaneously two hours prior to surgery, continuing twice daily for 7 days post-operatively. The primary study outcome was safety, defined by the occurrence of bleeding events within the 30-day post-operative period, as per international guidelines. Secondary outcomes included VTE and death up to 30 days post-operatively. Data analyses included descriptive and Wilcoxon Signed Rank test statistics. Ethics approval and informed consent were obtained.

Results: Forty-seven adolescents were consecutively enrolled, with a median age of 17 years (IQR 16-18), median weight/BMI of 136.3kg/47.1kg/m^2 (IQR 121.1-156; IQR 42-54), and median surgery duration of 116 minutes (IQR 86-146). Surgical techniques included: Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG), and gastric band (GB). In terms of potential risk factors for VTE, 44.7% of patients were found to have obstructive sleep apnea and 21.3% were receiving oral contraception prior to surgery. Two major bleeding events were reported in the SG group, both occurring within 24 hours post-operatively, with a cumulative major bleeding complication rate of 4.25% at 30 days. Both events were classified as surgical-related, requiring surgical re-intervention. A pre- and post-operative median hemoglobin (Hgb) level (g/L) comparison between the bleeding (bleeding+) and non-bleeding (bleeding-) groups confirmed the major blood loss nature (bleeding+: Hgb pre-134.5/post-92; bleeding-: Hgb pre-135/post-142); no difference occurred for pre/post-operative platelet counts. No anti-Xa levels were available at the time of bleeding. No VTE or post-operative deaths were reported.

Conclusion: A fixed-dose venous thromboprophylaxis protocol (~0.2-mg/kg/dose) starting pre-operatively was associated with bleeding in adolescents undergoing bariatric surgery. All bleeding events occurred early in the post-operative period. A better understanding of bariatric surgery modalities and their respective safety, in context of LMWH prophylaxis, is required.

Poster # 14

A SINGLE CENTER RETROSPECTIVE REVIEW OF LEMIERRE SYNDROME AND RELATED ANTICOAGULATION TRENDS

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Background: Lemierre syndrome (LS) is a rare oropharyngeal infection progressing to thrombosis and septic embolization. Management relies on high clinical suspicion and aggressive antimicrobial therapy. While disease pathogenesis and the role of antibiotics are well described, the use of anticoagulation remains controversial.

Objectives: Describe anticoagulation and clinical outcomes in children with LS and Lemierre-like syndrome (LLS) at a single center over 15 years.

Design/Method: We defined LS by 1) primary oropharyngeal infection; 2) bacteremia; 3) jugular vein thrombophlebitis; 4) metastatic infections. LLS was characterized by an oropharyngeal infection and any other two criteria. We conducted a retrospective chart review of 17 patients with LS or LLS between 2005-2020.

Results: In our cohort, 76.5% were diagnosed with LS and 23.5% LLS. The mean age was 12.4 (*SD* 6.8, range 8 months-18 years). Ninety-four percent had internal jugular vein thrombi, while one patient had an external jugular vein thrombus. Twelve percent experienced central sinus venous thrombosis and 76.5% demonstrated pulmonary septic embolization. Veno-occlusion was complete in 47.1% and partial in 52.9%. *Fusobacterium species* was cultured in 66.7%. Inflammatory markers were elevated, with mean CRP 45.9 (*SD* 62.3) and mean ESR 48.5 (*SD* 25.9). Eighty-two percent required intensive care unit admission. Thrombophilia evaluation was performed in 70.6% of patients, with abnormalities detected in 47.1%, including elevated Factor VIII level (n=7), low protein C and S activity (n=1 and n=3, respectively), positive anticardiolipin antibody (n=3), and positive lupus anticoagulant screen (n=2). These abnormalities resolved at 3-month follow-up. One patient had a heterozygous Factor V Leiden mutation. Anticoagulation was used in 88.2% of patients: low molecular weight heparin (LMWH; 58.8%), unfractionated heparin and LMWH (11.8%), tissue plasminogen activator before LMWH (11.8%), and LMWH bridge to warfarin (5.9%). Anticoagulation duration ranged from 18-182 days (mean 86.4, *SD* 56.2). Median time to thrombus resolution was 39 days (*IQR* 23.5 - 68), without significant difference in time to resolution based on degree of veno-occlusion (p=0.7). At 6-month follow-up, 82.4% demonstrated thrombus resolution; 14.3% had vascular stenosis with collateral circulation. One patient was lost to follow-up. Two patients experienced persistent thrombosis. The patient treated with warfarin experienced oozing at a catheter site; otherwise, there were no bleeding complications and no recurrent embolic events.

Conclusion: The majority of patients presented with systemic complications and transient thrombophilic abnormalities reflecting inflammatory epiphenomena. In the absence of bleeding

complications, anticoagulation is a safe adjunctive modality to prevent thrombi propagation and embolic complications in children with LS and LLS.

Poster # 15

FIBRINOGEN CONCENTRATE PHARMACOKINETICS AND DOSING IN PATIENTS WITH CONGENITAL FIBRINOGEN DEFICIENCY

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Background: The rare bleeding disorder, congenital fibrinogen deficiency (CFD), is characterized by a lack of/low levels of functional fibrinogen in the blood which can lead to hemorrhage. Bleeding in CFD patients can be treated with human fibrinogen concentrate (HFC).

Objectives: Provide an examination of HFC (*Fibryga*®, Octapharma) pharmacokinetic (PK) profile in adult, adolescent, and pediatric patients, and investigate dosing differences between age groups.

Design/Method: FORMA-01/FORMA-02/FORMA-04 were multinational, prospective, open-label studies in CFD patients. FORMA-01 was a Phase 2 PK study in patients ≥12 years, while FORMA-02 and FORMA-04 were Phase 3 efficacy and safety studies in adult/adolescent patients (≥12 years) and pediatric patients (<12 years), respectively. FORMA-01/FORMA-04 assessed PK endpoints at baseline and eight time points up to 14 days following a single HFC infusion (70 mg/kg per bodyweight). FORMA-02/FORMA-04 assessed hemostatic efficacy of HFC for on-demand treatment of bleeding events (BEs) and surgical prophylaxis, using an objective 4-point efficacy scale adjudicated by an Independent Data Monitoring and Endpoint Adjudication Committee (IDMEAC).

Results: In the PK analysis, the median (range) patient age was 23 years (12–53) in FORMA-01 (n=22) and 6 years (1–10) in FORMA-04 (n=13). Mean PK parameters for AUC, C_{max}, IVR, T_{max}, $T_{1/2}$, MRT and V_{ss} in pediatrics were numerically lower compared to adults/adolescents, while clearance was numerically higher. In the analysis of treatment in bleeding and surgery, the median (range) patient age was 26.5 years (12–54) in FORMA-02 (n=24) and 6 years (1–10) in FORMA-04 (n=8). There were 89 BEs and 12 surgeries in adults/adolescents, and 10 BEs and 3 surgeries in pediatrics. The median (range) total HFC dose per BE was 59.41 mg/kg (32.12–273.80) in adults/adolescents and 73.91 mg/kg (47.45–262.50) in pediatrics. For surgery, the median (range) loading dose was 70.00 mg/kg (58.46–127.91) in adults/adolescents and 75.00 mg/kg (52.50–108.10) in pediatrics, with median total dose per surgery of 85.80 mg/kg and 108.10 mg/kg respectively. The IDMEAC rated overall hemostatic efficacy as successful for 99% of BEs and 100% of surgeries, comparable between age groups.

Conclusion: The PK profile of HFC is favorable and does not deviate from the pattern already described for other coagulation factors in adults/adolescents versus pediatric patients. Pediatric

patients received a numerically higher HFC dose compared to adult/adolescent patients. Despite differences in PK and dosing, HFC was efficacious for on-demand BE treatment and surgical prophylaxis in CFD patients across age groups.
Studies funded by Octapharma.

Poster # 16

VENOUS THROMBOEMBOLISM RISK AND ROLE OF THROMBOPROPHYLAXIS IN YOUTH WITH POTS

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Background: Adolescents and young adults with Postural Orthostatic Tachycardia Syndrome (POTS) often have difficulty with oral/enteral feeds and fluids. Sometimes this necessitates placement of a Central Venous Catheter (CVC) for intravenous (IV) fluids to provide nutrition & fluids and improve the quality of life. Placement of a CVC increases the risk of venous thromboembolism (VTE) as these patients often have other comorbidities that may increase this risk. In our clinical experience, a high frequency of CVC-related VTE was noted in patients with POTS, so in 2017, we implemented a targeted anticoagulant thromboprophylaxis (AT) protocol to be considered in any patient with POTS who required a CVC.

Objectives: To describe the frequency and characteristics of CVC-related VTE in patients with POTS and report the usefulness of AT.

Design/Method: We conducted a retrospective study of patients with POTS who were followed at our institution since 2012 and identified all patients who received anticoagulation for treatment or prevention of VTE. To assess the impact of a recently implemented institutional AT protocol, we assessed the frequency of objectively confirmed symptomatic CVC-related VTE and anticoagulant-related bleeding complications according to the International Society of Thrombosis and Haemostasis bleeding definitions. Relevant data were extracted from the electronic medical records and were summarized using descriptive statistics.

Results: A total of 17 adolescents with POTS who required a CVC between 2012-2020 were included in this study. All patients were females with a median age of 15.5 years (range 12-19 years). More than one VTE risk factor was present in all patients. At least 1 thrombophilic trait was identified in 10/17 patients. Prior to implementation of the AT protocol (2012-2016), 8 patients with POTS developed a VTE [7 CVC-related deep vein thrombosis (DVT) and 1 Non-CVC-related provoked DVT] and received therapeutic anticoagulation. Since the implementation of AT protocol in 2017, 9 patients with POTS who required a CVC received AT [Rivaroxaban (5 patients), Apixaban (2 patients), Enoxaparin (2 patients)]. Only 1/9 patients developed VTE while on AT with an overall prevalence of CVC-related-VTE of 0.14 event per 1 000 CVC days. There were no major bleeding episodes. One patient on Enoxaparin AT developed clinically relevant non-major bleeding event.

Conclusion: We observed a high incidence of CVC-related thrombosis in patients with POTS. Administration of AT in our population was associated with a reduction in CVC-related thrombosis without evidence of major bleeding episodes.

Poster # 17

FIBRINOGEN CONCENTRATE FOR SURGICAL PROPHYLAXIS IN PATIENTS WITH CONGENITAL FIBRINOGEN DEFICIENCY

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Background: Congenital fibrinogen deficiency (CFD) is a rare blood coagulation disorder that puts patients at increased risk of surgical bleeding. Human fibrinogen concentrate (HFC) can be administered prophylactically prior to surgery, and during surgery to prevent blood loss during and after surgical procedures in CFD patients. Currently, limited data are available on the use of HFC for perioperative management in CFD.

Objectives: Here we report data from two Phase 3 studies on the use of HFC to prevent surgical bleeding in adult, adolescent, and pediatric patients.

Design/Method: FORMA-02 and FORMA-04 were international, multicenter, prospective, open-label Phase 3 studies of the efficacy and safety of HFC (*Fibryga*®, Octapharma) in adult/adolescent and pediatric patients respectively with CFD. Efficacy was assessed by the investigating physicians and an Independent Data Monitoring and Endpoint Adjudication Committee (IDMEAC), both intra- and post-operatively using an objective 4-point Likert scale (excellent; good; moderate; none). All efficacy assessments were adjudicated by the IDMEAC and overall hemostatic efficacy was assessed as success/failure.

Results: In total, 11 patients (3 pediatric: <12 years, 1 adolescent: 12 years, and 7 adults: ≥18 years) received HFC for the prevention of surgical bleeding in 14 surgeries. There were two major surgeries, 1 adult (right eye enucleation with socket reconstruction) and 1 pediatric (splenectomy); all remaining surgeries were minor. For the minor surgeries, mean±SD HFC dose administered prior to surgery was 77.64±19.99 mg/kg (68.98±5.74 mg/kg for adult, 127.91 mg/kg for adolescent, and 78.53±27.96mg/kg for pediatric patients). Four of the minor adult surgeries required additional HFC infusions during surgery, with 2–5 total doses given and a mean±SD total dose of 132.87±29.06 mg/kg. The adult and pediatric major surgeries required 8 and 6 total HFC infusions, respectively, with loading doses of 102.56 mg/kg and 53.00 mg/kg, and total doses of 225.33 mg/kg and 450.00 mg/kg.
Intra-operative and post-operative efficacy were assessed as excellent by the IDMEAC for all patients except for the adult patient undergoing major surgery, where intra-and post-operative efficacy was assessed as good. All surgeries (100%) were given a final adjudication as successful by the IDMEAC. One serious adverse event was considered possibly related to treatment; a case of portal vein thrombosis in the pediatric patient undergoing splenectomy. No

allergic/hypersensitivity reactions or deaths were observed.

Conclusion: In conclusion, HFC administration for bleeding prophylaxis during surgery was efficacious for this ultra-rare disease in adult, adolescent and pediatric patients with CFD. Studies funded by Octapharma.

Poster # 18

FIBRINOGEN CONCENTRATE IN PEDIATRIC AND ADOLESCENT PATIENTS WITH CONGENITAL FIBRINOGEN DEFICIENCY

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Background: Congenital fibrinogen deficiency (CFD) is a rare disorder characterized by a lack of/low levels of functional fibrinogen. Human fibrinogen concentrate (HFC) is administered for bleeding episode (BE) treatment and for preventing blood loss during surgery in patients with CFD.

Objectives: Here we report data from adolescent and pediatric patients (aged <18 years) in two Phase 3 studies of HFC for on-demand BE treatment and surgical prophylaxis.

Design/Method: Both FORMA-02 and FORMA-04 were international, multicenter, prospective, open-label, uncontrolled Phase 3 studies of HFC (*Fibryga*®, Octapharma) efficacy and safety in adult/adolescent and pediatric patients with CFD. Hemostatic efficacy was assessed by the investigators and adjudicated by an Independent Data Monitoring and Endpoint Adjudication Committee (IDMEAC) using an objective 4-point scale (excellent; good; moderate; none). Adverse events (AEs) were recorded.

Results: A total of 11 pediatric (aged 0–11 years) and 7 adolescent (aged 12–17 years) patients received HFC for either BE treatment or surgical prophylaxis.
Of these 18 adolescent and pediatric patients, 14 received HFC for treatment of 21 BEs; 19 minor and 2 major (left knee/thigh bleed and intraperitoneal from spleen). The median (range) total dose per BE was 78.57 mg/kg (37.78–91.30) for adolescents and 73.91 mg/kg (47.45–262.50) for pediatric patients. Overall hemostatic efficacy was rated as successful (excellent/good rating) for 100% of BEs by the IDMEAC.
A total of 4 patients (aged 1, 3, 5 and 12 years) received HFC for 4 surgeries; 1 major (splenectomy) and 3 minor (circumcision, pulpectomy for two teeth, and extraction of tooth). The median (range) HFC loading dose prior to surgery was 91.50 mg/kg (53.00–127.91). Only 1 infusion was required for each of the 3 minor surgeries, while the major surgery required 6 infusions at a total dose of 452.00 mg/kg. Overall hemostatic efficacy was successful (excellent rating) for 100% of surgeries by the IDMEAC.
A total of 15 AEs occurred in 7 pediatric and adolescent patients (38.9%), including 11 treatment-emergent AEs. One serious AE (portal vein thrombosis following splenectomy) was

observed in one pediatric patient receiving HFC for major surgery. No allergic/hypersensitivity reactions or deaths were observed.

Conclusion: Across two Phase 3 clinical trials, HFC was efficacious for on-demand treatment of BEs and perioperative prophylaxis in adolescent and pediatric patients with CFD, which is comparable to adult patients with CFD. Hemostatic efficacy of HFC was comparable for adolescent and pediatric patients, with a favorable safety profile.
Studies funded by Octapharma.

Poster # 19

TESTICULAR THROMBOTIC MICROANGIOPATHY: AN UNRECOGNIZED COMPLICATION

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Background: Thrombotic microangiopathy (TMA) causes global endothelial damage and injures multiple organs systems. Multiple subtypes of TMA exist, including TMA after hematopoietic cell transplant (HCT). No study has described reproductive organ involvement in TMA and the effect of TMA on fertility is unknown.

Objectives: Our study aimed to identify and characterize testicular involvement in TMA.

Design/Method: We reviewed autopsies from 4 males who underwent HCT complicated by systemic, complement-mediated TMA. Testicular tissue was compared with an age-matched, healthy control who underwent testicular biopsy for a benign mass. All specimens were reviewed with a senior pathologist. Previously recognized histologic findings used to diagnose TMA in other organ systems were used to evaluate testicular tissue.

Results: Three patients had striking histologic evidence of testicular TMA. The median age at time of HCT for patients with testicular TMA was 18 years old (range 14-29) and the HCT patient without testicular TMA (patient 4) was 23 years old at time of HCT. All HCT patients died from complications related to infection (n=4) and/or graft versus host disease (GvHD, n=3). The maximum sC5b-9 values for patients with testicular TMA were 628ng/mL (patient 1), 769 ng/mL (patient 2) and 385ng/mL (patient 3; normal range, < 244ng/mL). Blood sC5b-9 levels were not available for patient 4. The severity of TMA histology varied but was most notable in a patient with an X-linked lymphoproliferative disease-like condition (patient 1). Testicular tissue had chronic damage to the vasculature (small and moderate sized vessels) and surrounding stroma. Capillaries had abnormal wall thickening, lamellated basement membranes and thickened intima. The surrounding testicular stroma was expanded with significant hyalinization. These abnormal stromal findings are consistent with testicular hypoxia due to markedly increased capillary wall to lumen ratios and chronically diminished tissue perfusion. Patient 4 did not have evidence of TMA in the testicles and had essentially normal testicular histology. This confirmed that abnormal testicular histology was not universal after HCT.

Conclusion: Our study suggests TMA injures the testicles and testicular involvement in TMA is underdiagnosed. The fertility implications of TMA-mediated testicular damage are unknown, but further attention must be paid to fertility after TMA diagnosis. Our discoveries are perhaps most pertinent to patients with recurrent TMA syndromes, in whom infertility is not commonly considered. Confirmation of a clinical impact of TMA on male fertility would result in widespread clinical practice changes for patients with TMA.

Poster # 20

EVALUATION OF NEUTROPHIL EXTRACELLULAR TRAPS AND CANCER ASSOCIATED THROMBOSIS IN CHILDREN

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Background: Children with cancer are at a high risk for thrombosis. The prothrombotic state of cancer is not well understood in children. Neutrophil extracellular traps (NETs) are a unique framework of externalized DNA with histones and granular proteases that contribute to cancer associated thrombosis (CA-T) in adults. The role of NETs in CA-T in children is unknown.

Objectives: 1) To evaluate NETs in pediatric cancer patients (at initial diagnosis or relapse) as compared to matched non-cancer pediatric patients.
2) Examine the effects of chemotherapy on NETs.
3) Measure the contribution of NETs to the prothrombotic state.

Design/Method: This is an IRB approved prospective observational cohort study consisting of two groups: research and control subjects. Research subjects consist of pediatric patients with a newly diagnosed or relapsed cancer. Control subjects consist of age and sex matched patients who do not have a cancer diagnosis. For research subjects there are three timepoints at which bloodwork is being obtained. Samples are drawn at the time of diagnosis or relapse, prior to a central line insertion or initiation of chemotherapy. The second sample is obtained after central line placement and immediately prior to the start of systemic chemotherapy. The third sample is obtained at the end of the first cycle of chemotherapy completion after neutrophil recovery. Control subjects will only have a one-time blood draw. NETs are measured from the plasma of the research and control subjects by the citrullinated histone H3 (CitH3) and Myeloperoxidase-DNA complexes (MPO) assays. Measurement of thrombin generation is conducted on platelet poor plasma samples with and without thrombomodulin.

Results: Thirteen research subjects (8 females, 5 males; age range 15 months -16years) have been enrolled in this ongoing study. Diagnoses include Langerhans cell histiocytosis, B- cell acute lymphoblastic leukemia, primary mediastinal B cell lymphoma, Hodgkin lymphoma, acute myeloid leukemia, Burkitt lymphoma, osteosarcoma, and T cell leukemia. Research subjects have been matched with controls for age and sex. Preliminary data show that NETS are elevated

in patients with cancer as compared to the controls. Early analysis comparing CitH3 and MPO as biomarkers for measuring NETs reveals that MPO may be a better marker in the pediatric cancer population for detecting NETs.

Conclusion: Our study investigates the role of NETs in pediatric cancer and will provide critical information in understanding the prothrombotic state of childhood cancer. Enrollment continues with further statistical analysis to be conducted once accruement of patients is completed and all three timepoints are collected.

Poster # 21

CONGENITAL BLEEDING DISORDERS IN FEMALE ADOLESCENTS WITH MENORRHAGIA AND IRON DEFICIENCY ANEMIA

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Background: Congenital bleeding disorders are characterized by deficient or dysfunctional coagulation factor activity levels, abnormal platelet function, or defects within the fibrinolytic system. Menorrhagia and iron deficiency anemia are common presenting signs of bleeding disorders among post-pubertal adolescent females. Epidemiologic studies suggest that 25% of women with menorrhagia have an underlying bleeding disorder. However, identification of a causal bleeding disorder is often delayed. The consequences of undiagnosed and untreated bleeding disorders have significant clinical and psychological ramifications. Early recognition by pediatric providers is crucial.

Objectives: To report the prevalence of congenital bleeding disorders among post-pubertal female patients referred to a hemophilia treatment center for menorrhagia with or without iron deficiency anemia.

Design/Method: A retrospective chart review was performed after IRB approval was obtained. Patients included were post-pubertal females younger than 22-years-of-age referred for evaluation of menorrhagia or iron deficiency anemia between January 2015 and November 2020 to the University of Miami-Hemophilia Treatment Center. Patients were identified by ICD-10 code. Excluded patients were those with a prior bleeding disorder diagnosis.

Results: Eighty-one patients met the inclusion criteria. Thirty-three (40.7%) patients were referred for iron deficiency anemia only, 23 others (28.4%) for menorrhagia. Twenty-five patients (30.9%) carried both diagnoses.

Thirty-three patients (40.7%) were ultimately diagnosed with a congenital bleeding disorder. The most common diagnosis was type 1 von Willebrand Disease (VWD) (n=18, 54.5%), followed by factor 7 deficiency (n=11, 33.3%). Hemophilia A carrier status and factor 11 deficiency were identified in one patient, each. Two patients (6%) had a platelet function disorder and 1 patient was diagnosed with both type 1 VWD and factor 7 deficiency. Interestingly, while family history

of abnormal bleeding symptoms was present in 84.8% of the referred patients diagnosed with a congenital bleeding disorder, only 28.6% (n=8) had a known family history of a previously diagnosed congenital bleeding disorder.

Conclusion: Our interim analysis confirms that congenital bleeding disorders are prevalent among adolescents with menorrhagia and iron deficiency anemia. The presence of a family history of abnormal bleeding symptoms is highly predictive of an underlying bleeding disorder and should warrant referral for specialized work-up and evaluation.

Poster # 22

SAFETY OF DIRECT ORAL ANTICOAGULANTS FOR TREATMENT OF THROMBOEMBOLISM IN PEDIATRIC CANCER PATIENTS

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Background: Children with cancer who develop venous thromboembolism (VTE) have an increased risk of thromboembolism recurrence, morbidity and mortality. Thrombosis risk is multifactorial resulting from the interaction of tumor and therapy-related risk factors, hypercoagulability, and the presence of central venous lines. Standard of care for the treatment of VTE is low molecular weight heparin (LMWH), however the mode of administration by subcutaneous injection impacts quality of life and potentially medication adherence.
Direct oral anticoagulants (DOACs) represent a class of oral medications to treat VTE. DOACs are subject to potential problems in cancer patients, which stem from altered gastrointestinal function and absorption from direct cancer effect, cachexia, vomiting, or direct gut lining damage from chemotherapy. There are also a host of drug interactions from chemotherapy and supportive care. Given adult studies showing the safety and efficacy of DOACs, many pediatric providers question using them in cancer patients. There are currently limited studies on the use of DOACs in the general pediatric population and most do not include cancer patients, highlighting a gap in pediatric thrombosis knowledge.

Objectives: The main aims are to evaluate the safety and efficacy of DOACs when used to treat acute VTE in pediatric cancer patients.

Design/Method: My study is a retrospective chart review of patients 1-18 years old treated at Children's Wisconsin (CW) from 1/2012 to present. Using the I2B2 network, I was able to identify 14 total patients receiving DOACs for VTE treatment and 27 comparative patients receiving LMWH. I extracted data regarding their weight/BMI, oncologic diagnosis, VTE diagnosis, bleeding events and any end of therapy imaging. I will compare 3 main factors: 1) number of significant bleeding events 2) number of platelet transfusions and 3) efficacy of therapy.

Results: Data collection is complete and preliminary statistical analysis shows non-inferiority of DOACs compared to LMWH, with equal efficacy and bleeding rates. The size of our study does

not allow for statistical significance.

Conclusion: The overarching goal of this project is to improve medication compliance and quality of life in a population that is already medically traumatized. We hope that this initial pilot study will be followed by a larger study using the national CHAT database, which we are currently gaining access to. Ultimately, with the increasing use of DOACs in pediatric patients, my goal is to ensure that it is safe and effective in this unique population.

Poster # 23

THE RELATIONSHIP BETWEEN WEIGHT STATUS AND JOINT FUNCTION IN PATIENTS WITH HEMOPHILIA: A PILOT STUDY

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Background: Hemophilia is an X-linked inherited bleeding disorder in which blood does not clot normally as it lacks one of the coagulation factors. People with hemophilia (PWH) are at higher risk for joint damage compared to the general population due to recurrent bleeds in joints. Obesity has been identified as a risk factor for arthritis in individuals not having hemophilia. Very few studies have examined the relationship between weight status and severity of joint dysfunction in PWH.

Objectives: To describe the relationship between joint dysfunction and weight status in pediatric and adult PWH. Additionally, to examine relationships among weight status, hemophilia disease severity, and patients' self-perceived functional ability.

Design/Method: Patients aged 2-year-old and older with Hemophilia A or B of all severities receiving care at Charleston Area Medical Center (CAMC) Hemophilia Treatment Center (HTC) located in Charleston, WV were recruited for the study. Weight, height, and body mass index (BMI) were prospectively obtained. A prospective assessment of the level of joint dysfunction was performed by a certified physical therapist using a modified Hemophilia Joint Health Score (HJHS). Questionnaires evaluating patients' self-perceived functional ability using the Hemophilia Activities List (HAL) and Pediatric HAL (pedHAL) were provided to all enrolled participants. Demographic and disease characteristics were obtained by chart review. Patients were stratified into 3 groups based upon disease severity: mild, moderate, or severe.

Results: Data analysis was performed for 38 patients (age range: 2 to 69 years, with nine participants under the age of 18 years) having either Hemophilia A (n=24) or Hemophilia B (n=14) of all severities. Compared to normal and overweight patients, obese patients had higher HJHS scores representing worse functional status. These differences did not reach statistical significance ($P = 0.11$). However, when HJHS scores of the ankle joint were analyzed independently, obese patients had higher scores that reached statistical significance ($P = 0.03$).

There was no association between BMI classification and either HAL scores or hemophilia severity.

Conclusion: Although only statistically significant in the ankle joint, the higher HJHS scores in obese patients suggest worse functional status compared to PWH of normal weight. The small sample size is a study limitation. Larger and multi-institutional studies are needed to further describe the association between BMI classification and joint function in hemophilia patients.

Poster # 24

DOES INTRAVENOUS IMMUNOGLOBULIN USE AFFECT OUTCOMES IN NEONATES WITH ABO INCOMPATIBILITY?

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Background: ABO incompatibility occurs in approximately 15-25% of pregnancies and is a common cause of Hemolytic Disease of the Newborn (HDN). HDN can be associated with severe hyperbilirubinemia and anemia requiring packed red blood cell (pRBC) transfusions. The American Academy of Pediatrics recommends intravenous immunoglobulin (IVIG) in addition to phototherapy to prevent the need for exchange and simple transfusions. IVIG has a role in severe disease with evidence extrapolated from its use in Rh mediated HDN; data are limited regarding use in ABO incompatibility and HDN.

Objectives: To determine if treatment with IVIG of neonates with ABO incompatibility (without Rh incompatibility) results in decreased number of transfusions and phototherapy use.

Design/Method: An IRB-approved, single institution retrospective study was conducted. Neonates ≥35 weeks gestational age born between 01/01/2007 and 12/31/2016 with ABO incompatibility were included. The comparison among groups was performed using Chi square and Fisher exact test for categorical variables; continuous variables were assessed by Kruskal-Wallis test.

Results: Six hundred and sixty-eight neonates with ABO incompatibility met inclusion criteria, 579 patients were included in the analyses. From those, 431 (74%) neonates had positive Direct Antiglobulin Test (DAT); 98 (17%) received IVIG and 352 (61%) received phototherapy. Thirty-six (6%) neonates received pRBC and 6 (1%) required exchange transfusions. Only 3 (0.5%) infants received pRBC transfusions post discharge, by 3 months of age.

Neonates requiring IVIG had lower initial hemoglobin 13.6 g/dL [11.8 – 15.1] compared to 16 g/dL [14 – 17.8] in the non-IVIG group ($p < 0.0001$). They had higher bilirubin at start of phototherapy 9.1 mg/dL [7.4 – 10.7] vs 8.1 mg/dL [6.5 – 10.5] in the non-IVIG group ($p=0.0064$).

From the 42(7%) neonates who received simple and exchange transfusions, IVIG use was not associated with decreased use or number of transfusions (p=0.5148 and 0.3333, respectively).

Newborns with A+ and B+ blood types had comparable initial hemoglobins, DAT positivity, APGARs, and bilirubin. However, infants with B+ blood were more likely than A+ to require phototherapy (p<0.001), receive IVIG (p=0.003), and need phototherapy for a longer duration (p=0.001).

Conclusion: The results of this large retrospective study reveal that neonates with ABO incompatibility who received IVIG in the newborn period did not have reduced need for simple or exchange transfusions. Newborns with B+ blood type required more phototherapy and IVIG. Further studies are needed to better stratify neonates who would benefit from IVIG use in order to optimize treatment strategies and avoid unnecessary risks and adverse events.

Poster # 25

SAFETY AND EFFICACY OF DEFERIPRONE VS DEFEROXAMINE FOR TRANSFUSION-DEPENDENT ANEMIAS

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Background: FIRST was a multicenter, randomized, open-label, noninferiority trial of deferiprone (DFP) vs deferoxamine (DFO) in iron-overloaded patients with sickle cell disease (SCD) or other transfusion-dependent anemias. The primary endpoint (change in liver iron concentrations) showed DFP was noninferior to DFO. Here we report the 12-month safety and secondary efficacy outcomes from FIRST.

Objectives: To assess the safety and efficacy of DFP compared to DFO in iron-overloaded patients with SCD or other anemias.

Design/Method: Eligible patients ≥2 years old were randomly assigned (2:1) to receive DFP or DFO. Secondary efficacy endpoints were the change from baseline to 12 months in cardiac MRI T2*, serum ferritin (SF), and patient-reported quality of life using the Short-Form 36 (SF-36) questionnaire. All adverse drug reactions (ADRs; adverse events that were considered to be possibly related to the study product) were recorded.

Results: Patients (N=228) were 46.9% female, with a mean (SD) age of 16.9 (9.6) years. Most (82%) had SCD; 18% had other anemias. Most DFP (n=106/152; 69.7%) and DFO (n=58/76; 76.3%) patients completed 12 months of treatment. There were no significant (*P*>0.05) differences between the DFP and DFO intent-to-treat groups in the secondary efficacy measures. Mean changes from baseline to 12 months in log cardiac MRI T2* were similar for the DFP (1.01) and DFO (1.00) groups. Mean (SD) changes from baseline to 12 months for SF were 15.7

(2060.3) μg/L in the DFP group and −351.7 (2169.1) μg/L in the DFO group. Mean (SE) SF-36 questionnaire scores were similar between the DFP and DFO groups for the Physical Summary (43.1 [1.8] vs 43.0 [2.0]) and Mental Summary (44.7 [2.7] vs 40.9 [2.9]) parameters. Common ADRs (≥5% of patients) in the DFP group were abdominal pain (17.1%), vomiting (14.5%), pyrexia (9.2%), increased alanine transaminase (9.2%), increased aspartate aminotransferase (9.2%), neutropenia (5.9%), and nausea (5.3%). Common ADRs in the DFO group were pyrexia (9.2%) and injection site pain (6.6%). Serious ADRs in DFP patients were neutropenia (2.6%), increased transaminases (1.3%), and agranulocytosis, sickle cell crisis, epididymitis, Propionibacterium infection, bacterial sinusitis, vascular device infection, and migraine (0.7% each). Serious ADRs in DFO patients were abdominal pain, arthritis, and headache (1.3% each).

Conclusion: FIRST study secondary efficacy data support DFP as being noninferior to DFO in iron-overloaded patients with SCD or other anemias. DFP was well tolerated with no new safety concerns.

ApoPharma Inc. (now Chiesi) sponsored this study. Medical writing support was provided by Oxford PharmaGenesis and funded by Chiesi.

Poster # 26

BETI-CEL GENE THERAPY OUTCOMES IN PEDIATRIC PATIENTS WITH TRANSFUSION-DEPENDENT β-THALASSEMIA

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Background: The phase 3 studies evaluating betibeglogene autotemcel (beti-cel, formerly LentiGlobin for β-thalassemia) gene therapy for transfusion-dependent β-thalassemia (TDT), HGB-207 (non-β^0/β^0 genotypes; NCT02906202) and HGB-212 (β^0/β^0 , $\beta^0/\beta^{+IVS\text{-}I\text{-}110}$, $\beta^{+IVS\text{-}I\text{-}110}/\beta^{+IVS\text{-}I\text{-}110}$ genotypes; NCT03207009), demonstrated transfusion independence in 83% (10/12) of adult patients. The studies also enrolled pediatric patients <18 years old.

Objectives: We describe interim efficacy and safety of beti-cel in pediatric patients treated in HGB-207 and HGB-212.

Design/Method: Autologous CD34+ cells were transduced ex vivo with BB305 lentiviral vector to produce beti-cel drug product. Patients underwent pharmacokinetic-adjusted busulfan myeloablation and infusion with beti-cel. Transfusion independence (TI; weighted average hemoglobin [Hb] ≥9 g/dL without packed red blood cell transfusions for ≥12 months) is the primary endpoint in HGB-207 and a secondary endpoint in HGB-212. Data are presented as median (min–max).

Results: As of 3 March 2020, 24 pediatric patients <18 years old (n=17 non-β^0/β^0 genotype; n=7

β^0/β^0 genotype) were treated and followed for 15.5 (1.1–29.5) months, including 13 patients <12 years (HGB-207: n=8; HGB-212: n=5) and 11 patients ≥12–<18 years (HGB-207: n=6; HGB-212: n=5). TI was achieved in 87% (13/15) of patients evaluable for TI for an ongoing duration of 14.9 (12.2–21.6) months, including 2 patients with β^0/β^0 genotypes. Weighted average Hb during TI was 11.3 (9.4–12.8) g/dL. Gene therapy-derived adult Hb, HbA^{T87Q}, ranged from 5.1–10.9 g/dL at last assessment, representing 51%–88% of total Hb. In 92% (12/13) of patients with TI, soluble transferrin receptor levels decreased from baseline of 118.2 (65.9–197.6) nmol/L to 59.4 (25.9–89.4) nmol/L at Month 12. Myeloid:erythroid (M:E) ratio increased from baseline to Month 12 in 75% (9/12) of patients who achieved TI suggesting that ineffective erythropoiesis was modulated.

Non-hematologic Grade ≥3 adverse events in ≥3 patients <18 years old were stomatitis (n=14), febrile neutropenia (n=12), decreased appetite (n=5), epistaxis (n=4), increased alanine aminotransferase (n=3), hypoxia (n=3), and pyrexia (n=3). Grade 4 veno-occlusive liver disease (VOD) was a serious adverse event that occurred in 2 patients ≥12–<18 years; one grade 2 VOD event occurred in a patient <12 years; all resolved after treatment with defibrotide. There was no replication-competent lentivirus, clonal dominance, insertional oncogenesis or death**.**

Conclusion: Children <18 years of age achieved TI with rates comparable to adults after beti-cel gene therapy, suggesting that beti-cel is a suitable treatment option for patients with TDT without regard to age. The treatment regimen had a safety profile consistent with busulfan myeloablation. Sponsored by bluebird bio.

Poster # 27

REGIONAL ANESTHESIA FOR SICKLE CELL DISEASE VASO-OCCLUSIVE CRISIS: A SINGLE-CENTER CASE SERIES

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Background: The most common sequela associated with sickle cell disease (SCD) is recurrent, severe vaso-occlusive pain crisis (VOC). Acute pain management for VOC is extremely challenging due to limited treatment modalities. Regional anesthesia, including continuous peripheral nerve blocks (CPNB), have been found to be safe and effective in the pediatric population for perioperative analgesia and adjunctive pain management. There are few studies investigating the role of CPNB for pediatric patients with SCD VOC.

Objectives: To describe the hospital course of a cohort of patients with SCD and opioid refractory, focal VOC before and after the placement of a continuous peripheral nerve block (CPNB) for analgesia.

Design/Method: We conducted a retrospective chart review of hospital admissions for three discrete patients with SCD hospitalized for VOC.

Results:
Three patients ages 16 (HbSS, 60kg), 13 (HbSS, 59kg), and 11 (HbS/beta-0-thalassemia, 59kg) presented with upper extremity VOC pain. Pain persisted despite escalation of parenteral opioid regimens, and regional anesthesia was instituted. Ultrasound-guided CPNBs (supraclavicular, interscalene and interscalene, respectively) were placed with continuous cardiopulmonary monitoring under minimal sedation. Patients received an initial bolus of ropivacaine 0.2-0.5 % with or without dexmedetomidine, and subsequent infusions of ropivacaine 0.1% at 0.1 - 0.2 mg/kg/hr. The patients' average daily opioid consumption (morphine equivalents) of 149mg, 48.5mg, and 93.06mg preceding nerve block placement, decreased to 35.5mg, 15.8mg and 12.4mg, respectively, 24-hours proceeding nerve block infusions. Daily numeric pain scores ranged from 7-9/10 prior to nerve block placement and decreased to 0-3/10 thereafter. At the conclusion of therapy, CPNB catheters were removed at the bedside. No complications were observed with the placement, infusion, or removal of the nerve block catheters. Following hospitalizations ranging 2-8 days prior to CPNB placement, all three patients were discharged within 2 days of the nerve block therapy.

Conclusion: Three pediatric patients with opioid refractory, focal VOC pain experienced dramatic declines in pain scores and parenteral opioid usage after CPNBs were introduced. CPNBs may represent a beneficial adjunct to managing focal VOC in patients with SCD. Further prospective investigations of the efficacy of CPNBs for VOC are warranted.

Poster # 28

USE OF BETA BLOCKER TO TREAT DIASTOLIC DYSFUNCTION IN CHILDREN WITH SICKLE CELL DISEASE

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Background: Cardiac abnormalities seen in sickle cell disease (SCD) are common and include left ventricular diastolic dysfunction. Diastolic dysfunction has an estimated prevalence ranging from 11-77%. While the etiology of diastolic dysfunction in SCD is still unclear, it is an independent risk factor for early mortality in adults, and exercise intolerance in adolescents with SCD. [1, 2] The effect of disease-modifying therapy on diastolic dysfunction is unclear and the treatment has been evolving. Beta-blockers could be beneficial as they modulate the sympathetic nervous system resulting in increased diastolic filling time and reduced myocardial wall tension.

Objectives: To determine the effect of beta-blocker on left ventricular diastolic function.

Design/Method: SCD patients seen at St Jude Children's Research Hospital were placed on cardiac-selective Beta-blocker (atenolol, metoprolol) for diastolic echocardiographic parameters categorized as abnormal using normative age-specific ranges. [3] These parameters included early diastolic mitral annular velocity (lateral e'), ratio between early mitral inflow velocity and early diastolic mitral annular velocity (lateral E/e') and left atrial end systolic volume index

(LAESVi). Echocardiographic measurement of diastolic function was done before and after initiation of beta-blocker. Retrospective chart review was performed to ascertain echocardiogram data prior to introduction of beta-blocker and during treatment. Paired t-test was used to compare the change in the mean diastolic parameters prior to after initiation of beta-blocker

Results: Twenty-one patients with SCD (18 HbSS, 1 HbSβ^0thalassemia, 1 HbSC, 1 HbSβ^+thalassemia) ages 7 to 18 years were treated with beta blocker for a median of 22 months (11-30 months). Sixty-two percent were on hydroxyurea, 19% on monthly transfusions, and 9.5% on both. In the overall study population, after beta-blocker initiation, there was a mean decrease in LAESVi (3.82 ml/m^2, p= 0.01) and Lateral E/e' (1.03, p <0.001), with no change in hemoglobin (p=0.49).

Conclusion: In SCD patients on disease modifying therapy (hydroxyurea, monthly transfusions or both), a significant improvement in elevated LAESVi and Lateral E/e', markers of diastolic dysfunction, were seen after initiation of beta-blocker, despite no amelioration in anemia. Possible benefits of beta-blocker include improved myocardial filling time, reduced myocardial wall tension and potential antifibrotic properties. Further studies are needed to validate these finding in a larger cohort to define the role of beta blockers in the treatment of diastolic dysfunction and to understand the pathophysiology of diastolic dysfunction in SCD.

1. Sachdev et al, J Am Coll Cardiol, 2007.
2. Sachdev et al, Circulation, 2011.
3. Eidem et al, J Am Soc Echocardiogr, 2004

Poster # 29

LACK OF DOCUMENTATION OF SICKLE CELL TRAIT WITHIN THE EHR: ISSUE OF HEALTH EQUITY AND DATA INTEGRITY

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Background: The hemoglobinopathy newborn screen performed on all neonates in the United States aims to detect sickle cell disease (SCD) and allow access to life-saving medical care. As a byproduct of testing, sickle cell trait (SCT) is revealed. Knowledge of one's SCT status allows for identification of medical complications associated with SCT and informed reproductive planning regarding the risk for having a child with SCT or SCD. Few adults report knowing their SCT status, associated medical complications, or reproductive implications of SCT. Documentation of SCT within the electronic health record (EHR) may be a first step to accurate retention and transmission of SCT status.

Objectives: To evaluate the incidence of SCT documented within the EHR problem list, medical history list, and diagnosis billing codes for the patients within Nemours Children's Health System's pediatric primary care networks (Delaware Valley & Florida, US) as compared to the

expected incidence of SCT (15/1000 persons nationally, 3/1000 white persons, 73.3/1000 Black persons, Ojodu, et al, MMWR Morb Mortal Wkly Rep. 2014).

Design/Method: Demographic data, problem list, medical history, and billing codes were extracted for all patients seen for well-child examinations within 3 years of data extraction (May 2020). To account for differences in racial distribution of our sample versus the national population, standardized incidence ratios (SIRs) of observed cases of documentation versus expected cases of SCT were calculated. We calculated the relative risk (RR) of documentation in EHR versus the nation by racial group.

Results: Our sample included 182,402 patients (27% Black, 48% white). SCT was documented in 2421 for an overall incidence of 13/1000. Accounting for race, the overall SIR was 0.54 (0.52, 0.57 95% CI). SIRs for Pennsylvania, Delaware, and Florida were nearly identical. The RR for documentation for Black and White patients was 0.54 (0.51, 0.56, 95% CI) and 0.67 (0.57, 0.78, 95% CI), respectively.

Conclusion: While accounting for race, the SIR of 0.54 highlights significant gaps in documentation of SCT within the EHR with 46% less documentation than expected when compared to a national population. Additionally, the RR for documentation of SCT was lower in Black individuals than white indicating more under-documentation in Black individuals and potential disparities in care. We must evaluate causes and solutions to the under-documentation of SCT to facilitate reliable communication, integrity of 'big data' research evaluating medical complications of SCT, reduce disparities of care, assure health equity, and allow informed reproductive decision making for individuals with SCT.

Poster # 30

EFFECT OF AZITHROMYCIN ON ANTI-INFLAMMATORY MARKERS IN BLOOD OF PATIENTS WITH SICKLE CELL DISEASE

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Background: Patients with sickle cell disease (SCD) demonstrate varying degrees of inflammation and this inflammation is associated with many complications leading to significant morbidity and mortality. This may be ameliorated by lowering inflammation. Azithromycin, a safe, easily available antibiotic, lowers inflammation in patients with cystic fibrosis (CF).

Objectives: To determine anti-inflammatory effect of azithromycin in patients with SCD, we measured inflammatory markers in blood and white blood cells (WBCs) before and after 8 weeks of either oral placebo or azithromycin.

Design/Method: Seventeen of 23 patients (6-18 years,Mean±SD: 12.1±2.9 yrs) completed a 20 week placebo controlled double blind crossover study. One capsule of 250 mg azithromycin or

placebo was given orally to children under 30 kg and two capsules for larger children was given thrice weekly for 8 weeks. The azithromycin or placebo was switched after 4 weeks of washout. Blood samples were collected before and after each eight week period.
Whole blood was used to determine WBC subsets with flow cytometry. Lymphocyte phenotyping was accomplished by direct immuno-fluorescence labeling of cell surface antigens with mouse anti-human monoclonal antibodies conjugated to different (PerCP/Cy5.5, FITC, PE, APC, PE/Cy7, APC/Cy7) fluorochromes (BioLegend, CA, USA). Along with physical parameters (FS/SS) PerCP labeled antiCD45 Abs were used for leukocyte gating of granulocytes, monocytes, lymphocytes as well as lymphocyte subsets T-cells (CD3+), T-helper cells (CD3+4+), T-cytotoxic cells (CD3+8+), and NK-cells (CD3-CD56+). Samples were analyzed on BD FACSCalibur cell analyzer (Beckman Coulter, CA, USA).
Centrifuged plasma frozen at -80^{O}C was subsequently analyzed for markers of vascular damage. Concentrations of Myoglobin (Myo), Myeloid-related Protein 8/14 (MRP8/14), Lipocalin A (NGAL), C-Reactive Protein (CRP), Matrix Metalloproteinases (MMP) 2 and 9, Osteopontin (OPN), Myeloperoxidase (MPO), Serum Amyloid A (SAA), insulin-like growth factor-binding protein (IGFBP) 4, Intercellular Adhesion Molecule (ICAM) 1, vascular cell adhesion molecule (VCAM) 1, and Cystatin C were measured by flow cytometry using LEGENDplex bead-based immunoassay (BioLegend, CA, USA). Acquired raw data was analyzed using LEGENDplex Data Analysis Software v.7 (VigeneTech, Carlisle, MA, USA).

Results: WBC, absolute neutrophil count (ANC) and CRP were significantly lower (p=0.04, p=0.023 and p=0.036 respectively) after azythromycin therapy. Plasma levels especially of MRP8 (p=0.002), NGAL (p=0.002), and all other studied parameters of vascular damage including MRP8/14, NGAL, SAA, IGFBP4, ICAM1, and MMP9 decreased after azithromycin at different degrees with overall significance P=0.026.

Conclusion: Azithromycin significantly lowered markers of inflammation and vascular damage in our pediatric patients with SCD. Larger study would help conclusively verify our findings.

Poster # 31

IMPLEMENTATION OF A PAIN ACTION PLAN FOR PEDIATRIC PATIENTS WITH SICKLE CELL DISEASE

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Background:
Vaso-occlusive episodes (VOE) is the most common reason for hospital admissions and emergency room visits for patients with sickle cell disease (SCD). Education of patients and parents in appropriate management of pain is a key factor in reducing emergency room visits and hospital admissions. This quality improvement project addresses gaps in parent and patient knowledge through the implementation of a sickle cell pain action plan (SPAP).

Objectives:

The aim of this study was to decrease ER visits and hospitalizations for pain, increase utilization of non-opioids for pain management as a first line and decrease number of missed school days.

Design/Method:
A convenience sample of 23 patients age 2-21 years with sickle cell disease who are treated at The Jimmy Everest Center for Children with Cancer and Blood Disorders at The University of Oklahoma Health Sciences Center in Oklahoma City, Oklahoma was utilized.
A patient specific SPAP was created for patients and reviewed with patients/parents during routine clinic visits as well as a copy provided for them to take home. Active data collection occurred over a 3-month period (January 2020-March 2020) as well as a retrospective chart review of the same period the year prior (January 2019-March 2019).

Results:
Results that the utilization of a SPAP in pediatric and adolescent sickle cell patients significantly reduced the number of ER visits for pain (p 0.0491) and opioid prescriptions filled (p 0.0001). Although there was a decline in number of hospitalizations for pain, this was not found to be statistically significant (p 0.0829).

Conclusion:
This study shows that the utilization of a SPAP in pediatric and adolescent sickle cell patients significantly reduces number of ER visits for pain and opioid prescriptions filled. Patients and parents expressed appreciation for having a visible tool from which to refer to for pain management. Additionally, the SPAP provides standard communication regarding pain management across providers. A larger study conducted over a longer time frame would be beneficial in the future. At The Jimmy Everest Center at The University of Oklahoma Health Sciences Center, the SPAP will continue to be used to help better facilitate pain management for our sickle cell patients as well as introduce its use into the ER and hospital discharge process.

Poster # 32

SICKLE CELL AND VITAMIN-D: FRIEND OR FOE?

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Background: Sickle cell disease (SCD) is a very common genetic disease that results in structurally abnormal hemoglobin. These patients have limited therapeutic options and experience chronic pain, anemia, more infections and decreased quality of life. Literature reviews suggest SCD patients with chronic pain are susceptible to have Vitamin D deficiency which can lead to impaired bone health, cardiovascular disease, asthma and nephropathy. Cure for SCD is bone marrow transplant, while blood transfusions, vaccines, antibiotics, pain relievers and hydroxyurea are all designed to prevent and decrease vaso-occlusive crisis. Although the causal role of Vitamin D deficiency in SCD is not entirely clear, it can be easily and

inexpensively used as a treatment option with minimal risk.

Objectives: The goal of this retrospective study was to examine if supplementing vitamin-D deficient pediatric SCD patients with vitamin-D lowered pain crises, decreased the number of emergency room visits, reduced vaso-cclussive crisis and therefore, improved quality of life.

Design/Method: Using the selection criteria, a total of 19 pediatric patients (1-21year-old, both gender) with SCD were identified. A retrospective chart review was performed, and lab values were statistically analyzed using paired t-test and Pearson's correlation.

Results: In the consolidated analysis, vitamin D had a significant relationship to hemoglobin ($r=0.364$, $p = .001$) demonstrating a moderate and positive relationship. There was also a significant relationship between vitamin D levels and the number of visits to the ED ($r = 0.268$, $p = 0.019$) and hospitalizations ($r = 0.284$, $p = 0.013$), both indicating a positive correlation that was weak. When the analysis was stratified by year, the relationship between vitamin D and hemoglobin followed the same pattern in 2016 ($r= 0.628$, $p = 0.009$) and 2019 ($r = 0.553$, $p = 0.034$) demonstrating strong and positive correlations. In 2017, vitamin D also had a significant correlation with the number of pain crises ($r = 0.219$, $p = 0.049$) demonstrating a weak and positive relationship between these two variables.

Conclusion: Anemia in SCD is highly indicative of symptoms, the assumption still holds that Vitamin D has the potential to be a major factor in the treatment of SCD. While the study was limited due to retrospective nature, small sample size, and nonadherence, many of these are representative of a clinic that caters to inner-city populations. Nonetheless, these preliminary data calls for closer scrutiny via an RCT with better methodology to explore further the nature of relationship between vitamin-D and SCD in pediatric patients.

Poster # 33

RISING PEDIATRIC THALASSEMIA DIAGNOSES AND CONCURRENT REFERRAL GAPS BETWEEN 2010-2019 IN MINNESOTA

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Background: Thalassemias are common worldwide with evolving prevalence in different countries due to migration patterns. However, community prevalence across most of the United States is unknown. Minneapolis/St. Paul has a relatively large immigrant community including ethnic clusters from areas with high thalassemia prevalence. Statewide data show that these ethnic minority populations are growing; whether thalassemia prevalence mirrors these migration trends is unclear.

Objectives: To analyze the demography and disease characteristics of children with thalassemias diagnosed and receiving healthcare between January 1, 2010-December 31, 2019 within the University of Minnesota/M Health Fairview (MHF) system.

Design/Method: An IRB-approved electronic medical record (EMR) review was undertaken. Patients born January 1, 2001 or later were included if thalassemia diagnosis was confirmed and regular medical care was within the system. Thalassemia type, demography, labs, treatment, and specialist involvement were detailed and compared to available state demography data. Descriptive and comparative statistical analyses were performed for the full group and by thalassemia type.

Results: A total of 404 patients were included, representing 48 country or region-specific ethnicities, 17 known birth countries, and 30 separate languages. Karen (15%), Hmong (10%), and Vietnamese (5%) were most commonly represented, matching the 14th, 2nd, and 6th-largest Minnesota immigrant communities, respectively. Statewide, the Asian population grew by 32% (69,800 people) between 2010-2018. New thalassemia diagnoses also increased nearly every year, with Karen patients representing the largest proportional increase.

α-thalassemias (63%) were more frequently diagnosed than β-thalassemias. Most had either α-thalassemia or β-thalassemia traits (86%). Eleven (2.7%) and 2 (0.5%) had hemoglobin H disease and α-thalassemia major, respectively. β-thalassemia intermedia, major, and Hemoglobin E disease were collectively 5.9% of all patients (54% of these were transfusion-dependent). Excluding those categorized by default as "American" (28.1%), β-thalassemia patients were more likely to be Karen (24.3%), while those with α-thalassemias were frequently Hmong (14.4%). Five underwent marrow transplantation. Only 16% were seen by a hematologist within MHF, with fewer referrals in the final five years despite more diagnoses overall. English-speaking patients were more likely to have seen hematology than non-English speakers (20% versus 12%, P=0.04).

Conclusion: Pediatric thalassemia diagnoses are increasing within MHF, represent significant ethnic and language diversity, and highlight a need for improved culture-specific awareness and resources. MHF has one of two statewide pediatric hospitals providing dedicated thalassemia care, so these data likely under-represent the local prevalence. Most never receive hematologist evaluations, particularly if not English-speaking. The cause for this gap is unclear and requires further evaluation.

Poster # 34

VITAMIN D DEFICIENCY AND PAIN IN SICKLE CELL DISEASE

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Background: Sickle cell disease (SCD) is an inherited hemoglobinopathy which leads to vaso-occlusive crises (VOC) and increased erythrocyte adhesiveness to vascular endothelium. VOC is responsible for creating a state of chronic vascular inflammation that explains many features of SCD, especially chronic pain. With increased catabolism and deficits in nutrient intake, individuals with SCD suffer multiple macro- and micro-nutritional deficiencies, including

Vitamin D deficiency. Vitamin D decreases inflammation and deficiency in SCD patients leads to lower bone density, risk of bone fracture and may cause an increase in acute and chronic pain.

Objectives: To evaluate if there is a relationship between Vitamin D deficiency and pain in patients with sickle cell anemia.

Design/Method: Through retrospective review of electronic medical records (EMR) we evaluated patients with SCD followed at Marian Anderson Sickle Cell Center at St. Christopher's Hospital for Children. Patients with Vitamin D levels performed within the last 3 years were included in the analysis. Vitamin D was classified as sufficient (≥30), insufficient (20-29) or deficient (<20). The external pharmacy record was used to assess medication use. Associations between vitamin D and pain variables were explored with linear and rank order correlations, ANOVA, Chi Square, and Kruskal-Wallis tests as appropriate.

Results: Total of 103 patients were included in the study (47% female and 56% male; 75.7% had Hb SS, 19.4% HbSBeta+ and 4.9% HbSBeta0). Of these patients, 61.2 % were deficient in Vitamin D, 27.2% were insufficient and 11.7% were sufficient. We found that pain indicators increased consistently as vitamin D levels decreased. Mean VOC hospitalizations: deficient= 1.0, insufficient=0.5714, sufficient=0.1667, and self-reported pain scores: deficient= 3.5196, insufficient=2.2202, sufficient=1.9167, although these differences are not statistically significant (p=0.247 and 0.207, respectively). Vitamin D was significantly correlated with hemoglobin (p-=<0.001), MCV (p= 0.50), LDH (p=0.009), platelets (p=0.032) and WBC (p=<0.001)

Conclusion: In our data, hospitalizations and pain scores increased as Vitamin D levels decreased. Although the associations were not statistically significant, the power of the study is an issue, and we believe the pattern of increasing pain measures with decreasing Vitamin D levels merits further research. No significant differences in outcomes were seen between patients on Vitamin D supplementation and those who were not.
Further studies need to be done to develop treatment recommendations for vitamin D supplementation in pediatric SCD patients.

Poster # 35

SECRETORY PHOSPHOLIPASE A2 IN EXHALED BREATH CONDENSATE OF SICKLE CELL ACUTE CHEST SYNDROME

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Background: Acute chest syndrome (ACS) is a life-threatening complication of sickle cell disease (SCD). While ACS is defined by particular clinical findings, the underlying pathophysiology varies. Most current techniques to identify underlying triggers for ACS or to study inflammatory lung damage are uncomfortable for the patient and/or invasive and are limited in scope.

Plasma levels of secretory phospholipase A2 (sPLA2) are significantly elevated SCD during ACS compared with levels during vaso-occlusive crisis and at baseline.[1] While plasma sPLA2 may prove an effective biomarker to aid in ACS diagnosis, monitoring disease progression and response to therapy, its measurement requires frequent blood draws from already anemic patients in sickling crises. Exhaled breath condensate (EBC) collection is simple, non-invasive, and contains biomarkers with properties similar to those of sPLA2. EBC has not previously been used to evaluate sPLA2.

Objectives: We hypothesized sPLA2 would be measurable in EBC from patients with SCD during ACS.

Design/Method: In this single-institution feasibility study, plasma and EBC levels of sPLA2 from pediatric and adult patients with SCD were measured during ACS episodes and at baseline. The definition of ACS used for this study required a new radiographic pulmonary infiltrate of at least 1 complete lung segment, and 2 or more of the following: fever, chest pain, dyspnea, tachypnea, hypoxia.
Within 48 hours of ACS diagnosis, 3 patients with SCD (type HbSS) each had 3 EBC samples collected (at least 1 hour apart). A corresponding plasma sample was obtained at time of first EBC collection. For comparison, 3 patients with SCD at baseline had 1 collection of EBC and plasma. Human sPLA2 Type IIa levels were measured in all samples by a commercially available ELISA.

Results: Of 9 subjects screened, 7 were enrolled and 5 completed the study. Only 1 subject who completed collection during ACS returned for baseline collection. An additional 2 were enrolled for baseline collection. Incidentally, all participating subjects were female. All participants tolerated sample collection well.
sPLA2 reached level of detection in the ACS subject with the largest radiographic pulmonary infiltrate and who also reached the highest level of respiratory support when compared to the other ACS subjects. This patient also had the highest level of plasma sPLA2.

Conclusion: It is feasible to measure EBC sPLA2 levels in patients with SCD and ACS. sPLA2 is detectable in EBC. Further studies are warranted to evaluate measurability and reproducibility of sPLA2 in EBC, and its relationship to disease states.

(Styles, Blood, 1996)

Poster # 36

PATTERNS AND ATTITUDES AROUND DISCLOSURE OF SICKLE CELL ANEMIA: EXPERIENCES OF CHILDREN AND FAMILIES

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Background: Children with Sickle Cell Disease (SCD) may have frequent medical appointments and hospitalizations. However, complications of SCD are often not visible, allowing people to delay or avoid disclosure of the diagnosis. Decisions to disclose depend on weighing perceived risks and benefits in a given context. Little is known regarding patterns of disclosure of SCD, for young people and their families in Canada.

Objectives: 1)Understand motivating factors and implications of disclosure of SCD among children and families.
2)Identify if children and parents differ in attitudes toward disclosure.

Design/Method: A survey was administered to families while attending hematology clinic appointments in Edmonton, Canada. Parents/guardians of a child with SCD could complete the parent survey. Children 8-18 years, with SCD, completed the patient survey. Data were analyzed with quantitative and descriptive statistics.

Results: 42 families participated (42 parents, 14 children) with a total of 50 children with SCD. Median age of children with SCD was 7.5 years, with the majority born in Canada. The majority of parents were born outside Canada. Median age of children completing the survey was 13 years, 43% were born in Canada.

Parents reported disclosure of the diagnosis to all of the child's grandparents (60%), some grandparents (24%), and to at least one other extended family member (70%). 73% disclosed to at least some of the child's teachers. 46% had not disclosed to their employer. Among patients, 77% disclosed to at least one friend. 98% of parents indicated they always disclosed to a Family Doctor/Pediatrician. They were less likely to always disclose to a walk-in-clinic (86%), or emergency room doctor (90%). 5% felt they/their child had been treated badly by a nurse or doctor because their child had SCD. 22% of parents, and 15% of children regret telling someone. 15% and 32% of children and their parents felt they/their child were treated differently after disclosure, respectively.

Patients reported disclosing so others could understand if they are sick or need help. Reasons not to disclose included fear of being treated differently, and desire for privacy. Parents commonly reported motivation for disclosing so that others could take care of their children. Children and parents identified the importance of only disclosing to trusted individuals.

Conclusion: These data help us better understand challenges our patients and their families face and highlights the need for ongoing education of healthcare providers to ensure patients are confident they can disclose a diagnosis of SCD and continue to receive unbiased care.

Poster # 37

AWARENESS OF SICKLE CELL STATUS AMONG ADOLESCENTS AND CAREGIVERS IN AN INNER-CITY COMMUNITY HOSPITAL

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Background: Despite universal newborn screening available in the United States (U.S.), babies with sickle cell disease (SCD) are often born to parents who did not know they had sickle cell trait (SCT) before pregnancy.

Objectives: The objective of this study was to assess the knowledge of SCD and SCT among adolescents and their caregivers in our community.

Design/Method: It was a descriptive cross-sectional study. Self-administered anonymous questionnaires were distributed by convenient sampling method to adolescents and their caregivers in the general ambulatory and in-patient setting in an inner-city hospital. Multivariable adjusted logistic regression models were used to determine predictors of awareness of SCT.

Results: A total of 157 surveys were completed between April 2019 and February 2020. The mean age was 22 years (SD of 7.6 years). 35% and 58% of respondents identified as Black and Latino respectively. Overall, 72% of respondents stated they knew they had SCT and 28% did not know their status. 46.5% and 62.4% of respondents had never heard of SCD and SCT respectively, while 66.9% had never been spoken to about SCD by a healthcare provider. Respondents older than 21 years were more likely to know their SCT status compared to those who were 21 years or younger, OR = 2.74 (95% CI: 1.24 - 6.09). There was no statistical difference in SCT status knowledge between respondents who reported being born in the United States or outside the United States.

Conclusion: A significant fraction of respondents were not aware of their SCT status among a population with significant sickle cell prevalence (approximately 10% of U.S. SCD patients are in New York). These findings support the need for more education and awareness and the need for improved mechanisms to be put in place in order to communicate SCT status (universally available through the newborn screen) to adolescents early enough to be able to consider family planning practices using the knowledge of their SCT status. We believe that this awareness of one's SCT status would lead to a reduction in the incidence of SCD.

Poster # 38

EXPLORATORY UNDERSTANDING OF PHYSICAL ACTIVITY PRACTICES AND SAFETY IN CHILDREN WITH SCD

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Background: Though physical activity (PA) is beneficial in healthy individuals and in those with chronic disease, its impact on children with sickle cell disease (SCD) remains poorly

studied. Moreover, patients may refrain PA given a perceived fear of SCD complications exercise.

Objectives: 1/ Evaluate whether SCD children engage differently in PA compared to their peers. 2/ Evaluate the cardio-pulmonary impact of PA in a group of SCD patients.

Design/Method: Prior to the beginning of the pandemia, SCD children aged 8-17 y.o were consented to answer PA questionnaire (PAQ), and have their school peers answer the same PAQ. PAQ is a standardized questionnaire evaluating PA during the last 7 days and is a well described surrogate marker of PA. Patients and their peers were approached only during school year. The study was performed prior to the beginning of the COVID19 pandemia. A set of HbSS patients were invited to participate in a supervised exercise test including pre and post-effort PFT, echocardiograpy, ECG, measurement of troponins and NT-proBNP; a metacholine challenge was performed on day 2 to evaluate exercise-induced bronchial hyperreactivity.
T-test was used as statistical analysis, using SPSS V24. The study received IRB approval

Results: Questionnaires from 25 SCD (13 SS and 12 SC) were compared with 36 matched-school peers. SCD patients were overall less active (p=0.04). While their level of activity was similar at school, SCD patients were less active overall after school (p=0.028), in the evening (p=0.008) and weekends (p=0.049). While the difference was both significant for SS and SC patients, SS were less active than SC although the difference was staitstically not significant.
5 HbSS patients on HU were subjected to exercise test. There were no statistical differences in the pre and post-PA evaluations including measurements of troponin, nt-proBNP and functional testing. None of them had exercise-induced hyperreactivity.

Conclusion: Overall, SCD patients are less active than their peers, mostly outside schools. The absence of cardio-pulmonary modifications during PA is reassuring, although our study was limited to 5 HbSS on HU. Whether HU has a protective role cannot be excluded. Our results encourage us to further evaluate PA interventions outside school in SCD patients. Interventional studies evaluating the risk-benefit raio of PA in SCD children are further needed.

Poster # 39

ADHERENCE TO HYDROXYUREA THERAPY IN SICKLE CELL ANEMIA PATIENTS DURING THE COVID 19 PANDEMIC

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Background: Sickle Cell Anemia (SCA) is an inherited disease of hemoglobin that affects over 30,000 children in the United States. Hydroxyurea is a medication that promotes an increase of fetal hemoglobin (HgF) allowing for reduced disease complications. COVID-19 has placed numerous strains on the healthcare system so it can be expected that barriers to medication management will increase. While healthcare utilization and adherence to hydroxyurea in youth has been previously studied, it is unclear how the current COVID-19 pandemic has affected this

adherence.

Objectives: The purpose of this study is to evaluate patient adherence with hydroxyurea therapy along with the barriers to adherence during peak incidence of COVID-19 in children with SCA compared to one year prior to the emergence of COVID-19.

Design/Method: We performed a retrospective chart review for patients with SCA followed at the Marian Anderson Center at St. Christopher's Hospital for Children (SCHC) between ages 2-25 years. All patients were on hydroxyurea therapy between 02/2019 to 11/2019 (pre-COVID) and 02/2020 to 11/2020 (peak COVID). Data was collected and compared between the time periods for various biomarkers of anemia, hemolysis, as well as liver and kidney function. A paired t-test was used to compare data between the pre-COVID and peak-COVID time periods.

Results: We analyzed a total of 58 children with SCA (60% male, 40% female), 84.5% subtype HgbSS and 15.5% HgbSβ0thalassemia. Average HgbF% pre-COVID was 14.9, while average HgbF during peak-COVID was 13.9, showing significant decrease in HgbF% (-4.6%, p=0.039). Our data also showed increases in hematocrit, mean corpuscular volume, reticulocyte count, bilirubin, AST, ALT, BUN and creatinine although statistically not significant.

Conclusion: The COVID-19 pandemic brought a variety of challenges to healthcare, particularly for patients with higher healthcare needs such as those with SCA. Those on hydroxyurea therapy showed a decrease in their HgbF% from the pre-COVID to peak-COVID time period. This decrease is possibly related to less adherence with hydroxyurea therapy due to barriers accessing healthcare or obtaining medication during the pandemic. In addition, these patients showed worsening liver and kidney function indicating worsening SCA disease. Further survey of these patients will help identify which barriers to healthcare influenced their decrease in compliance.

Poster # 40

CLINICAL AND LABORATORY FINDINGS OF OSTEOMYELITIS IN SICKLE CELL DISEASE USING A STANDARD MRI

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Background: Sickle cell disease (SCD) is an inherited blood disorder leading to frequent pain due to bone infarction and increased susceptibility to infection. Osteomyelitis (OM) is a severe infections that requires prompt diagnosis and treatment. Distinguishing between bone infarcts and OM is difficult. Clinically, the presenting symptoms are often the same. Laboratory and radiographic evidence also overlap. There is no single, widely used definition of OM by MRI.

Objectives: We retrospectively applied a single, published MRI definition of OM to cases at our center to determine whether we could identify clinical or laboratory differences between patients

with SCD with MRI-defined OM versus patients with SCD without MRI-defined OM.

Design/Method: All patients with SCD admitted to Texas Children's Hospital with an ICD diagnosis code of OM were identified from 2000-2020. Data extracted by review of the electronic health record including clinical history, images, and laboratory results. The MRI results were re-classified using a previously published definition of OM in SCD.

Results: Fifty-nine admissions were identified, including five admissions with MRI criteria for definite (n=4) or probable (n=1) OM and 54 with MRI findings that did not meet the criteria for OM (NOM). Among the NOM group, 38 MRIs were suggestive of bone infarction according to the definition used. Within the OM group, 3 patients (60%) presented with fever, whereas 46 (94%) in the NOM presented with fever (p=0.20). Among the OM group, all patients (100%) complained of focal pain at admission, whereas 34 (59%) of patients with NOM had focal pain (p=0.16). Two patients (40%) in the OM group had positive blood cultures, compared to 18 (33%) in the NOM group (p=1.00). Across all groups, 8 of 24 patients had a pathogen grown from a bone biopsy, including 5 pathogens that matched the blood culture. Of these 8 positive bone biopsy, one patient had MRI criteria for OM (p=1.00). Of 47 patients with a ESR during the admission, 28 had ESR greater than 60s (OM=2; NOM = 26; p= 0.38). Three other OM and 16 NOM patients had ESR less than 60s.

Conclusion: In our cohort, we did not demonstrate a significant difference in clinical and laboratory data between patients with SCD and MRI-defined OM versus patients without MRI-defined OM. Additional refinements to the MRI definition of OM in SCD or to clinical data collected when OM is suspected should be explored to standardize the definition of OM in this patient population.

Poster # 41

SELENIUM LEVELS IN SCD PATIENTS AND IMPACT OF SELENIUM DEFICIENCY ON A SCD MOUSE MODEL

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Background: Sickle cell disease (SCD) is caused by a mutation in the β-globin gene resulting in a disease that affects more than 100,000 Americans and millions worldwide. Though pain is the hallmark of SCD, patients also have multisystem organ damage and a shorter lifespan. Elevated levels of reactive oxygen species (ROS) contribute to the pathology associated with SCD. ROS can be generated within the RBC by the auto-oxidation of HbS. Micronutrient selenium (Se) plays a key role in redox regulation through its incorporation into selenoproteins such as GPX1. ROS generated in the red blood cells can also be detoxified by glutathione peroxidase 1 (GPX1). It was reported that the of GPX1 reduced in the RBC's of SCD patients compared to a control group due to the oxidation of the amino acid selenocysteine that occurs at the active site of the enzyme. Selenium levels are lower among African Americans in the Chicago area and

elsewhere. In this regard, it is notable that in the United States, African Americans represent the majority of those with SCD.

Objectives: To investigate the relationship between selenium levels and SCD.

Design/Method: 1) We have utilized a mouse model of SCD to examine the impact of a reduced intake of selenium on parameters associated with SCD pathology. SCD mice on a selenium-deficient diet (<0.01 mg/kg diet) were compared to mice fed with a selenium-adequate diet (0.1mg/kg).
2) Blood samples were collected from SCD patients (steady-state) and control subjects (non-SCD) at the University of Illinois Hospital & Health Sciences System Sickle Cell Center. Patients of both sexes were enrolled for the study, and samples of blood for analysis was obtained when patients come in for their routine clinic visits.

Results: 1) SCD mice in the selenium-deficient group exhibited an increase Hb levels (Se deficient 5.7± 0.17 g/dl, n=3 vs. Se adequate 7.0± 0.83 g/dl, n=4 $p<0.05$. 2)Total of 17 blood samples from patients with SCD disease and 4 blood samples from control non-SCD individuals were collected in heparin tubes for plasma selenium, sodium and chloride analysis. It was observed that the levels of selenium were significantly (P=0.02) lower in the sickle cell patients plasma.

Conclusion: This data suggest that selenium deficiency in SCD should be further investigated. The establishment of providing a safe dietary selenium supplement to a portion of the SCD community could be a novel strategy that could be further established in clinical trials.

Poster # 42

UTILIZATION OF THE EMERGENCY DEPARTMENT DURING COVID19 PANDEMIC IN PEDIATRIC SICKLE CELL CENTER

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Background: In the United States, individuals with sickle cell disease (SCD) have an estimated 1,500,000 Emergency Department (ED) visits every. During the early COVID-19 pandemic NSSP found that ED visits declined 42%. Patients with SCD are at higher risk for complications related to COVID 19 due to multiple reasons, including higher rate of comorbidities, involving heart and lungs conditions. Delay in obtaining medical for patients with chronic medical conditions could lead to increase in adverse outcomes.

Objectives: To evaluate patient experience with ED visits and trends in healthcare utilization during the COVID-19.

Design/Method: We performed phone interviews of patients with SCD followed at St. Christopher's Hospital for Children. Patients who have been seen in the ER during COVID 19

pandemic were offered the questionnaire. Answers were given on a 1 to 5 Likert scale, with 1 signifying strong disagreement and 5 signifying strong agreement. Analysis of covariance was performed to compare means. Two-tailed p-values less than 0.05 were considered significant.

Results: Twenty-nine patients participated in the study (16 HgSS, 9 HgbSC, 3HgbS Beta0thalassemia, and 1 HgS/HPFH), 55% male. The data was analyzed based on participant's age, gender, hemoglobin genotype, race, and SCD severity. Severity of the disease was classified based on history of acute chest, stroke, cerebral vasculopathy and recent admissions for VOC. Seventeen patients were considered severe and 12 not severe. Most of the patients did not report significant changes in pain symptoms with 4 (14%) patients reporting improvement and 5 (17%) worsening of the symptoms. Main concerns related to ER visit included waiting area exposure 6 (20%); contact with other patients 9(31%) and contact with providers 2 (6%). Patients reported that they did not delay going to the ED or use additional home treatments (mean 2.23 and 2.40 respectively); but there was a significant difference when analyzed by hemoglobin genotype (mean 2.00 for HgSS, mean 3.08 for other genotypes, p=0.04). Finally, patient's satisfaction of the overall ED visit was slightly better (overall mean 3.27 with 3.4 for Children's Hospital ED and 2.5 for Adult Hospital ED, p 0.02).

Conclusion: Preliminary results suggest that the COVID-19 pandemic has not significantly affected patient satisfaction of ED visits nor their baseline SCD symptoms. Participants reported waiting longer and trying more medications at home prior to coming to the ED, which may correlate to the nationwide decrease in SCD-related ED visits. A larger trial with more participants is ongoing.

Poster # 43

PRACTICE STANDARD FOR MANAGEMENT OF NUTRITIONAL IRON DEFICIENCY ANEMIA IN THE EMERGENCY DEPARTMENT

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Background: Iron deficiency anemia (IDA) occurs in 2 to 3% of young children in the US due to a low-iron diet. Patients with severe anemia may be referred to the emergency department (ED) given the risk of serious complications and need for urgent intervention. A lack of consensus guidelines for children with moderate to severe IDA leads to variability in their management.

Objectives: To standardize the evaluation and management of patients (age 9 months to 5 years) with nutritional IDA presenting to the ED by developing an institutional algorithm.

Design/Method: A retrospective chart review of ED encounters for patients with nutritional IDA from June to November 2019 was conducted. A literature search was performed to identify any

existing clinical algorithms for management of patients with IDA in the ED. Both informed the creation of a draft algorithm, which was presented to all providers within the Section of Hematology/Oncology who manage patients with IDA. A 32-question pre-/post-survey was administered to elicit feedback. Survey questions probed clinical decision-making and explored attitudes using a 5-point Likert scale. The algorithm was revised and presented to the Section of Emergency Medicine in the same iterative manner, and input was obtained directly from our hospital's Blood Bank Director. A final draft algorithm was reviewed, edited, and approved by our Section's Practice Standard Committee. Implementation began in September 2020.

Results: Forty-two patients were captured on chart review (60% male, median age 22.5 months, mean hemoglobin of 5.5 g/dL [range 2.8-9.8], mean ferritin of 3.1 ng/ml [range 0-10]). Fifty percent (21/42) received oral iron, 45% (19/42) packed red blood cell transfusions, and 14% (6/42) intravenous iron. Survey evaluations were completed by 88% (53/60) of hematology providers and 44% (50/114) of ED providers. All hematology respondents reported the algorithm would be helpful for patients; 96% that it would be useful for providers. Majority consensus was achieved regarding PRBC transfusion threshold (74% of providers) and disposition from ED guidelines (82%) for the algorithm. We are currently assessing algorithm utilization using Model for Improvement methodology and measuring whether laboratory evaluation, therapy, and disposition decisions are made according to the practice standard.

Conclusion: A multi-disciplinary institutional practice standard for the management of young children with nutritional IDA was developed with the input of key stakeholders. Ongoing assessment of its implementation should provide insight into its long-term feasibility and impact on specific patient-centered outcomes.

Poster # 44

RETICULOCYTE HEMOGLOBIN CONTENT TO IDENTIFY IRON DEFICIENCY IN VERY LOW BIRTH WEIGHT INFANTS

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Background: Very low birth weight (VLBW) infants are at high risk for iron deficiency due to low iron stores, high growth velocity, low levels of erythropoietin, and a small circulating blood volume relative to iatrogenic blood loss. It is crucial to identify the infants who are iron deficient to prevent neurocognitive impairment. Reticulocyte hemoglobin content (CHr) is a reliable early indicator of iron deficiency.

Objectives: The aim of this study is to assess the iron status shortly after birth and at the time of discharge for VLBW preterm infants and to assess the effect of low early CHr on CHr at the time of discharge.

Design/Method: Retrospective analysis on all surviving VLBW infants (≤1500 grams) born

between 1/2015 and 09/2020 who had CHr performed shortly after birth and near discharge. Low CHr was defined as <29 pg. A descriptive analysis was performed, and the infants with low initial CHr were compared with those infants who had normal initial CHr.

Results: A total of 384 VLBW infants met the inclusion criteria. The median (IQR) initial CHr was 30.4 (28.1-32.4) and 29.4% of infants had low initial CHr. The median (IQR) CHr prior to discharge was 30.9 (28.4 – 32.5). In 118 infants (30.7%), the CHr was low prior to discharge. The infants with low CHr initially had a lower birth weight, a lower gestational age and required more blood transfusions. More infants in the low initial CHr group had low CHr at discharge.

Conclusion: Approximately 30% of VLBW infants had a low CHr initially and near the time of discharge, suggesting they were iron deficient. Infants with low initial CHr are likely to have low CHr near the time of discharge. Therefore, we speculate that CHr content can be used to guide iron supplementation in VLBW and improve iron status at discharge as well as the long-term neurocognitive outcomes.

Poster # 45

FAMILY PERCEPTIONS OF ANIMAL ASSISTED INTERACTIONS FOR CHILDREN WITH ADVANCED CANCER

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Background: The psychological and physical burden of relapsed/refractory childhood cancer takes an immense toll on ill children and their caregivers, jeopardizing quality of life. Children often endure prolonged hospitalizations, additional surgeries and procedures, unpleasant side effects of intensive chemotherapy, debilitating cancer pain, and increased stress and anxiety. Caregivers are frequently distressed by their child's suffering and unknown future. Animal-assisted interactions (AAI) have shown promising benefits for children with chronic conditions and their families. Little is known about child and caregiver perspectives on AAI participation for children with advanced cancer.

Objectives: To explore child and caregiver perspectives of their experiences with AAI during oncology clinic or hospital visits for children with advanced cancer.

Design/Method: Children (ages 3-17) with relapsed or refractory cancer and their caregiver(s) were recruited to participate in a 2-group randomized trial. Participants in the intervention group (n=14 families) completed approximately weekly 15-minute AAI sessions with a trained dog and handler during children's oncology clinic visits or hospitalizations for up to 12 weeks. Assessments included semi-structured interviews at study end to assess participant perceptions of AAI. Content analysis identified themes within the qualitative data.

Results: Nine families (N=17 participants; 7 children and 10 parents) completed interviews. Eight themes emerged from the data: (a) positive and, (b) negative aspects of the intervention, (c)

preferred changes to the intervention, (d) pet ownership impact on helpfulness of intervention, intervention effects on (e) communication, (f) anxiety/stress, and (g) child's willingness to come to clinic, and (h) value of the study. Two researchers coded the data with an initial inter-rater reliability of 0.9; three researchers ultimately reached consensus. Sixteen (94%) participants shared positive aspects (e.g. enjoyment, anticipation) of AAI. No participants reported negative aspects. The only requested change was more time with the canine team. Six of 10 (60%) parents expressed the importance of the study's purpose without prompting. Additional code counts, frequencies, and exemplar quotes will be presented.

Conclusion: Families of children with advanced cancer perceive AAI as beneficial with few requested changes. Further studies are needed to fully evaluate impact of AAI. Providers should recognize that families value supportive interventions, such as AAI, and advocate for their patients to receive these services during cancer treatment.

Poster # 46

TRENDS IN PEDIATRIC CANCER CARE IN FLORIDA FROM 1981-2020: A REVIEW OF THE FAPTP DATABASE

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Background: The Florida Association of Pediatric Tumor Programs (FAPTP) has used the Statewide Patient Information Reporting System (SPIRS) since 1980 to track all new cases of pediatric cancer in the state from birth through 21 years of age.

Objectives: Our objective was to review the last 40 years of SPIRS data to see how pediatric cancer care in Florida has evolved as the state's population has grown and FAPTP centers have increased from 13 to 17.

Design/Method: We retrospectively analyzed the SPIRS data from 1980 through 2018, looking at numbers of new diagnoses, care delivery sites and trial enrollment in COG studies. There was no distinction between biologic and therapeutic studies. We looked at the data in 5-year increments starting in 1981-1985 and ending in 2016-2020 with data from 2019-2020 projected based on 2016-2018.

Results: From 1981-2020 Florida's population grew 87%. Simultaneously the population under 21 grew only 61% while new pediatric cancer diagnoses increased 347% to over 1,000 new cases/year. The median age of pediatric cancer patients increased over that time from 6 to 9 years old with a consistent gender breakdown of 55% male and 45% female. From 1981 through 2020, the percentage of patients treated at FAPTP centers grew from 30% to 64% with an average annual percentage change (AAPC) of 12% (95% Confidence Interval [CI] of 3 to 21%) and those with known follow-up rose from 65% to 95%%, an AAPC of 4.6% (95% CI of 3.2 to 6%). The number of patients enrolled on COG trials increased 150% over the this time, but the rate of clinical trial enrollment for established patients decreased from 32% in 1981-1985 to 20%

for the period ending in 2020, after a peak of 42% in 1986-1990, for an AAPC of -9% (95% CI of -13.4 to -4.3%).

Conclusion: The data demonstrate a striking increase in pediatric cancer cases in Florida over the last 40 years out of proportion to the population growth. There was a significant increase in the percentage of these patients receiving care at FAPTP centers, which should equate to greater access to clinical trials. Although the overall number of patients enrolled on COG trials increased, there was a decrease in the rates of enrollment. While there has been improvement in access to specialized care for these patients, this has not translated into a higher rate of clinical trial enrolment, which merits further investigation and ongoing initiatives.

Poster # 47

IMPLICATIONS OF INCIDENCE OF COVID-19 AT RUSH UNIVERSITY HOSPITAL PEDIATRIC ONCOLOGY CLINIC

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Background: Cook County, Illinois, the home of Rush University Medical Center, was the epicenter of COVID-19 in the US during the spring of 2020, resulting in tension between timely and life-saving therapy and the risk of coming into the pediatric and adolescent/young adult (AYA) oncology clinic. Chicago's initial shelter period required non-emergent hospital visits to be postponed. Currently, the nation is experiencing a second COVID-19 surge similar or perhaps worse than the previous surge in the spring of 2020.

Objectives: The objective is to see if patients can continue treatment during the COVID-19 pandemic while preventing infection in vulnerable patients.

Design/Method: Corresponding to the shelter period, chart reviews identified COVID-19 nasal swabs and SARS-CoV-2 IgG results for patients who came to clinic between 3/13/2020-6/13/2020. A positive test was defined as a positive COVID-19 nasal swab or an IgG antibody detected within 14 days after start/end of the period. Data from Johns Hopkins Coronavirus map and Chicago Department of Public Health was used within the same time period.

Results: During the shelter period, there were 165 visits to Rush's pediatric oncology clinic with a mean of 4.8 patients in clinic per day. Of the 54 patients, 94% (n=51) were immunocompromised including 50% (n=27) on active immunosuppressant treatment. There was a mean of 3.1 visits to the oncology clinic per patient (median=1) and 4.0 total hospital visits per patient (median=2). For ages 0-17, 18-29, and 0-29, the positivity percentages were 3.4%, 7.1%, and 4.9% respectively (3 of 88 tests; 4 of 56 tests; 7 of 144 tests). The positivity percentages compared to 15.9% (ages 0-17), 16.9% (18-29), and 16.7% (0-29) in Chicago and 5% (0-17) and 8% (18-24) at Rush University Hospital overall. For each age group: 0-17, 18-29, and 0-29, the p-values were that of p=0.00069, p=0.02559, and p=0.0001 respectively.

Conclusion: The positivity percentages for COVID-19 cases in the pediatric oncology clinic during the shelter period were significantly lower than the Chicago data during the shelter period for each age group. The COVID-19 positivity percentages for all ages of pediatric oncology patients were lower than the overall Rush University Hospital positivity percentages too. This data shows that masking, distancing, and hand washing can help prevent COVID-19 acquisition even in a clinic setting. These results support that vulnerable pediatric patients can be protected without deferring their treatment during viral outbreaks.

Poster # 48

PREVALENCE OF AUTISM SPECTRUM DISORDER IN CHILDHOOD CANCER PATIENTS: SINGLE INSTITUTION EXPERIENCE

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Background: The strong underlying genetic etiology for both autism and cancer suggests the possibility of a common pathway between the two diseases. An increasing number of literature have been focusing on understanding the shared genetics between cancer and autism. We are reporting a single institution experience on the prevelence of Autism Spectrum Disorder (ASD) in childhood cancer patients.

Objectives: Significant literature evidence suggests shared genetic variants and metabolic pathways between ASD and cancer. Few research had studied the prevelence of ASD in children with cancer.

Design/Method: This is a retrospective study based on chart review of 220 cancer patients at Palm Beach Children's Hospital between 2012 and 2020. We evaluated the percentage of patients diagnosed with autism before the onset of cancer and compared it to the national prevalence of autism reported by the Centers for Disease Control (CDC) in 2016. We excluded from our cohort patients who were less than 2 years of age as it is difficult to make the diagnosis of ASD prior to 2 years. We also excluded patients who were diagnosed with ASD after the diagnosis of cancer.

Results: Our cohort showed over two-fold increase in the incidence of ASD in with childhood cancer patients compare to the general population (5.0% vs. 1.8%). We performed the Chi-square test, and the P-value was 0.38, reflecting statistically insignificant results likely due to the small sample size. We did not find correlation between ASD and specific type of cancer, the male:female ratio was similar compare to the CDC report in general population.

Conclusion: Our study showed increase incidence of cancer in children's with autism, however, the result was statistically insignificant.

Poster # 49

LONG-TERM COMPLICATIONS OF STAPHYLOCOCCUS AUREUS BACTEREMIA IN PEDIATRIC CANCER PATIENTS

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Background: In children with cancer, central venous catheter (CVC)-associated *Staphylococcus aureus* (*S. aureus*) blood stream infections (BSI) are common and associated with complications. Though guidelines recommend CVC removal in *S. aureus* BSI, attempted CVC salvage is common practice. Data clarifying the indications for CVC removal are limited in pediatric cancer patients.

Objectives: To identify factors associated with long-term complications from *S. aureus* BSI in pediatric cancer patients to determine indications for CVC removal.

Design/Method: A chart review was conducted on all cases of *S. aureus* BSI in children with cancer or post stem cell transplant at Monroe Carell Jr. Children's Hospital at Vanderbilt between 2005-2020. Long-term complications were assessed up to 6 months from BSI presentation and included *S. aureus* BSI recurrence, defined as repeat BSI after ≥2 consecutive negative blood cultures at least 24 hours apart, osteomyelitis, endocarditis, meningitis, deep abscess, and exit site infection identified >72 hours after presentation. Categorical and continuous variables were compared with long-term complications (Yes vs. No) using Fishers exact test and Wilcoxon rank sum, respectively.

Results: There were 60 *S. aureus* BSI episodes. In 16.7% of episodes (10) no CVC was present. In those with a CVC, CVC was removed in 58.0% of episodes (29) and salvaged in 42.0% (21). Long-term complications occurred in 18.3% of episodes (11). The first complication in each of these episodes were BSI recurrence (4), meningitis (1), deep abscess (3), exit site infection (1) and death (2). Complication rate by CVC status was 17.2% (5) in removal group, 14.3% (3) in the salvage group, and 30% (3) in the no CVC group. In cases where the CVC was removed, there was a trend that complications occurred more frequently in those who had a delay in CVC removal (n=5 with complications, median 103 hours [94-260] vs. n=24, 79 [36-119], p=0.065). In univariate analysis, MRSA (45.5% in those with complication versus 20.4% without, p=0.122), and need for ICU care <24 hours from presentation (36.4% in those with complication versus 16.3% without, p=0.206) trended towards an association with long-term complications.

Conclusion: MRSA bacteremia or ICU care at presentation trended towards association with long-term complications in pediatric cancer patients with *S. aureus* BSI. While it is unclear if CVC removal is necessary in all cases, decreasing time to line removal may result in fewer long-term complications. More data is needed to further elucidate indications for CVC removal.

Poster # 50

EFFECT OF PLATELET TRANSFUSION ON HEMOSTASIS IN PATIENTS WITH ALL OR LLY RECEIVING PEG-ASPARGASE

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Background: Acute lymphoblastic leukemia (ALL) is the most common childhood malignancy. Despite improved cancer outcomes, venous thromboembolism (VTE) is a source of significant disease- and therapy-related morbidity. PEG-aspargase and glucocorticoids, mainstays of ALL and lymphoblastic lymphoma (LLy) treatment, are risk factors for thrombosis. While many patients require platelet transfusions during induction, the impact of transfusions on VTE risk is unknown.

Objectives: To examine the effect of platelet transfusion on the clotting milieu during induction chemotherapy using thromboelastography (TEG) parameters maximal amplitude (MA) and clot strength (G) to determine if changes were predictive of VTE risk.

Design/Method: This observational, prospective study was conducted from 11/2014 to 1/2020 at a tertiary care hospital. Children weighing greater than or equal to 17 kg with ALL or LLy were eligible. Complete blood count (CBC), PT, aPTT, fibrinogen and TEG were collected prior to day 4 PEG-aspargase administration, and on days 8 and 15 of induction. These studies were also collected before and within 1 hour after platelet transfusions given during induction. Comparisons between TEG parameters pre- and post-transfusion were made. Mixed effects general linear modeling was used for analysis of pre vs. post-transfusion.

Results: Of 26 patients enrolled, 11 (5 males, 6 females) received platelet transfusions on or after day 4 of induction. The age was 7.5$\pm$3.5 years (mean$\pm$SD), with the majority having standard risk B-ALL (45.5%). Expectedly, increases in MA (26.7$\pm$9.8 vs. 46.4$\pm$8.6, $p < 0.001$), and G (1.9$\pm$0.9 vs. 4.6$\pm$1.5, $p < 0.001$) occurred following platelet transfusion (pre vs. post-transfusion, respectively).

Ten and 4 patients were transfused platelets on or within 96 hours of day 8 and day 15, respectively. When compared to 12 non-transfused patients on day 8, and 16 non-transfused patients on day 15, post-transfusion MA and G parameters were not statistically different for transfused compared to non-transfused patients. None of the transfused or non-transfused patients had significant bleeding. Two of 26 patients developed VTE. Neither received a platelet transfusion on or after day 4 PEG-aspargase.

Conclusion: Platelet transfusion was associated with statistically significant increases in TEG parameters MA and G, with correction of abnormally low parameters pre-transfusion to the normal range post-transfusion. However, there was no difference in MA and G parameters for patients post-platelet transfusion compared to non-transfused individuals. Overall, platelet

transfusion did not increase the risk for VTE during induction. More research is needed to understand factors that contribute to VTE risk in ALL/LLy patients undergoing induction chemotherapy.

Poster # 51

RISK FACTORS FOR DELAYED CLEARANCE AND NEPHROTOXICITY FROM HIGH-DOSE METHOTREXATE IN PEDIATRIC ALL

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Background: High-dose methotrexate (HD MTX) is a key component of treatment in many regimens for pediatric acute lymphoblastic leukemia (ALL), yet it entails significant adverse effects such as nephrotoxicity and increased health resource utilization such as extra hospital admission days.

Objectives: We described the prevalence of nephrotoxicity and delayed MTX clearance in pediatric ALL patients and evaluated demographic and clinical risk factors for these outcomes.

Design/Method: We performed a chart review of ALL patients who received HD MTX doses between 1000-5000mg/m2 at Texas Children's Cancer Center from September 2010 to December 2017 and collected data including percent creatinine increase from baseline, MTX clearance time (measured from the start of infusion), and key clinical and demographic variables. Bayesian hierarchical ordinal regression was performed to estimate odds ratios (OR) and 95% compatibility intervals (CI) to evaluate associations between risk factors and outcomes.

Results: We identified 423 patients who received 1590 HD MTX doses. Of the doses, 143 (8.9%) resulted in a Common Terminology Criteria for Adverse Events (CTCAE) grade 2 nephrotoxicity, five grade 3, and one grade 4. Among the 4000-5000mg/m2 doses, 333/1308 (25.4%) doses resulted in delayed MTX clearance > 72 hours that amounted to 573 extra hospital days. Of patients that experienced a delay, the median cumulative extra hospital days was 2 (interquartile range 1-4, max 16). The factors associated with delayed MTX clearance were age (OR=1.47 for 5-year increase in age [95% CI: 1.32-1.67]), pre-B ALL compared to pre-T ALL (OR=1.59[95% CI: 1.04-2.31]). Self-reported Black race was associated with a decreased risk of delayed MTX clearance (OR=0.69[95% CI: 0.48-0.99]. BMI <3% (OR=2.15[95% CI: 1.50-3.03])and Hispanic ethnicity (OR=1.38[1.08-1.78]) were associated with an increased risk of nephrotoxicity, and age (OR=0.76[0.66-0.87] per 5-year increase), Black race (OR=0.69[95% CI: 0.47-0.99]), and an institutional intensive monitoring protocol (IMP) (OR=0.44[95% CI: 0.26-0.74]).

Conclusion: We found that over 9% of HD MTX doses resulted in CTCAE grade 2 or higher nephrotoxicity and that doses of 4000-5000mg/m2 caused573 extra days of hospital time due to delayed clearance in the seven-year study period. Our analysis revealed that age, disease type,

race, sex, and BMI may play a role in the development of these adverse outcome and that the institutional IMP was protective against nephrotoxicity. Our findings can be used to improve risk prediction models for MTX toxicity and assist clinicians in decreasing the burden of toxicity in pediatric ALL.

Poster # 52

READMISSION FOLLOWING HOSPITALIZATION FOR FEBRILE NEUTROPENIA IN PEDIATRIC ONCOLOGY PATIENTS

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Background: Febrile neutropenia is a life-threatening complication of chemotherapy in pediatric oncology patients, which is associated with significant utilization of hospital resources. Prior studies have attempted to identify patients at low-risk of infection to facilitate early discharge. This is the first multicenter study to evaluate factors associated with readmission following hospitalization for fever and neutropenia.

Objectives: Our objectives were to describe the characteristics and hospital courses of pediatric oncology patients admitted with fever and neutropenia and to identify factors associated with an increased risk of readmission.

Design/Method: We utilized retrospective data from the 6 pediatric hospitals contributing to the Pediatric Health Information System Plus database from 2007-2012. We included inpatients 1-21 years with an ICD-9 code for malignancy and either febrile neutropenia or fever alone. We required a documented absolute neutrophil count (ANC) within 24 hours of admission (ANC <500 cells/microliter) and discharge. Patients were excluded if post bone marrow transplantation, admission for fever or infection within the previous 7 days and if mortality occurred during the admission. We evaluated demographic features, antibiotic management, infectious complications and utilization of hospital resources. We compared patients who required readmission within seven days following index hospitalization to those who did not to identify features associated with increased likelihood of readmission.

Results: We identified 4,029 hospitalizations among 2,349 patients. Readmission within 7 days took place following 342 hospitalizations (8.5%). Patients who required readmission had a longer mean length of stay during index hospitalization (9.0 days vs 7.1 days, p=0.003). There were no significant differences between patients who required readmission and those who did not as far as demographic features, antibiotic class exposure, diagnosis of invasive infection or G-CSF exposure. A greater proportion of patient who required readmission required ICU care during index hospitalization (9.6% vs 6.6%, p=0.03). There was no significant difference in the median ANC at the time of discharge. However, the readmission group had a significantly lower total phagocyte count at the time of discharge (520 vs 600 cells/microliter, p=0.02) and were more likely to have severe neutropenia (ANC <200 cells/microliter) at the time of discharge (28.7% vs 23.6%, p=0.04). On multivariate analysis, income in the first quartile was associated

with increased odds of readmission (OR 1.45, p=0.04).

Conclusion: A significant proportion of children are readmitted following hospitalization for fever and neutropenia particulary those with severe neutropenia at the time of discharge. Variation in patient management cannot predict the need for readmission.

Poster # 53

SECONDARY IMPACTS OF CONSTIPATION IN ACUTE LYMPHOBLASTIC LEUKEMIA IN U.S. CHILDREN'S HOSPITALS

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Background: Children with acute lymphoblastic leukemia (ALL) suffer from a litany of chemotherapy-induced side effects. Constipation secondary to vinca alkaloids, environmental changes, and opioid use are common issues for children newly diagnosed with leukemia. Our prior work identified that 34% of children with ALL undergoing induction chemotherapy in U.S. children's hospitals suffered from constipation[1]. Secondary impacts of constipation in pediatric oncology patients have not been reported in the literature.

Objectives: To investigate the morbidity associated with constipation including infections, mucositis, and healthcare burden in hospitalized children with ALL receiving induction chemotherapy.

Design/Method: We analyzed data from 48 children's hospitals in the Pediatric Health Information System, extracting patients 1-21 years of age with ALL, hospitalized for induction from October 2015 through December 2019. Induction admission was identified by the presence of vincristine, L-asparaginase, steroids, and intrathecal cytarabine. Constipation was defined as the presence of a constipation diagnosis code or having received at least two unique anti-constipation medications during hospitalization. All infection diagnoses were included in database search. Data were analyzed using nonparametric statistics, comparisons of outcomes between those with and without constipation were presented as odds ratios (OR).

Results: We identified 2,693 (56%) patients with constipation out of a total of 4,814 unique ALL patients in induction. Compared to patients without constipation during induction, patients with constipation were significantly more likely to have fever and neutropenia (OR=1.14; p=0.03), an infection (OR=1.42; p<.0001), mucositis (OR=3.73; p<.0001), abdominal imaging (OR=2.00; p<.0001), physical therapy consult (OR=2.39; p<.0001), or occupational therapy consult (OR=1.97; p<.0001). The median length of induction hospitalization was significantly greater in those with constipation compared to those without constipation (10 days vs. 8 days; p<.0001).

Conclusion: Children with ALL suffering from constipation during induction therapy have more

infections, mucositis, and healthcare burden compared to children with ALL and no evidence of constipation during induction therapy. Further research should explore the causative relationship between constipation and infections. Increased attention should be given to constipation prophylaxis, management, and treatment in patients with ALL at the start of induction therapy, particularly in patients with complications or prolonged hospitalizations.

1. (Belsky, Pediatr Blood Cancer, 2020)

Poster # 54

(1-3) -ß-D-Glucan (BDG): A DIAGNOSTIC MARKER OF INVASIVE FUNGAL DISEASE IN PEDIATRIC CANCER PATIENTS

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Background: Diagnosing invasive fungal disease (IFD) in pediatric patients is challenging as cultures are often negative and diagnostic efficacy of biomarkers such as β-d-glucan assay (BDG) and galactomannan assay (GM) is unclear. Pediatric fever and neutropenia guidelines have recommended against BDG to diagnose IFD in pediatric cancer patients given BDG false positivity driven by treatments such as intravenous immunoglobulins (IVIG) or albumin infusions.

Objectives: Our objective was to determine if having an optimal BDG positivity cut-off could help differentiate between true IFD versus false-positive cases.

Design/Method: A retrospective chart review of pediatric oncology patients was conducted at University of Chicago (Comer Children's Hospital) between July 2009 until December 2016 to determine the utility of BDG. Inclusion criteria for this study included patients with febrile neutropenia, at high risk for IFD (fever >5 days unresponsive to antibiotics or recurrent fever with persistent neutropenia), and who have had ≥1 BDG sent. IFD was diagnosed using the European Organization for Research and Treatment of Cancer and Mycoses Study Group criteria with patients divided into two groups: 1) proven/likely IFD and 2) less likely IFD. Data pertaining to possible causes of false-positive BDG was collected including the presence of bacterial infections, recipients of IVIG, albumin or certain antibiotics (i.e., ampicillin/sulbactam, piperacillin/tazobactam). BDG levels were reported to determine cut-off positivity of each group (true IFD versus false positive cases).

Results: Of the 230 febrile neutropenia episodes (FNEs) of high-risk IFD evaluated, there were 125 FNEs which had >1 BDG sent. There were 45 cases of total positive BDG serum levels >80 pg/ml, comprised of 35 cases of FNEs in the proven/likely IFD group and 10 false positive (FP) cases in the less-likely IFD group. The median value of the first reported BDG in the IFD group was higher than in the FP group (290 versus 150 pg/ml). The range of BDG levels in the IFD group was 83 to >500 pg/ml and the FP group was 106 to 250 pg/ml. Repeated serial BDG values were shown to trend down and normalize quickly in the 7-10 days post treatment, or FP

group.

Conclusion: No optimal cut-off value for BG assay in IFD exists, but a false positive BG assay cut-off may be as high as 250 pg/ml with a lack of clinical and .radiological symptoms suggesting IFD. This finding could help provide guidelines for physicians for IFD interpretation, early IFD diagnostics, and empiric treatment without novel fungal biomarkers.

Poster # 55

SINGLE DOSE RASBURICASE FOR CHILDREN AND ADOLESCENTS AND YOUNG ADULTS

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Background: Tumor lysis syndrome (TLS) is an oncologic emergency characterized by a rapid lysis of tumor cells and subsequent release of intracellular contents such as potassium, phosphate, and nucleic acids. This can lead to an increase in uric acid and precipitation of uric acid in the renal tubules which can lead to renal insufficiency and even renal failure. Standard prevention of TLS includes adequate hydration and allopurinol. Rasburicase is a recombinant enzyme that converts uric acid to a more soluble metabolite of uric acid, allantoin. The utilization of a single dose of rasburicase has become increasingly common and has been the standard at our institution for several years for patients with elevated uric acid levels and/or additional risk factors for TLS.

Objectives: Evaluate the effectiveness of a single dose of rasburicase in children and adolescents and young adults

Design/Method: This was a retrospective chart review. All patients who received rasburicase from 2014 through 2019 were included. Patients were identified and data was retrieved using the hospital's electronic medical record system, EPIC.

Results: Ten patients with a median age of 12 years (range: 4 months to 20 years) received rasburicase. The majority of patients had acute lymphoblastic leukemia but other diagnoses included T-cell lymphomblastic lymphoma and Burkitt lymphoma. The median baseline uric acid prior to rasburicase administration was 10 mg/dL (range: 5.1-15.7 mg/dL) and the median baseline white blood cell count prior to rasburicase administration was 60,690 k/uL. All patients received hydration and 9 received concomitant allopurinol. All patients received only 1 dose of rasburicase within 1-2 days of initiating treatment for the malignancy. The median dose of rasburicase was 4.5 mg (range: 1.5-4.5 mg). The median dose of rasburicase based on weight was 0.12 mg/kg/dose (range: 0.04-0.3 mg/kg/dose). Uric acid levels following rasburicase administration were reduced by a median of 60% within 10 hours. The median uric acid level at 24 hours was 0.35 mg/dL. The median duration of allopurinol therapy was 7 days. Uric acid levels did not exceeded the upper limit of normal at any point following rasburicase

administration.

Conclusion: This data demonstrates that a single, weight-based dose of rasburicase (max of 4.5 mg) effectively normalized uric acid in 100% of patients within 24 hours. Utilizing a single dose of rasburicase is a clinically effective and pharmacoeconomic approach for preventing TLS in children and adolescents and young adults.

Poster # 56

ASPARAGINASE-ASSOCIATED TOXICITIES & OUTCOMES IN OMANI CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Asparaginase has contributed to improved therapy outcomes in children with acute lymphoblastic leukemia (ALL). Notwithstanding its high therapeutic efficacy, asparaginase is associated with number of toxicities and may require alteration/ discontinuation. Failure to receive full course due to treatment-emergent toxicity has been associated with poor-outcomes. Of the available preparations our patients received PEG-asparaginase as a standard of care.

Objectives: We aimed to evaluate the profile of asparaginase-associated toxicities and outcomes in Omani patients with ALL.

Design/Method: Retrospective study on patients with ALL, at the Pediatric Hematology/Oncology Unit, Sultan Qaboos University Hospital, Muscat, Oman from June2006-Jan2020. Electronic medical records were used to obtain patients' details for asparaginase-associated toxicities and outcomes. Data were analyzed using SPSS software version 23.

Results: Of the 207 children with ALL, 48 children, aged 2-14 (median 7) years; developed asparaginase-associated toxicities.
Mild to moderate toxicities included local skin reaction at the site of injection and transient urticarial skin rash in 3 patients each with transient hyperglycemia in 23 patients, of whom 17 required short-term insulin therapy.
Severe toxicities in these children included clinical hypersensitivity in 2, pancreatitis in 4 and cerebral venous sinus thrombosis (CVST) in 8 patients with hemorrhagic infarction in one of them.
The two patients with clinical hypersensitivity were shifted to erwinia asparaginase and completed treatment uneventfully.

Asparaginase was discontinued in all 4 patients who developed pancreatitis, of whom two are in remission (duration 1 year and 5 years); both were standard-risk ALL.
The remaining two patients in whom asparaginase was discontinued died, both had high-risk ALL, one succumbed to the disease in delayed intensification, and the other developed

permanent diabetes mellitus requiring regular insulin therapy and died of complications post hematopoietic-stem-cell-transplant (HSCT).

All children with CVST received treatment with anticoagulation (unfractionated and/or low molecular weight heparin) and are alive. Neurological sequelae (permanent right-sided hemiplegia) occurred in one boy (2.5 years old), with high-risk ALL. He had extensive superior sagittal sinus thrombosis and massive left-sided fronto-parietal hemorrhage with midline shift, requiring urgent craniotomy and evacuation with interruption of chemotherapy. He was subsequently continued on treatment with asparaginase, but suffered a relapse and underwent HSCT.

Conclusion: Most of asparaginase-induced adverse reactions were transient and self-limited. Discontinuation of therapy might predict poor outcome for disease-free survival in high-risk ALL. Rapid identification and management of asparaginase-associated toxicity is necessary for maximal benefit from asparaginase therapy.

Poster # 57

BODY COMPOSITION AND CHEMOTOXICITY IN CHILDREN WITH CANCER

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Background: Body composition is an emerging predictor of chemotoxicity and survival in adults with cancer; however, its role in children with cancer has remained unexplored.

Objectives: Examine the association between body composition at cancer diagnosis and post-cancer chemotoxicity in children with hematologic malignancies (Hodgkin lymphoma [HL], non-Hodgkin lymphoma [NHL]) and solid tumors (neuroblastoma [NBL], rhabdomyosarcoma [RMS]).

Design/Method: We constructed a retrospective cohort of 128 patients (HL= 45, NHL= 42, NBL=21, RMS=20) diagnosed between 2000 and 2015 with available pretreatment abdominal computerized tomography (CT) scans. Body composition was assessed at the 3rd lumbar vertebral level using sliceOmatic (Tomovision, Quebec, CA) and included skeletal muscle index (SMI, cm^2/m^2), skeletal muscle density (SMD, Hounsfield units [HU]) and height-adjusted total adipose tissue (hTAT, sum of visceral, intramuscular and subcutaneous adipose tissue, cm^2/m^2). We calculated skeletal muscle gauge (SMG = SMI X SMD, expressed per 1000 in arbitrary units [AU]). We abstracted sociodemographics, disease characteristics and toxicities from medical record. We graded toxicities per Common Terminology Criteria for Adverse Events v5. We operationalized chemotoxicity as the proportion of chemotherapy cycles with grade ≥4 hematologic or grade ≥3 non-hematologic toxicities. Linear regression models were constructed to examine associations between body composition metrics and toxicities, after adjusting for age at diagnosis, gender, race/ethnicity, cancer diagnosis, body-mass index (BMI; measured as

percentile) or body-surface area (BSA).

Results: Median age at cancer diagnosis was 11.3y (range, 2-21y), 60.9% were male, and 57.8% were non-Hispanic white. Median BMI percentile at cancer diagnosis was 60 (0-100). The median values for body composition metrics were as follows: SMI (40.6 cm^2/m^2 (24.1-86.6), median SMD was 55.1 HU (35-84.5), median SMG was 2249 AU (961.4-4221.5) and median hTAT was 18.5 cm^2/m^2 (0-226.7). The mean proportion of chemotherapy cycles with toxicity were 45.9% for hematologic toxicity and 34.4% for non-hematologic toxicity. The correlation between BMI and skeletal muscle indices was poor (BMI and SMI: r^2=0.2; BMI and SMD: r^2=0.1; BMI and SMG: r^2=0.01) but was modest with adipose tissue index (BMI and hTAT: r^2=0.4). There was significant association between hematologic toxicity and skeletal muscle indices (SMD: β=-1.2, P=0.01 and SMG; β=-13.9, P=0.02, but not SMI: β=-0.2, P=0.5). BMI was not associated with hematologic toxicities (β=-0.1, P=0.2). Non-hematologic toxicities did not show any association with BMI or body composition indices.

Conclusion: We show that poor skeletal muscle density, reflecting myosteatosis, at diagnosis is associated with a greater likelihood of experiencing hematologic toxicities. The mechanism of this association needs to be investigated.

Poster # 58

FLUID OVERLOAD AND ACUTE KIDNEY INJURY IN CHILDREN WITH TUMOR LYSIS SYNDROME

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Background: Tumor lysis syndrome (TLS) is a common oncologic emergency among patients with pediatric hematologic malignancies. Biochemical derangements from TLS can lead to significant sequelae including acute kidney injury (AKI), arrhythmias, seizures, and sudden death. The mainstay of TLS management is aggressive intravenous (IV) hydration. However, the burden of fluid overload (FO) and AKI within this population is understudied. In this study, we aim to describe the incidence, severity and complications of FO and AKI among pediatric patients with TLS.

Objectives: In this study, we aim to describe the incidence, severity and complications of FO and AKI among pediatric patients with TLS.

Design/Method: Our retrospective single center cohort study involved pediatric patients aged 1-18 years with a new diagnosis of hematologic malignancy over a 10-year period including acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), Burkitt lymphoma and diffuse large B-cell lymphoma (DLBCL). Patients who met criteria for TLS were analyzed in two groups based on the severity of FO and AKI. Patients with severe AKI (≥ 2x increase in serum creatinine) were compared to those with no/mild AKI (< 2x increase in serum creatinine). Patients with severe FO (≥ 10%) were compared with those with mild/moderate FO (< 10%).

Charts were reviewed for complications associated with AKI and FO including hypoxemia, mechanical ventilation, hyponatremia, pulmonary edema, intensive care admission and need for renal replacement therapy (RRT).

Results: We identified 56 patients with TLS. We found severe FO occurred in 35.7% (n=20) and was more common in younger children (3.5 vs 6.5 years, p=0.004) with a primary diagnosis of Burkitt lymphoma (25% vs. 2.8%, p=0.01). PICU admission occurred in 35% of patients with severe FO compared to 8% in those with mild/moderate FO (p=0.013). Complications of hypoxemia (30% vs. 5.6%, p=0.012) and pulmonary edema (25% vs. 2.8%, p=0.01) were more common among those with severe FO. AKI occurred in 37.5% (n=21) patients and resulted in a significant increase in PICU admission and requirement for RRT (p=0.001 and p <0.001, respectively).

Conclusion: In one of the first pediatric studies analyzing the epidemiology of FO in TLS, we demonstrated a high burden of FO in our TLS patients. Our results show FO and AKI are common and often unrecognized complication of TLS associated with increased morbidity. Prospective, multi-center studies are needed to further dissect the burden of FO and AKI within this vulnerable population.

Poster # 59/Early Career Award Recipient

CHEMOTHERAPY-INDUCED SENSORY PERIPHERAL NEUROPATHY: THE ROLE OF PHOSPHOINOSITIDE 3-KINASE SIGNALING

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Background: Although therapeutic advancements have improved cancer-related outcomes, chemotherapy can be limited by toxicities that can be dose-limiting or prompt drug discontinuation, thereby impacting patients' quality of life and survival. Our work focuses on paclitaxel-induced sensory peripheral neuropathy (PIPN). Paclitaxel induces mitotic arrest by stabilizing microtubules and causes axonal degeneration, growth cone arrest, and retraction bulb formation. *In vitro* data suggests phosphoinositide 3-kinase (PI3K) signaling may be activated by paclitaxel and cause microtubule stabilization. "Hyper-stabilization" with loss of microtubule dynamic instability may contribute to PIPN.

Objectives: Characterize the involvement of PI3K in the stabilization of microtubules and axonal degeneration in paclitaxel-treated peripheral sensory neurons.

Design/Method: By utilizing human induced pluripotent stem cells differentiated into peripheral sensory neurons (iPSC-SNs), we intend to mimic human toxicity and extend genomic data to molecular mechanisms of PIPN. Cells treated with vehicle or paclitaxel with or without PI3K inhibitors are examined by immunofluorescence microscopy for growth cone and neurite morphological changes. Tubulin partitioning and Western blotting are performed to characterize

PI3K involvement in tubulin dynamics.

Results: iPSC-SNs treated for 48 and 72 hours with 1 µM paclitaxel demonstrated neurite network disruption and puncta formation. PI3K inhibitors (BKM-120, GDC-0941; 1 µM) attenuated this phenotype. Use of a PI3K activator (740-YP; 15 µM) alone consistently showed healthy neurite networks. However, cells treated with 740-YP and paclitaxel exhibited severe toxicity, highlighting a microenvironment-dependent PI3K response: PI3K promotes cell growth and proliferation but may have different effects in a toxic cellular environment induced by paclitaxel. Vehicle-treated iPSC-SNs revealed growth cones with extension of filopodia (filamentous actin staining). iPSC-SNs treated for 6 hours with 0.5 µM paclitaxel showed diminished filopodia extension and retraction bulb formation. BKM-120 (1 µM) added to paclitaxel improved this phenotype, revealing increased filopodia extending from growth cones. Tubulin partitioning to investigate the effects of PI3K on tubulin polymerization was unsuccessful and limited by our cell model. We will use reverse transcription-quantitative polymerase chain reaction to characterize PI3K involvement in tubulin stabilization by measuring tubulin unspliced pre-mRNA and spliced mRNA in cells treated with paclitaxel and PI3K inhibitors.

Conclusion: Based on our preliminary data, PI3K may be involved in PIPN. As other studies suggest, PIPN-related findings might extend to vinca alkaloids: microtubule stabilizers and destabilizers cause mitotic arrest with common downstream effects on gene expression and effector molecules. Future experiments and validation of preliminary data are necessary. Ultimately, identifying targetable pathways will promote therapeutic and preventive neuroprotective strategies and improve clinical outcomes.

Poster # 60

THERAPEUTIC PLASMA EXCHANGE IN CRITICALLY ILL PEDIATRIC PATIENTS WITH LEUKEMIA

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Background: Therapeutic plasma exchange (TPE) has well-documented applications in the adult population, outlined by the American Society of Apheresis (ASFA) 2019 guidelines. Limited data exists regarding the use of TPE in critically ill pediatric patients, however these reports rarely include patients with oncological diseases. Care for these patients poses certain clinical considerations including the safety of continuing chemotherapy, delayed clearance of chemotherapy secondary to end organ damage and mechanical clearance (i.e., continuous renal replacement therapy (CRRT) circuitry), and ability to tolerate chemotherapy once recovered. We aim to highlight the potential benefits of TPE in their acute management, so that it may be recognized as an earlier treatment modality.

Objectives: To describe the role of apheresis in pediatric patients with hematological malignancies.

Design/Method: Records for 7 pediatric patients with leukemia (0-18 years) who received TPE in Children's Mercy ICU from 2015-2020 were retrospectively reviewed. Data collected included demographics (including treatment protocol/cycle of treatment), TPE specifications (treatment indication, number of treatments, baseline and interval laboratory evaluation, procedure related complications), duration of time in the ICU, and outcome measures (mortality and ability to resume oncological treatment). Descriptive and survival analyses were performed.

Results: Our population (mean age 7.43 years, 57.1% female) consisted of 4 patients requiring extracorporeal membrane oxygenation (ECMO) and 6 requiring CRRT. Multi-organ failure (MOF) prompted the initiation of TPE in 85.7% of patients, 42.9% of whom were also diagnosed with hemophagocytic lymphohistiocytosis (HLH). Mean days in the ICU until apheresis initiation was 12.43 (range 1-68 days), not statistically different between those who did (n=4) and did not (n=3) survive 30 days post-TPE. While baseline laboratory evaluation noted similar creatinine, bilirubin, and CRP between the groups, survival analysis noted elevated liver enzymes in those who did not survive 30 days post-apheresis. Analysis of interval labs shows a statistically significant improvement in CRP and lactic acid in those who survived versus did not. Procedure-associated complications included circuit clotting, hypotension, and hypocalcemia; however, apheresis discontinuation was not required in any cases. All living patients were able to continue chemotherapy treatment, however 2 required protocol adjustments for residual decreased organ function.

Conclusion: Our cohort demonstrated MOF and HLH consistently as indications for TPE, currently AFSA category III indications (optimal role of apheresis is not yet established). Recognition of this treatment modality earlier in the clinical course for critically ill oncological patients may lead to improved outcomes, and a larger cohort study is needed to evaluate this further.

Poster # 61

IMPROVING POST-TREATMENT CARDIOTOXICITY SCREENING IN THE PEDIATRIC HEMATOLOGY/ONCOLOGY CLINIC

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Background: Anthracyclines are key components of many chemotherapy regimens for treating pediatric cancer. However, adverse effects of anthracycline use include cardiotoxicity. In version 5.0 of the Children's Oncology Group (COG) Long-Term Follow-Up Guidelines, recommendations for screening cancer survivors for anthracycline-induced cardiotoxicity were updated with changes to the screening frequency, dose exposure, and inclusion of electrocardiogram. Our team recognized an opportunity to improve adherence to the updated guidelines.

Objectives: Using quality improvement methods, we aim to increase the rate of timely and appropriate off-therapy cardiotoxicity screening for pediatric cancer patients from a baseline of 26% to greater than 90%.

Design/Method: At our institution, care for pediatric cancer survivors is shared between the acute pediatric oncology clinic and a dedicated survivorship clinic. Our population includes off-therapy patients (within the prior three years) with anthracycline exposure. We define appropriate initial post-treatment cardiotoxicity screening as an echocardiogram and electrocardiogram for any anthracycline exposure. For patients with history of mediastinal radiation exposure or >250 mg/m^2 cumulative dose of anthracycline, referral to cardio-oncology clinic is standard of care. Using a survivorship database and the electronic health record, upcoming visits for eligible patients are identified and reminders are sent to the provider about cardiotoxicity screening. After review of the current process, opportunities for improvement were identified. Working with the cardiology team, we have made significant revisions to the prior cardiotoxicity screening protocol and shared with faculty and staff. Chart reviews are performed weekly. A run chart is used to measure the proportion of eligible patients who have received the recommended screening.

Results: We identified 144 eligible patients who completed treatment between 1/19/2017 and 10/1/2020. With the addition of the email reminders, the percentage of patients who have received appropriate cardiotoxicity screening has increased from a baseline of 26% in May 2020 to 33% in September 2020. After the revised protocol was presented at a division meeting, the rate increased to 41% by November 2020.

Conclusion: The updates to the protocol, education, and email reminders have increased providers' awareness of patients eligible for post-treatment cardiotoxicity screening which led to improvement in overall compliance with screening recommendations. With knowledge that education and email reminders are not sustainable, we are also building an alert in the electronic health record as a person-independent post-treatment screening reminder for the eligible population. Repeat process evaluation and plan-do-study-act cycles are ongoing to help meet our goal for adherence to the guidelines.

Poster # 62

VINCRISTINE-INDUCED PERIPHERAL NEUROPATHY IN CHILDREN WITH CANCER: A REPORT FROM ARMENIA

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Background: Vincristine belongs to vinca alkaloids and is a cornerstone in the management of many types of childhood cancer and some non-malignant blood conditions. Vincristine has a wide range of side effects and one of them is peripheral neurotoxicity. Vincristine-induced peripheral neuropathy (VIPN) is characterized by serious sensorimotor peripheral neural

deficiency in children who received vincristine. The incidence of reported vincristine-induced neuropathy ranges from 1 to 35%. The reports from developing countries about the incidence, severity and management of VIPN is very limited.

Objectives: The aim of our study is to determine the incidence and severity of VIPN among children with solid tumors and lymphomas receiving treatment at the department of pediatric oncology of the Pediatric Cancer and Blood Disorders Center of Armenia (PCBDCA), Hematology Center after R. Yeolyan between February 2019 and July 2020. PCBDCA is the only institution in Armenia treating children with cancer and blood disorders.

Design/Method: Retrospectively the data of 97 unselected patients were collected and analyzed, of whom 36 (37.1%) were female, age range was 1-17 years, median age was 10.4 years. From the entire group, 61 (62.89%) patients received vincristine, from which 19 (31.14%) were patients with lymphoma, 11(18.0%) with neuroblastoma, 6 (9.83%) with rhabdomyosarcoma, 6 (9.83%) with medulloblastoma, 5 (8.2%) with Wilms tumor and 14 (22.9%) with other tumors. The severity was evaluated based on the scale of the World health Organization (WHO) Common Toxicity Criteria for Peripheral Neuropathy.

Results: VIPN was reported in 6 (9.84%) patients from which 3 (50%) were in patients with lymphoma, 2 (33.3%) with rhabdomyosarcoma and 1(16.7%) with neuroblastoma. The four (66.7%) patients developed grade 3 peripheral neuropathy and received gabapentin, which was effective in all patients. None of the patients required treatment adjustment.

Conclusion: As the cohort was retrospective there were distinctly unreported cases of neuropathy, which makes it difficult to evaluate the whole spectrum of the problem. Our data showed that VIPN was seen only in around 10% patients, and from them half of the cases were in patients with lymphoma. Although the study cohort was small, it showed that the incidence of VIPN reported at our clinic corresponds to the range reported in literature.

Poster # 63/Early Career Award Recipient

HIGH-THROUGHPUT SMALL MOLECULE SCREENING TO IDENTIFY NEW TREATMENTS FOR PLEUROPULMONARY BLASTOMA

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Background: Pleuropulmonary Blastoma (PPB) is the most common primary pediatric lung malignancy and hallmark cancer of *DICER1* Syndrome, a cancer predisposition syndrome driven by microRNA dysregulation. Standard treatment for Type II and Type III PPB utilizes a combination of surgery, radiation, and a standard sarcoma chemotherapy regimen that is non-specific to the underlying microRNA dysregulation. Outcomes for Type II and Type III, particularly in cases of metastasis or recurrence, continue to be dismal and represent a need for new treatment strategies. High-throughput drug screens can efficiently identify compounds that are highly effective in treating in vitro tumor models for further testing in vivo prior to human

clinical trials and are of particular importance in rare neoplasms such as PPB.

Objectives: To identify new treatment options for PPB using a high-throughput drug screen of drugs that are FDA approved or in clinical trials.

Design/Method: Patient derived xenograft cell lines of PPB were optimized for growth in 384-well plates. Drugs that were FDA approved or in clinical trials were added to the cells and cell viability was measured at 96 hours via cell-titer glow with dimethyl sulfoxide and brefeldin A as the negative and positive controls, respectively. We used a step-wise approach to narrow the drugs down from 2736 compounds to a top three best performing drugs to proceed with in vivo and mechanistic testing. We identified the best performing drugs at each step based on toxicity level, minimizing the number of drugs from a single drug class, and prioritizing drugs with clinical experience and safety data for ease of future in vivo testing and incorporation into clinical trials.

Results: 2736 compounds were added at a single dose to a PPB cell line. The top 60 performing drugs were then added in triplicate at three doses to two PPB cell lines. The top ten performing drugs were then added in triplicate at 12 doses to the PPB cell lines as well as two control cell lines for comparison of maximal effect and IC50 doses. The top 3 drugs were identified as triptolide, dinaciclib, and flavopiridol.

Conclusion: Using a stepwise in vitro approach based on cell viability assays and clinical experience, 2736 compounds were narrowed down to the three top performing drugs against Pleuropulmonary Blastoma, triptolide, dinaciclib, and flavopiridol. All three drugs are involved in inhibition of RNA transcription and represent a possible therapeutic vulnerability in Pleuropulmonary Blastoma. Further in vivo and mechanistic studies are ongoing.

Poster # 64

PRECISION NANOMEDICINE: A NOVEL THERAPEUTIC APPROACH FOR PEDIATRIC LEUKEMIA

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Background: Overall survival rates in pediatric leukemia have been dramatically improved through the use of intensive, high dose, multi-agent combination chemotherapy; however, outcomes remain poor in certain high-risk subsets, including early T-precursor acute lymphoblastic leukemia (ETP-ALL), infant ALL and acute myeloid leukemia (AML). Additionally, patients in high-risk subsets are exposed to more toxic therapy and have a high prevalence of late effects. Therefore, novel therapeutic approaches are needed for these patients.

Objectives: To address this challenge, our research utilizes a novel high-throughput drug screening and formulation method that exploits synergy between small molecule inhibitors of the receptor tyrosine kinases MER (MERTK) and FLT3 and the anti-apoptotic protein BCL-2 in

AML, infant ALL and ETP-ALL models. Our overall aim is to develop a clinically translatable nanoscale combination therapy that improves the therapeutic index via synergistic drug encapsulation. We hypothesize that conditionally synergistic co-delivery of molecularly targeted therapies, utilizing a dual MERTK/FLT3 inhibitor and BCL-2 inhibitors, will improve the growth inhibition (GI) of pediatric AML, ETP-ALL, and infant ALL cells in vitro.

Design/Method: We will utilize a high-throughput screening strategy to identify optimal ratiometric dosing for pairwise drug combinations targeting MERTK/FLT3 and BCL-2 across twelve different leukemia cell lines to provide the comprehensive concentration- and ratiometric-dependent resolution needed to nominate synergistic drug combinations. In addition, we will look for transcriptomic correlates at hot spots of conserved drug synergy to understand the biological molecular mechanisms of drug synergy identified via this screening. We will develop methods to encapsulate nominated synergistic drug combinations in nanoparticle liposomes and optimize drug loading conditions to enable co-delivery of synergistic ratios. We will engineer liposomes using sonication of rehydrated lipid foam filled by high pressure extrusion to make unilamellar vesicles. Nominated synergistic combinations of drug will be loaded by passive rehydration and chemical buffer gradient. We will investigate the maintenance of drug ratios of nanoparticles in storage and following cell delivery via LC-MS and characterize the degree of cytotoxicity mediated by ratiometric drug formulations.

Results: High throughput screening studies are complete and results demonstrate synergy between MERTK/FLT3 and BCL-2 inhibitors in cell line models. We have successfully identified a ratio that is both effective (high GI) and synergistic and are engineering methods for co-delivery by encapsulation in liposomal nanocarriers.

Conclusion: High throughput screens demonstrate synergy between small molecule inhibitors of MERTK/FLT3 and BCL-2 that is conserved across cell lineages for AML, infant ALL and ETP-ALL.

Poster # 65

GENOMIC COMPARATIVE ANALYSIS OF HIGH RISK NEUROBLASTOMA AT DIAGNOSIS AND RELAPSE

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Background: Genomic alterations such as MYCN amplification and ALK mutations have shown to be important in the prognosis and treatment of neuroblastoma (NB) Further genomic understanding for therapeutic targets is needed.

Objectives: Compare genomic analysis of high-risk NB at diagnosis and at relapse. Develop an understanding of MYCN-driver status to provide better prognostic biomarkers. Characterize differences in DNA and transcriptomes and evaluation of novel subgroups by looking at the

association between somatic genetic changes and expression reflecting cancer driver pathway activation.

Design/Method: Genomic Analysis was performed on patients enrolled on Beat Childhood Cancer Research Consortium Precision Medicine trials at both diagnosis and relapse. Whole-exome sequencing (WES) and RNA-Seq were performed and were compared to a normal whole-body reference and a pediatric cancer reference. Differential expression data was interpreted in the context of systems biology.

Results: Tumor WES was performed on 128 patients (81 diagnosis, 47 relapse). RNA-Seq was performed on 127 patients (69 diagnosis, 58 relapse). DNA analysis exhibited fewer mutations in primary diagnosis compared to relapse (median 53[26-78] coding mutations per subject to 164[28-5000]). Most common mutations or copy number alterations (diagnosis, relapse) were seen in MYCN (30%,34%), ATRX (7%,30%), ALK (17%,11%), CDKN2A (0%,13%), PPM1D (0%,15%). RNA expression analysis was performed evaluating MYCN-driver status and to identify subsets of patients with high/low expression of genes in diagnosis versus relapse. Overexpression and positive correlation of TRIM71 with LIN28B and MYCN was seen in MYCN amplified tumors, with the opposite in non-amplified tumors. Investigation of Chr17q proximal gene IGF2BP1 and its implication in mediating the effect of Chr 17 gain and in cancer driver pathway activation was performed. IGF2BP1 has a positive correlation with MYCN and LIN28B genes in MYCN amplified, non-amplified and chr17q gain tumors but differed in diagnosis and relapses tumors. SSX1 and SSX2 genes were overexpressed in relapse (43%, 34%) and mutually exclusive when compared to diagnosis (20%,14%). We identified two expression subtypes within MYCN amplified tumors. The first was characterized by low SSX1, SSX2/high MYCN expression (SSX1/SSX2 was low in 95% of MYCN amplified tumors vs 56% of MYCN negative tumors). The second was characterized by high HOXD13/high MYCN expression (HOXD13 was overexpressed in 65% of MYCN amplified tumors vs 28% MYCN non-amplified tumors).

Conclusion: Genomic sequencing for precision therapy was feasible both at diagnosis and relapse and identified genomic differences. Genomic analysis may identify novel treaments and subtypes which may be used to stratify patients and develop further understanding of relapse.

Poster # 66

GENOMIC ANALYSIS AND PRECISION THERAPY FOR RECURRENT AND RESISTANT SARCOMA

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Background: Sarcomas account for less than 5% of all childhood cancer but are the second most common group of malignant solid tumors. Despite improvements, approximately 30% of patients with non-metastatic sarcoma have refractory or recurrent disease after therapy; 10-20%

of patients with metastatic disease at presentation have a survival of < 20%, and <10% of patients with residual/recurrent tumor are curable with current therapy, underscoring the need for new approaches to treatment.

Objectives: To identify, via Whole Exome Sequencing (WES) and RNA Sequencing (RNA-Seq), rare variants and novel biomarkers in sarcomas predictive of potential response to conventional and targeted agents.

Design/Method: Patients were enrolled on NMTRC008/009: "Feasibility Trial Using Molecular Guided Therapy for Patients with Relapsed/Refractory Childhood Cancer". WES and RNA-Seq were performed at the Translational Genomics Research Institute. RNA expression levels were compared to a normal whole-body reference and a pediatric cancer reference. Differential expression data were interpreted in the context of systems biology.

Results: Tumor WES was performed on 71 patients (18 rhabdomyosarcoma (RMS), 18 Ewing Sarcoma (ES), 15 osteosarcoma (OS), 5 undifferentiated sarcoma (US), 5 Desmoplastic Small Round Cell Tumor (DSRCT), and 10 other sarcomas), and RNA -Seq on 61 patients (17 RMS, 13 ES, 13 OS, 5 US, 4 DSRCT, 9 other sarcomas). The median tumor mutation burden was 1.2 mutations per Mb (range: 0.02 – 5.8). Genomic analysis identified 67% (n=12/18) of ES with *EWSR1-FLI1* fusion and one ES with EWSR*1-ERG* fusion; 100% (n=5/5) of DSRCT with *EWSR1-WT1* fusion; 33% (6/18) of RMS with *PAX3-FOXO1* fusion; 67% (n=2/3) of synovial sarcomas with *SS18-SSX2* fusion; and one US with *SUZ12-DNAH2* fusion. *TP53* was the most frequently altered gene, with mutations or deletions detected in ES, OS, RMS and other sarcomas. *MYC* amplifications were seen predominantly in OS, and *RB1* deletions were seen in OS, RMS, ES, DSRCT. Gains of 5p and 8q (containing *TERT* and *MYC*) showed enrichment in OS, ES, DSRCT, RMS, and other sarcomas. Other large-scale chromosome events included 10p, 10q, 17p, and Yp loss. *TP53* mutations were enriched in tumors with 17p deletion, suggesting biallelic inactivation of *TP53*. We identified 78 cosmic genes that were variably expressed across tumors; in particular, *HOXD13, SSX2, HMGA2, TERT* were highly overexpressed in 40% of tumors.

Conclusion: Genomic sequencing of refractory/relapsed sarcomas showed a low mutation burden. RNA analysis resulted in identification of potential novel therapeutic targets. Further analysis of patient molecular subgroups and therapeutic strategies is ongoing.

Poster # 67

NOVEL MUTATIONS AND ROLE OF MOLECULARLY TARGETED THERAPY IN PEDIATRIC SPINDLE CELL RHABDOMYOSARCOMA

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Background: Spindle cell rhabdomyosarcoma (SCRMS), a rare and aggressive subtype of rhabdomyosarcoma, results in poor outcomes due to a lack of effective response to standard

treatments. There is a critical need to understand tumor biology and identify molecularly targetable treatments. Previous studies uncovered distinctive somatic aberrations in MYOD1 and PIK3CA. Genomic sequencing of a SCRMS cell line, OHSU-SARC001, derived from a patient treated at our institution revealed uncharacterized GNAS$^{p.R201C}$ and novel PIK3CA$^{p.I459_T462del}$ mutations allowing for opportunities to investigate their oncogenic role in SCRMS and targetable treatments. The role of GNAS activation of the MEK/ERK pathway in SCRMS is unknown.

Objectives: The objectives are to elucidate the role of novel PI3KCA and GNAS mutations in oncogenesis and investigate the efficacy of targeted inhibitors based on molecular aberrations in the tumor (including LY3023414, a compound identified by the COG MATCH trial).

Design/Method: Activity of the novel GNAS and PIK3CA mutations was assessed by utilizing OHSU-SARC001 (a validated patient-derived cell line) and gain of function heterologous model cell systems. Biochemical techniques were used to characterize effects of the novel GNAS and PIK3CA mutations on the AKT/mTOR and MEK /ERK signaling pathways as well as after OHSU-SARC001 drug treatments. Single agent and combination treatments with dual mTOR/PIK3CA, PIK3CA, mTOR, MEK, AKT inhibitors, and chemotherapeutic agents were conducted on OHSU-SARC001.

Results: No differences in AKT/mTOR and MEK/ERK activation were observed in cells expressing GNAS and PIK3CA mutants, respectively, as compared to wildtype proteins. Cell viability studies revealed that targeting PI3K/mTOR or RAS/MAPK pathways with a single agent approach was ineffective despite these inhibitors having on-target effects on cognate signaling proteins as determined by immunoblotting with phospho-specific antibodies. Combination treatment of OHSU-SARC001 cells that included concurrent inhibition of mTOR/PIK3CA with LY3023414 and doxorubicin or mTOR inhibition with rapamycin combined with vincristine exhibited some functional synergy.

Conclusion: The novel PIK3CA $^{p.I459\_T462del}$ mutation is not a catalytically activating mutation, and the GNAS$^{p.R201C}$ mutation does not activate the MAPK pathway in murine myoblast lineage cells. While LY3023414 and rapamycin biochemically inhibited the PI3K/AKT pathway significantly, single drug agents did not result in cell death. However, combination therapy involving LY3023414 with doxorubicin and rapamycin with vincristine showed synergistic effect. Our results demonstrate the importance of utilizing a preclinical patient-derived model to assess efficacy of molecularly targetable treatments to better understand future treatment options with the potential to translate findings back to the bedside.

Poster # 68

NOVEL BIOMARKER DISCOVERY FOR CHILDHOOD RHABDOMYOSARCOMA USING URINARY METABOLITES

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Background: Metabolic reprogramming is a hallmark of tumor cells in which the tumor cells change their metabolic phenotypes to promote their proliferation and progression. Metabolomics analysis can be used to develop diagnostic and therapeutic strategies targeting pathways of energy metabolism in tumor cells. Childhood rhabdomyosarcoma is rare and difficult to treat; therefore, novel biomarker discovery and therapeutic strategy development are expected through metabolomics analysis.

Objectives: The aim of this study was to identify biomarkers for childhood rhabdomyosarcoma by comprehensively analyzing urinary metabolites from pediatric patients with or without rhabdomyosarcoma.

Design/Method: This study was conducted at Nagoya University Hospital, Nagoya, Aichi, Japan. Urine samples were collected from 15 pediatric patients with rhabdomyosarcoma and 39 pediatric patients without rhabdomyosarcoma. Urine metabolites were extracted using liquid chromatography/mass spectrometry (LC/MS) or capillary electrophoresis mass spectrometry (CE/MS). Biomarker candidates were identified using the Wilcoxon rank-sum test, random forest method, and orthogonal partial least squares discriminant analysis between patients with and those without rhabdomyosarcoma.

Results: Approximately 2000 metabolites, such as amino acids, nucleic acids, and lipids, were detected in one urine sample. Ten urine metabolites were significantly increased in patients with rhabdomyosarcoma compared to those in patients without rhabdomyosarcoma. In this study, we developed an AI technology that efficiently searched for urine tumor markers based on the detailed medical information of each urine sample and used them to construct cancer test models.

Conclusion: Through metabolomic analysis of urine metabolites in pediatric patients with and without rhabdomyosarcoma, we identified ten urine tumor marker candidates for childhood rhabdomyosarcoma. In the future, in addition to urine samples, we plan to conduct a comprehensive analysis (LC/MS, CE/MS) of the metabolites in blood and sarcoma tissue samples. We will identify the metabolic pathways of the 10 metabolites found in this study and detect the metabolic pathways specific to childhood rhabdomyosarcoma in order to investigate whether they can be disease-specific biomarkers or therapeutic targets.

Poster # 69

ANALYSIS OF CANCER PREDISPOSITION SURVEYS IN SURVIVORS OF PEDIATRIC CANCER USING MIPOGG ALGORITHMS

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Background: Studies show that about 10% of children and adolescents with cancer carry germline variants that can be classified as cancer predisposition syndromes (CPSs), but many go undiagnosed. As subsequent malignant neoplasms are a major cause of morbidity and mortality in survivors of pediatric cancer, identifying CPSs in this population is especially important. We conducted a study to compare our practice's referral patterns for genetic counseling for CPSs to MIPOGG (McGill Interactive Pediatric OncoGenetic Guidelines) algorithms' recommendations.

Objectives: To retrospectively apply decision-making algorithms to survivors of pediatric cancer and analyze differences in algorithm-recommended and provider-recommended screening for CPSs.

Design/Method: Patients in a pediatric cancer survivorship clinic were given a family cancer history survey. MIPOGG algorithms for genetic referral for CPSs, which include universal criteria (criteria that are identical for all tumor types) and tumor-specific criteria, were applied to the patients' family history surveys and medical histories retrospectively. Application of the MIPOGG algorithms generated a binary recommendation, either for or against a genetics referral for CPS evaluation. The universal criteria alone recommendations and full MIPOGG recommendations were compared to whether the patients were actually referred to genetics for a CPS evaluation using chi-squared analysis.

Results: One hundred and fifty-nine patients completed the surveys. Thirteen patients had been referred to genetics by their treating physicians based on their clinical judgment for CPS evaluation. Six of these were diagnosed during cancer treatment with a CPS (Li-Fraumeni Syndrome n=2, Beckwith-Wiedemann Syndrome n=2, Constitutional Mismatch Repair Deficiency n=1, pathogenic *RB1* mutation n=1). Four of the thirteen patients were negative upon testing for CPSs. Three patients were referred to genetic counseling but did not receive testing. Applying the MIPOGG universal criteria alone to each patient yielded 22 recommendations for a genetics referral to evaluate for CPSs, which was not statistically different from clinical practice ($p > 0.05$). Applying the MIPOGG tumor-specific and universal criteria together resulted in 52 recommendations for genetics referrals, which was statistically higher than clinical practice ($p<0.001$), All thirteen clinically referred patients would have also been identified by MIPOGG (9 by universal criteria, 4 by tumor-specific criteria). These results suggest that there are patients whose underlying risk for CPS was underestimated when applying only the universal criteria or the routine clinical judgment of the treating oncologist.

Conclusion: MIPOGG algorithms can potentially identify patients who could benefit from genetic counseling for genetic cancer predispositions. Further prospective studies to validate the predictive value of MIPOGG are needed.

Poster # 70

SURGICAL AND MEDICATION TREATMENT AMONG PATIENTS WITH PIK3CA-RELATED OVERGROWTH SPECTRUM

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Background: PIK3CA-related overgrowth spectrum (PROS) is an umbrella term used to describe a group of rare disorders characterized by abnormal growth of various parts of the body, due to somatic mutations in the PIK3CA gene. There is a significant gap in literature to describe the overall population of PROS patients in terms of comorbid conditions, associated complications, and real-world health care utilization and treatment patterns.

Objectives: This study described surgical interventions and medication treatment among patients diagosed with PROS related conditions identified in electronic health records (EHR) data.

Design/Method: This retrospective real-world descriptive observational study identified patients with a presumptive diagnosis of PROS (all ages) from the Optum EHR database using key PROS-related clinical terms found in provider notes between 1/1/2007-12/31/2019. The first date observed with the PROS-related term was the index date. Patients were further categorized into PROS-specific (PS) and PROS-non specific (PNS) cohorts based on the presence of clinical terms unique to PROS (e.g. CLOVES) or less specific terms (e.g. Klippel-Trenaunay). Patients needed to have EHR records starting at least 1 month prior to and at least 3 months following the index date. Evidence of surgeries (orthopedic, debulking, and/or neurosurgery) were described during the baseline and follow-up time periods. Use of medications (anti-seizure, pain, mTOR inhibitors, and AKT inhibitors) were also described for the two cohorts in the follow-up period.

Results: A total of 657 PROS patients were identified [PS (n=120) and PNS (n=537)]. Total mean observation time was 86 months, with follow-up contributing nearly half (39.7 months). Mean age was 28.8 years (SD: 22.3), 39.7% (n=261) of the patients were <18 years, and 60% (n=394) were female. For the entire study period (baseline and follow-up), approximately half (43.5%; n=286) of the overall study patients had a surgical procedure [PS: (61 patients (50.8%); PNS: 225 patients (41.9%)], while 13.6% (n=89) of the study patients showed evidence of mutiple types of surgical interventions [PS: 20 patients (16.7%); PNS: 69 patients (12.9%)]. During the follow-up period, nearly half (40.0%, n= 263) [PS: 51.7%; PNS: 37.4%] of all study patients used anti-seizure and pain medications (62.9%; n=413) [PS: 68.3%; PNS: 61.6%].

Conclusion: This retrospective observational study demonstrated a clinical burden, in terms of the number of surgeries and use of medications, amongst the patients with a presumptive PROS diagnosis identified in an EHR database.

Poster # 71

LEVOFLOXACIN VERSUS CIPROFLOXACIN PROPHYLAXIS IN PEDIATRIC CANCER PATIENTS AT HIGH RISK OF INFECTION

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Background: Patients with cancer and those undergoing chemotherapy are at risk of developing bacterial infections due to myelosuppression. Patients undergoing the most intensive chemotherapy regimens are at a higher risk for morbidity and mortality due to profound neutropenia. Antibacterial prophylaxis is given to reduce the incidence of infection in those at highest risk. Starting March 1, 2016 our institution used ciprofloxacin for antibacterial prophylaxis however recent literature, including the COG trial ACCL0934, supports using levofloxacin in certain high risk (HR) populations due to greater efficacy in reducing neutropenic fever (NF) and bacteremia. Therefore, we switched to this April 1, 2019 and used this change in our standard of care (SOC) as an opportunity to evaluate instances of NF and bacteremia between the two fluoroquinolones.

Objectives: To determine if there is a significant difference in the incidence of NF and bacteremia in patients with malignancies at HR for infection [defined as acute myeloid leukemia (AML), relapsed acute lymphoblastic leukemia/lymphoma (ALL), infant ALL, Down Syndrome ALL, Burkitt lymphoma, and those who have undergone autologous or allogenic HSCT] in those who have received levofloxacin compared to ciprofloxacin prophylaxis.

Design/Method: This is a retrospective chart review study of patients at HR for infection and who received bacterial prophylaxis with levofloxacin and/or ciprofloxacin. We reviewed charts individually and collected data including patient demographics, details regarding antimicrobial prophylaxis and the incidence of NF and bacteremia.

Results: A total of 132 patients were included. Median age was 6 years, 58% were male, and 62% were white. There were 85 patients who received ciprofloxacin encompassing 13 months prior to the switch in SOC and 47 patients who received levofloxacin in the 15 months after SOC change. Observation periods were equivalent for both groups (p=0.47). Patients were found to have 1+ instances of NF in 82.4% of those who received ciprofloxacin and 68.1% of those who received levofloxacin (p=0.06). Additionally, 42.4% of patients who received ciprofloxacin experienced bacteremia whereas this occurred in 29.8% of patients who received levofloxacin (p=0.15). There was also a significant reduction in median number of NF episodes in the levofloxacin recipients (p=0.04). The impact on PICU and hospital utilization, treated related mortality, or potential rises in fungal or Clostridioides difficile infections is also reviewed.

Conclusion: Our data shows that the use of levofloxacin more effectively prevented neutropenic fever and bacteremia than ciprofloxacin in children with high-risk malignancies.

Poster # 72

PROPHYLACTIC PLATELET TRANSFUSION PRACTICES FOR BRAIN TUMORS PATIENTS- SURVEY OF PEDIATRIC EXPERTS

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Background: Thrombocytopenia is a risk factor for bleeding in patients with brain tumors. The Canadian[17] council recommends prophylactic platelet transfusion for brain tumors patients undergoing chemotherapy and radiation therapy at platelet count <30,000/cumm, however no such guidelines exist in United States (US) and practices vary within and amongst institutions.

Objectives: To understand clinical practices, attitudes and experiences of pediatric hematologists/oncologists regarding platelet transfusions for patients with brain tumors undergoing treatment.

Design/Method: This study was approved by the Institutional Review Board of the Wayne State University (WSU). Questions were developed in Survey Monkey®, pretested and sent via an online link to pediatric hematologist oncologists at teaching/academic US centers and to the members of the Hemostasis Thrombosis Research Society. Results are reported as descriptive statistics.

Results: One-hundred-fourty-two eligible clinicians responded to the survey with a completion rate of 72% (102/142). Sixty-four (63%) participants were female, and majority (96%) worked in academic centers. The median clinical experience of participants was 10-14 years. Seventy-four (73%) participants agreed that platelet transfusion guidelines are needed. Ninety-seven (74%) participants had institutional criteria for platelet transfusion with cutoffs varying from <50,000/cumm to <10,000/cumm with median of <30,000/cumm. Twenty-four (20%) participants reported 66 episdoses of intracranial bleeding (ICH) but only 10 participants provided additional details about the bleeding episodes. As per the respondents' experience, ICH was associated with high grade glioma 7 (32%), medulloblastoma 5 (23%), low grade glioma 5 (23%), germ cell tumor 1 (4.5%) and choroid plexus tumor (4.5%). Platelet count at the time of bleeding was reported to be > 50,000/cumm in 5 patients (23%), ranging between <10,000-50,000. PT/PTT and fibrinogen levels were reported as normal in 5 patients. Twelve patients had residual disease at the time of bleeding (55%), and the location of bleeding was within the resection cavity for 9 patients (41%).

Conclusion: Our results demonstrate that in the US, there is considerable variation in platelet transfusion thresholds for pediatric brain tumors patients undergoing therapy. Moreover, there is a strong desire among the experts for evidence-based guidelines. Respondents also reported ICH with platelet counts >50,000/cumm indicating that platelet count alone may not be predictive of bleeding risk. Further investigations including the use of global assays need to be evaluated.

Poster # 73

CHARACTERIZING PROTEINS THAT MEDIATE CALM-AF10 LEUKEMOGENESIS

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Background: *CALM-AF10* leukemias, which account for ~10% of childhood T-cell acute lymphoblastic leukemia (T-ALL) and a subset of acute myeloid leukemia (AML), have a poor prognosis. These leukemias exhibit increased *HOXA* gene expression, which is dependent on the interaction between CALM-AF10 and the CRM1/XPO1 nuclear export receptor: interruption of the CALM/CRM1 interaction abrogates both *HOXA* gene activation and leukemogenesis. However, since neither CALM-AF10 nor CRM1 contains a recognized DNA binding domain, the mechanism by which CRM1 interacts with *HOXA* genes is not currently understood. We utilized a biotin ligase (BioID2) proximity based-labeling approach to detect candidate CALM-AF10-interacting proteins that could potentially mediate binding to *HOXA* genes.

Objectives: Identify candidate proteins that interact with the CALM-AF10/CRM1 protein complex

Design/Method: We prepared a *BioID2-CALM-AF10* expression plasmid and determined that it transcriptionally activates *HOXA* genes and promotes leukemogenesis, similar to *CALM-AF10*. Human Embryonic Kidney 293 (HEK293) cells were transiently transfected with *BioID2-CALM-AF10* and grown in the presence or absence of biotin, and mass spectrometry (MS) identified candidate interacting proteins. Initial validation of candidate proteins was confirmed via co-immunoprecipitation (co-IP) in HEK293 cells transiently transfected with *CALM-AF10*.

Results: Three independent transfections/MS experiments identified 12 biotin-labeled proteins that interact with CALM-AF10. Importantly, these include two proteins that validate our approach: **DOT1L**, a protein known to interact with AF10, and **NUP214**, a nuclear pore protein with a potential role in *CALM-AF10* leukemias. Among the remaining ten proteins, we identified epidermal growth factor receptor substrate 15 (**EPS15**), a known CRM1 interacting protein that is also involved in *KMT2A* translocations, and Cortactin (**CTTN**), a protein that is overexpressed in adult CLL and pediatric B-ALL. Triplicate Co-IP studies showed that EPS15 and CTTN directly interact with CALM-AF10. In addition, we identified several other candidate proteins that potentially interact with CALM-AF10, including **DDX3X**, **DVL2**, and **DVL3** – each of which plays a role in oncogenesis. CoIP studies are underway to investigate direct interactions of these proteins with CALM-AF10.

Conclusion: Proximity-based labeling using biotin ligase is a novel approach for identifying proteins that interact with CALM-AF10. Among the candidates we identified, EPS15 and CTTN are known to bind to CRM1 and are involved in signal transduction and transcriptional regulation. Our demonstration that they also directly interact with CALM-AF10 suggests a potential role in *CALM-AF10* leukemogenesis. EPS15 and CTTN knockdown studies in *CALM-AF10* leukemia cells are currently underway to evaluate effects on leukemogenesis and gene expression.

Poster # 74

POPULATION-BASED LATE EFFECTS IN CHILDHOOD ACUTE LEUKEMIA SURVIVORS WITH DOWN SYNDROME

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Background: The risks of late effects of therapy among childhood cancer survivors have been well characterized. Whether these risks are equivalent in survivors with Down syndrome (DS) is unknown.

Objectives: To compare mortality and morbidity outcomes between childhood leukemia survivors with DS and control cohorts of DS patients without childhood cancer and non-DS leukemia survivors by linking population-based clinical and health services data.

Design/Method: We identified all 5-year survivors of childhood leukemia diagnosed in Ontario, Canada between 1987-2013. Survivors were divided into those with and without DS (DS survivors and non-DS survivors). DS survivors were matched by birth year and sex to individuals with DS but no history of childhood cancer (DS controls) in a 1:10 ratio. Demographic, disease, and treatment details were obtained through a provincial registry. Linkage to population-based health services data identified specific morbidity and mortality outcomes [overall survival (OS), chronic heart failure (CHF), subsequent malignant neoplasm (SMN), cataracts, dementia] using validated algorithms. Starting at the index date of 5-year survival, we compared outcomes between the cohorts.

Results: We identified 86 DS survivors, 2,229 non-DS survivors, and 860 DS controls. DS survivors experienced inferior overall survival (OS) compared to both non-DS survivors (20-year from index date OS ± standard error 84.5%±5.6% vs. 97.4%±0.4%; $p<0.0001$) and to DS controls (96.2%±1.0%; $p=0.0001$). When adjusted for covariates, the increased hazard of death was maintained compared to both non-DS survivors [adjusted hazard ratio (aHR) 7.8, 95% confidence intervals (95CI) 3.3-16.1; $p<0.0001$] and DS controls (aHR 4.4, 95CI 1.8-9.6; $p=0.0005$).
There was no difference in the incidence of CHF between DS survivors and either non-DS survivors or DS controls. No DS survivor experienced a SMN, compared to a 20-year cumulative incidence of 4.4%±0.7% among non-DS survivors ($p=0.16$). Neither the 20-year cumulative incidence of cataracts nor of dementia differed between DS survivors and DS controls.

Conclusion: In this population-based analysis, DS survivors were at substantially higher risk of late mortality than both non-DS survivors and DS controls. This excess mortality risk was not attributable to cardiac- or SMN-related late effects, historically the main causes of late mortality among non-DS survivors. Though limited by small absolute risks, chronic morbidities associated with DS, such as dementia and cataracts, were not increased among DS survivors compared to DS controls. Further follow-up is justified to determine whether excess risk becomes evident as DS survivors continue to age. DS-specific surveillance guidelines may be warranted.

Poster # 75

THE SIX1 HOMEOBOX PROTEIN IS A NOVEL THERAPEUTIC TARGET IN CALM-AF10 LEUKEMOGENESIS

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Background: The *CALM-AF10* chromosomal translocation is found in 5-10% of T-cell acute lymphoblastic leukemias (T-ALL) and some acute myeloid leukemias (AML), and is associated with increased *HOXA* gene expression. Since *HOXA* genes are critical to hematopoiesis, they are not suitable drug targets. In order to identify potential alternative targets, we carried out RNA-sequencing on *CALM-AF10* transduced hematopoietic stem cells. Since CRM1 is critical for CALM-AF10-dependent *HOXA* gene activation, we also performed microarrays on murine *CALM-AF10* leukemia cells treated with the CRM1 inhibitor, Leptomycin B (LMB). Eleven genes were found in both gene sets, including 7 *Hoxa* genes and the homeobox gene *Six1*. Six1 and its cofactor EYA2 are overexpressed in solid tumors, but little is known of their role in leukemias.

Objectives: Evaluate the role of Six1 in *CALM-AF10* leukemias.

Design/Method: Gene expression was evaluated by RT-qPCR. The interaction between CALM-AF10 and the *Six1* gene was examined using Chromatin Immunoprecipitation-qPCR (ChIP-qPCR). Methylcellulose colony assays were used to assess self-renewal potential, and Cell-titer-Glo (CTG, Promega) assays measured cell proliferation. An inhibitor of the SIX1/EYA2 interaction (Compound 8430) was used in RT-qPCR experiments and CTG assays.

Results: We confirmed increased expression of *Six1* in *CALM-AF10* leukemia cells and that LMB decreases *Six1* expression in *CALM-AF10* leukemia cells, with ChIP showing that CALM-AF10 binds the *Six1* gene locus. *Six1* Overexpression was sufficient to immortalize murine fetal liver hematopoietic progenitors. Compound 8430 slowed cell growth in *CALM-AF10* murine leukemia cells and a human *CALM-AF10* cell line (U937), compared to cells treated with DMSO. 8430 also slowed proliferation of T-cell ALL lines (Jurkat/Molt4), and to a lesser extent B-cell ALL lines (REH/NALM6), with little effect on AML lines (OCI-AML5/NOMO1). Expression of downstream targets of *Six1 – Slc2a1, Cdk2, Cyclina2* – was decreased in 8430-treated *CALM-AF10* leukemia cells.

Conclusion: Six1 has previously been implicated in solid tumor oncogenesis, including breast and cervical cancers, as well as Wilms Tumor. Our results show that Six1 may also play an important role in leukemogenesis based on observations in *CALM-AF10* leukemia cells. Moreover, an inhibitor of the SIX1/EYA2 interaction slows the growth of *CALM-AF10* and other ALL cell lines, indicating that Six1 may be important in leukemia cell proliferation. Ongoing studies include knockout of *SIX1* in leukemia cell lines and assessing the effects of 8430 in other

leukemia cells. Our findings suggest that Six1 plays a role in leukemogenesis, and may be a novel therapeutic target in *CALM-AF10* and other leukemias.

Poster # 76

PHASE-SPECIFIC RISKS OF EMERGENCY VISITS AND HOSPITALIZATIONS DURING COG-BASED ALL TREATMENT

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Background: Therapy for childhood acute lymphoblastic leukemia (ALL) is associated with substantial healthcare utilization and thus burden on families. Little is known about patterns of healthcare utilization during specific treatment phases.

Objectives: To determine the risks of unanticipated emergency department (ED) visits and hospitalizations during ALL treatment. This will inform healthcare providers, counselling of families, and complement clinical trial data.

Design/Method: All children diagnosed with ALL between 2002-2012 at age <18 years in Ontario, Canada and treated according to COG protocols were identified using a provincial pediatric cancer registry and linked to population-based healthcare databases. All ED visits and hospitalizations were identified. Patient, disease, treatment, and outcome-related variables were identified through chart abstraction, including treatment phase start and end dates. In addition to comparing standard and intensified versions of each treatment phase, we also compared patients receiving different steroids (dexamethasone vs. prednisone) and different versions of Interim Maintenance (IM) (Capizzi vs. high-dose methotrexate (HDMTX)). All comparisons were adjusted for prognosticators including age, sex, risk group, immunophenotype, and time period.

Results: 631 children met inclusion criteria. Intensified therapy was associated with dramatically higher rates of ED visits and hospitalizations. For example, 76.2% of patients were hospitalized at least once while receiving Intensified Consolidation compared to 32.3% of patients receiving Standard Consolidation ($p<0.0001$). Similarly, 72.9% of patients receiving Intensified Delayed Intensification were hospitalized during this phase compared to 50.3% of patients receiving Standard Delayed Intensification ($p<0.0001$). Among patients receiving a 4-drug Induction, those receiving dexamethasone had an 85% higher rate of ED visits (adjusted rate ratio (aRR) 1.85, 95th confidence interval (95CI) 1.14-3.00; $p=0.01$) and a 44% higher rate of hospitalization (aRR 1.44, 95CI 1.24-1.68) compared to those receiving prednisone. Neither ED nor hospitalization rates during Maintenance varied by steroid received. Among high risk B-ALL and T-ALL patients in IM, Capizzi MTX was not associated with an increased rate of ED visits vs. HDMTX.

Conclusion: These population-based results can be used to inform both healthcare providers and anticipatory guidance for families. Families of children undergoing intensified therapy on COG protocols should in particular be counselled on the high risk of ED visits and hospitalizations during phases such as Intensified Consolidation and Intensified Delayed Intensification. Our results also suggest that clinical trials demonstrating increased toxicity rates associated with dexamethasone vs. prednisone may in fact underestimate the true magnitude of this increased risk.

Poster # 77

IGH CLONAL DIVERSITY MAY RELATE TO A LESS DIFFERENTIATED LEUKEMIA CELL OF ORIGIN IN B-ALL

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Background: There is profound variability in the extent of immunoglobulin heavy chain (IGH) clonal diversity in B cell acute lymphoblastic leukemia (B-ALL) resulting from the activity of recombination activating genes (RAG1 and RAG2) and activation induced cytidine deaminase (AICDA). B-ALLs with greater IGH clonal diversity may demonstrate distinct clinical and biologic characteristics from clonally homogeneous leukemias.

Objectives: We aimed to test whether RAG1-RAG2 and AICDA expression corresponds to the extent of IGH clonal diversity in each B-ALL and whether clonally diverse leukemias demonstrate distinct gene expression patterns from clonally homogeneous B-ALLs.

Design/Method: We used ultradeep next generation sequencing (NGS) of IGH to test the extent of RAG- and AICDA-mediated clonal diversification in 22 patients' newly diagnosed B-ALL. Using RNA sequencing (RNAseq) of a subset of cases with available viably frozen, pre-treatment tissue (N=13), we compared gene expression profiles (GEP) between clonally diverse (N=6) and clonally homogeneous (N=7) cohorts.

Results: At least one IGH clone was detected in 19 of 22 cases, consistent with established rates of VDJ-recombined IGH clone detection. In 9 of 19 cases (the "diverse cohort"), evidence of extensive RAG-mediated subclone diversification was observed, with a median of 595 subclones derived from each progenitor clone (range 3-4570). In the remaining 10 cases (the "homogeneous cohort"), all detectable progenitor clones were instead uniformly comprised of a homogeneous sequence signature without subclone diversification. There was no statistically significant difference in bulk RAG1-RAG2 or AICDA expression between clonally diverse and clonally homogenous cohorts. However, the clonally homogeneous cohort demonstrated an unexpected trend toward RAG1-RAG2 and AICDA upregulation, suggesting that these cases may have derived from a more mature, completely VDJ-recombined leukemia cell of origin (COO). In support of this idea, statistically significant enrichment of genes involved in cell fate commitment was observed in the clonally homogeneous cohort. Conversely, the clonally diverse

cohort demonstrated greater homeobox (HOX) gene expression, specifically of HOXA9, MEIS1, HOXA10, HOXC4, and HOXB3a, all genes for which high expression has been associated with a less differentiated cell state. Likewise, the diverse cohort demonstrated statistically significant enrichment of genes associated with Gene Ontology (GO) terms related to regulation of a hematopoietic stem cell state.

Conclusion: Our data show gene expression patterns suggestive of an earlier developmental stage among B-ALLs with IGH clonal diversity. These observations support the notion that B-ALLs with extensive IGH clonal diversity may be biologically distinct from clonally homogeneous cases.

Poster # 78

OUTCOMES PREDICTORS OF INFANT ALL, HYPODIPLOID ALL AND MPAL IN CANADA: A POPULATION-BASED STUDY

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Background: The prevalence, prognostic factors and outcomes of children diagnosed with infant acute lymphoblastic leukemia (ALL), hypodiploid ALL and mixed-phenotype acute leukemia (MPAL) in Canada are unknown.

Objectives: The main objective of this study was to describe the prevalence, prognostic factors and outcomes of three poor prognosis ALL subtypes in Canada.

Design/Method: This was a retrospective study using the Cancer in Young People-Canada (CYP-C) database, a national population-based childhood cancer surveillance program. Patient characteristics were presented for all patients and by subtype. Event-free survival (EFS) and overall survival (OS) were described by the Kaplan-Meier method and compared using the log-rank test for all patients and stratified by subtype. Univariate and multivariable Cox proportional hazard regression models of EFS and OS were performed for all patients and stratified by subtype.

Results: Among 2626 children aged 0-14 years diagnosed with B-ALL between 2001 to 2018, 227 (8.6%) patients were identified to be infant ALL (n=139; 5.3%), hypodiploid ALL (n=43; 1.6%) or MPAL (n=45; 1.7%). The median age and WBC at diagnosis were 7 (4-10) months and 105.5 (23.8-358.1) $x10^9$/L for infant ALL; 7 (3-14) years and 12.8 (5.0-26.1) $x10^9$/L for hypodiploid ALL; 7 (4-12) years and 12.9 (3.8-54.4) $x10^9$/L for MPAL. The 5-year EFS was significantly worse in the infant ALL subgroup (38.9 ±4.6%) compared to that of hypodiploid ALL (63.0 ±8.6%; p=0.0006) and MPAL (58.8 ±8.1%; p=0.0025). The 5-year OS was significantly inferior in infant ALL (58.9 ±4.6%) compared to hypodiploid ALL (75.2 ±7.2%;

p=0.0273) and MPAL (74.9 ±7.0%; p=0.0353). For the entire cohort, presenting WBC≥50x10^9/L and CNS-3 status were significant prognostic factors in univariate analyses of EFS. However, only presenting WBC≥50x10^9/L (HR: 2.4, 95% CI 1.6-3.6) retained significance in multivariable analyses. For the entire cohort, presenting WBC≥50x10^9/L, CNS-3 status, cytogenetics and treatment prior to 2010 were significant prognostic factors in univariate analyses of OS. However, only presenting WBC≥50x10^9/L (HR: 2.5, 95% CI 1.3-4.8) and CNS-3 status (HR:2.6, 95% CI 1.1-6.2) were significant in multivariable analyses. In infant ALL, age < 3 months at diagnosis and presenting WBC≥100x10^9/L were independent adverse predictors of EFS and OS. For the MPAL subgroup, age≥10 years old at diagnosis was an independent negative predictor of EFS and OS.

Conclusion: Infant ALL, hypodiploid ALL and MPAL represent 8.6% of childhood ALL and are associated with poor prognosis in Canada. WBC≥50x10^9/L at diagnosis represents an independent adverse factor of EFS/OS, irrespective of ALL subtype.

Poster # 79

VENETOCLAX FOR ACUTE LYMPHOBLASTIC LEUKEMIA IN PEDIATRIC PATIENTS: THE MD ANDERSON CENTER EXPERIENCE

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Background: Venetoclax is an inhibitor of the anti-apoptotic protein, B-cell lymphoma-2 (BCL-2), which restores apoptotic ability of cells. It has been successfully used in the treatment of relapsed/refractory (RR) leukemia in the adult population. Expanding its use to the pediatric population has been investigated in acute myeloid leukemia and myelodysplastic syndromes but sparsely in acute lymphoblastic leukemia (ALL).

Objectives: To describe efficacy and adverse events of venetoclax use for lymphoblastic disease in pediatric patients.

Design/Method: Retrospective chart review identified patients </= 21 years with a diagnosis ALL, and who received venetoclax at MD Anderson. The Revised Recommendations of the International Working Group Response Criteria in Acute Leukemia were used for response criteria. Toxicities were graded per the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0.

Results: Nine patients were identified, 67% (n=6) with T- ALL and 33% (n=3) with B- ALL, aged 6-21 years. Histology consisted of 56% (n=5) precursor T- ALL and one ETP ALL. Refractory disease (>3) prior therapies in 67% (n=6.) History of prior hematopoietic stem cell transplantation (BMT) in 44% (n=4). All patients received venetoclax in combination with conventional chemotherapy.

The most common toxicity was myelosuppression; all nine patients developed grade 4 thrombocytopenia. Grade 4 neutropenia in 67% (n=6), febrile neutropenia in 33% (n=3), grade 3 or higher anemia in 33% (n=3), grade 3 hyperbilirubinemia in 44% (n=4), and grade 3 or higher sepsis in 33% (n=3) patients. One patient had grade 3 liver enzyme elevation, one grade 3 mucosal infection, one grade 4 pneumonia, and one grade 4 coagulopathy. Importantly, no deaths occurred within 30 days of the start of venetoclax combination therapy, and no deaths or grade 5 toxicities associated with venetoclax.

Complete Remission (CR) or CR with incomplete count recovery (CRi) was achieved in 44% (n=4), all with undetectable MRD (uMRD). All patients with CR/CRi had a diagnosis of T-ALL, 75% (n=3) had precursor T- ALL, and one had ETP ALL. To date, 75% (n=3) of patients who achieved CR/CRi remain alive without disease with a median follow up time of 17.4 months. One patient received consolidation with BMT, one is currently on maintenance with venetoclax combination and one is being monitored for recurrence.

Conclusion: This single-institution retrospective review found that (1) venetoclax was safe and well tolerated in combination chemotherapy regimens, (2) thrombocytopenia and neutropenia were the most common toxicities identified, and (3) patients with T- ALL may be particularly sensitive to combination chemotherapy with venetoclax.

Poster # 80

CHILDHOOD LEUKEMIA LONG-READ TRANSCRIPTOMICS BASED POINT OF CARE DIAGNOSIS

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Background: Genomic testing for leukemia is the standard of care in high income countries for diagnosis, risk stratification and treatment. Diagnostic testing for leukemia is not available for many patients in low income countries (LIC) leading to an inability to comprehensively diagnose leukemia, risk stratify patients, and provide treatment with appropriate chemotherapies/targeted therapies.

Objectives: To validate point of care RNA long-read sequencing (LRS) for the diagnosis of acute lymphoblastic leukemia (ALL) in patients. We hypothesize that RNA LRS can provide a fast, low-cost, and accurate point of care method of detecting genomic rearrangements and specific expression changes to allow for comprehensive diagnosis and care in M-LIC.

Design/Method: Our proof of principle initiative uses biobanked cells from patients with B-cell ALL. After RNA extraction, LRS of leukemia cells transcripts was performed using the Nanopore Promethion®. Primary sequencing of large transcripts allows identification of isoforms and detection of fusion products and point mutations. The expression pattern (number of reads per gene) allows allocation to genomic groups, including high hyperdiploidy,

translocation (9;22) or Ph-like leukemia (characterized by a specific transcriptome pattern).

Results: Forty-one biobanked samples with known genomics were identified. Using biobanked cells from different groups, 20 samples including high-hyperdiploidy, translocations (12;21), (9;22) or translocations involving KMT2A and Ph-like leukemia, were selected for deep Promethion sequencing (One flow cell per cell line).
Sequencing of a pilot sample harboring a BCR - ABL1 fusion cell line yielded 73 million reads. Expression of 415 isoforms from 408 genes showed very high expression level (>= 99th percentile, up to 10,000 copies). 122 of these genes are involved in leukemia or cancer pathways (Kegg database). Deep RNA sequencing of other leukemia groups is ongoing, as well as sequencing of bar-coded samples to decrease the testing cost.

Conclusion: Preliminary data has shown that RNA LRS can identify genomic mutations gene fusion and characterize RNA expression in bone marrow samples from patients with B-cell ALL. RNA LRS is a promising method to provide a fast, low-cost, and accurate point of care method of detecting genomic rearrangements and specific expression changes. Completion of phase 1 will allow for phase 2, a prospective study to validate our point of care approach by performing LRS in patients with leukemia diagnosed at Red Cross War Memorial Hospital and BC Children's Hospital and phase 3 point of care testing in unequipped units in LIC.

Grant support from Childhood Diseases 2020 Seed Grant Competition

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Poster # 81

USE OF HYPOMETHYLATING AGENTS IN RELAPSED/REFRACTORY PEDIATRIC ACUTE MYELOID LEUKEMIA

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Background: Hypomethylating agents (HMAs) have a low toxicity profile, making them attractive for heavily pretreated patients with relapsed/refractory acute myeloid leukemia (AML). Data in pediatrics regarding HMA use are scarce.

Objective: To describe the use of HMAs in relapsed/refractory pediatric acute myeloid leukemia.

Design/Method: A retrospective chart review of relapsed/refractory AML cases treated with HMAs between 2009 and 2018 was performed. Patients were classified according to indication: (1) curative intent to pursue hematopoietic stem cell transplantation (HSCT), (2) palliation, and (3) use with donor lymphocyte infusion (DLI).

Results: Twenty-five patients were identified with median age 8.31 years (range 1.4-21). Most were male (15/25) and 21/25 had relapsed disease. *KMT2A*-R (24%) was the most common

cytogenetic abnormality followed by monosomy 7/del 7q (16%). A total of 133 HMA cycles were given; mean of 5.3 cycles/patient (range 1-16). Of these, 65% were with azacytidine, 35% with decitabine and 5 patients had received both at different times during therapy. Most cycles (62%) involved HMAs as monotherapy. The indications for use were curative intent (42.5%), palliation (42.5%), or with DLI (15%). Seven patients received HMAs for more than one indication.

In 14 scenarios (13 patients) when HMAs were given with curative intent, 6 (43%) (5 patients) resulted in successful disease reduction allowing transition to HSCT. Of these 5 patients, one died from treatment-related mortality, while four others are survivors. In 4/6 scenarios, HMAs were combined with gemtuzumab ozogamicin (GO). Of the remaining 8 patients, one proceeded to CART therapy and is alive, while 7 showed progressive disease (6/7 died). Thirteen patients received HMAs for palliation, two of whom had significant heart failure. The median duration of palliation was 144 days, with patients receiving between 1 and 9 cycles. Five patients with relapse post HSCT received HMAs in combination with DLI. Successful MRD negative remission was induced in 3 patients while 2 died of progressive disease. All three patients eventually relapsed following a sustained period of remission, however all remain survivors.

Conclusion: We present our single center experience of using HMAs in pediatric relapsed/refractory AML. Our data suggests that HMAs can be an effective option to transition patients to HSCT and for palliation. HMAs can also induce sustained remissions in combination with DLI in patients with relapse post-HSCT. Randomized controlled trials are needed to determine whether use of HMAs is superior to other approaches when used for similar indications.

Poster # 82/Early Career Award Recipient

PREDICTORS AND OUTCOMES OF IMMUNOGLOBULIN SUPPLEMENTATION IN B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Although intravenous immunoglobulin (IVIG) supplementation occurs in approximately 30% of children with B-cell acute lymphoblastic leukemia (B-ALL), the evidence for indications and the benefits on outcomes is sparse.

Objectives: To compare disease and demographic characteristics by receipt of IVIG amongst children with B-ALL, and to evaluate outcomes following IVIG supplementation amongst IVIG recipients.

Design/Method: A retrospective analysis examined children age 1-21 years with B-ALL treated at Aflac Cancer and Blood Disorders Center from 2010 to 2017. Demographic, disease and

treatment data were collected from the electronic medical record. Outcomes included IVIG receipt, emergency department (ED) visits, hospitalization days, episodes of severe infection (Common Terminology Criteria for Adverse Events grade 3 or higher) and episodes of febrile neutropenia. These were stratified by chemotherapy phase (prior to or during maintenance). Multivariate logistic regression models were used to identify predictors of IVIG administration. For IVIG recipients, general estimating equation model with Poisson distribution was used to compare rates of outcomes between IVIG supplemented and non-supplemented days.

Results: In total, 383 patients met inclusion criteria. IVIG was administered to 123 (32%) patients. Median IgG nadir was lower for IVIG recipients vs non-recipients (410mg/dL vs 675mg/dL, $p<0.01$). IVIG recipients were younger at diagnosis (4 vs 6 years, $p<0.01$) and had more ED visits (8 vs 5, $p<0.01$), hospitalization days (51 days vs 35 days, $p<0.01$), severe infections (4 vs 2, $p<0.01$) and episodes of febrile neutropenia (3 vs 1, $p<0.01$). The odds of IVIG administration were lower for non-white patients (Odds ratio (OR) 0.36, Confidence interval (CI) 0.19-0.73), higher for patients with more than 2 severe infections (OR 4.48, CI 2.25-8.90) and higher for National Cancer Institute standard risk patients with IgG nadir <500mg/dL (OR 7.36, CI 3.48-15.6), adjusting for covariates. Among IVIG recipients, 45 (36.6%) started IVIG supplementation prior to maintenance and 78 (63.4%) started supplementation during maintenance. Rates of ED visits, hospitalization days, febrile neutropenia episodes and episodes of severe infections were lower during IVIG supplemented days vs non-supplemented days (Rate ratio (RR) 0.57, CI [0.47-0.70]; RR 0.39, CI [0.30, 0.50]; RR 0.33, CI [0.23, 0.47]; RR 0.45, CI [0.34, 0.58], respectively).

Conclusion: IVIG receipt was associated with hypogammaglobulinemia and number of severe infections. ED visits, febrile neutropenia and hospitalization days were favorably impacted by IVIG supplementation. Further studies to establish guidelines for IVIG administration in B-ALL will be especially important as immunotherapies are introduced into upfront regimens for ALL.

Poster # 83

THE PROGNOSTIC SIGNIFICANCE OF RESIDUAL MASSES IN CHILDREN WITH T-CELL ACUTE LYMPHOBLASTIC LYMPHOMA

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Background: T-cell lymphoblastic lymphoma (T-LLy) is an aggressive but curable disease. Most children with T-LLy respond to treatment, but the prognostic significance of slow response and residual tumor is not well defined.

Objectives: Describe tumor response at the end of induction and consolidation therapy and correlate with outcomes in patients diagnosed with T-LLy.

Design/Method: Retrospective chart review was performed for 24 pediatric patients from 2010 through 2019 at Children's Mercy Hospital.

Results: Twenty-four patients were analyzed: Mean age: 10.3 years (2 to 16yrs), Male: 54.3%, Race/ethnicity: Caucasians 62.5%(n=15), Hispanic 25%(n=6) and "other"12.5% (n=3). We evaluated tumor response including percent change in mass volume at end of induction and the greatest measurable diameter of mass at the end of consolidation. Among patients that underwent radiographic evaluation at the end of induction therapy, 20.8% (n=5) achieved complete remission (no evidence of disease), 75%(n=18) partial remission ($\geq$50% disease reduction) and 4% (n=1) no response. At the end of induction, no Hispanic achieved complete remission and one had no response. Mean volume reduction was 90 percent (range 59-99%) at the end of induction. Hispanics had a poorer response to induction therapy (87.1% volume reduction) compared to other races (92.9%). At the end of consolidation therapy 80% of Hispanics and 35.7% Caucasians/other respectively had a residual mass. Of patients imaged (n=20), 3 (15%) had residual mass at the end of consolidation $\geq$5cm in greatest measurable dimension representing 33.3% (n=2) of Hispanics and 7% (n=1) of Caucasians/other. The 3 patients that underwent biopsy/resection had mediastinal masses, 2 were PET-positive at the end consolidation, with residual mass volume 10.5-86cm^3 and all were Hispanic. Biopsy result was equivocal in one patient (predominantly necrotic) and no evidence of disease in the other 2 patients. These patients continued treatment with the addition of nelarabine due to slow response and remain in remission at 29, 32 and 99 months from initial diagnosis. One patient (partial response) relapsed during maintenance therapy and died. Two patients died of infectious complications (1 in induction and 1 after completing consolidation) and all other patients remain in remission.

Conclusion: Children with T-LLy have an excellent prognosis and our study suggests that tumor response may not be a useful prognostic factor and biopsies may be of limited value. Hispanic patients trended toward having a slower response to therapy and larger residual masses at the end of consolidation. While our numbers were small/not statistically significant, further investigation is warranted.

Poster # 84

MEASURABLE RESIDUAL DISEASE IN ACUTE LYMPHOBLASTIC LEUKEMIA TREATED WITH NON-MRD BASED PROTOCOL

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Background: Age, presenting total leukocyte counts, steroid response and cytogenetic are known prognostic markers for acute lymphoblastic leukemia (ALL). Measurable Residual Disease (MRD) (or minimal residual disease) after induction chemotherapy is well accepted prognostic marker in childhood leukemia.

Objectives: To study correlation of known risk factors with MRD at the end of induction therapy. Can MRD be avoided in various morphology based risk groups?

Design/Method: This is a retrospective analysis of newly diagnosed pediatric patients with ALL, who received their induction chemotherapy from September 2017 to August 2020. Patients were treated with IC-BFM 2002 protocol (non-MRD based), and were risk stratified into three risk groups as per protocol. At the end of induction chemotherapy, MRD was done by flow-cytometry on bone marrow sample. Statistical analysis was done to see correlation of various known risk factors and risk groups with MRD.

Results: Total 68 children were included over a 3-year period. Median age was 6 years (1-16 years) with male preponderance (male:female = 1.83). Median total leukocyte count was 14560/cu.mm (72390-330). Eighty-three percent (57/68) were B cell ALL and 16%(11/68) were T cell ALL. In B cell ALL, cytogenetic analyses done in 54/57 patients. t(12:21) was present in 8(15%) patients and was the commonest abnormality.Three (3.7%) were positive for t(9:22).Thirty-seven children (68%) had normal cytogenetic. Day-8(D8) steroid response was available for all 68 patients. Based on age, presenting counts, D8 response and cytogenetics, 21(29.4%) were in standard risk, 42(58.8%) were in intermediate risk and 5(11.7%) were in high risk group. Day-15(D15) marrow was done for 53 children, 51had M1,1had M2 and1had M3 marrow status. Seven out of Sixty-Eight children (10%), had positive MRD after 1 month of induction. All were pre B ALL. All standard risk except 1had negative MRD post induction chemotherapy. Seven perecent (3/42) of intermediated risk and 60% (3/5) of high risk had positive MRD post induction chemotherapy. Age, presenting counts, cytogenetic and D8 steroid response is not associated with MRD. D15 marrow morphology (P=0.015) and risk groups (P=0.001) had statistically significant association with MRD.

Conclusion: In resource constrained settings, MRD can be avoided in patients with standard risk ALL. Though morphology-based risk-group stratification allows identification of high-risk patients to some extent, still significant number of intermediate and high risk patients had positive MRD which was not identified by conventional risk stratification. MRD cannot be avoided in these risk groups, who require optimisation of therapy to prevent relapse based on their MRD status.

Poster # 85

RISK FACTORS AND OUTCOMES FOR PEDIATRIC PATIENTS WITH THERAPY-RELATED MYELOID NEOPLASMS

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Background: Therapy-related myeloid neoplasms (tMNs), including myelodysplastic syndrome (tMDS) and acute myeloid leukemia (tAML), are rare but devastating complications following exposure to chemotherapy or radiotherapy. In the pediatric population, tMNs differ genetically,

pathologically, and prognostically from their *de novo* counterparts and present as aggressive diseases cured only with allogeneic hematopoietic stem cell transplant (HSCT).

Objectives: We aim to describe exposures in patients who developed tMNs and outcomes based on treatment approaches for tMN.

Design/Method: We conducted a retrospective review of patients treated at UCSF Benioff Children's Hospitals between 1980-2019 and identified 33 patients with tMN, defined as any patient who developed a myeloid neoplasm after exposure to radiotherapy, chemotherapy or HSCT without an underlying cancer predisposition syndrome. Data pertaining to primary & secondary disease, treatment, and outcomes were reviewed.

Results: Thirty-two patients developed tMN after treatment for cancer, 1 after HSCT for sickle cell anemia. Twenty-three developed tAML and 10, tMDS. The most common primary diagnoses were acute lymphoblastic leukemia (n=11), bone sarcoma (n=6), and non-Hodgkin's lymphoma (n=3). All patients received chemotherapy, which included alkylators, anthracyclines and etoposide. Sixteen received radiation, including 2 who received metaiodobenzylguanidine (MIBG) therapy. Five patients underwent HSCT for their primary disease.
Median latency period between primary and tMN diagnoses was 3.8 years (SD 3.1 years). tMN cytogenetic data was available for 28 patients (22 unfavorable, 6 neutral). Four and 12 patients had chromosome 5 and 7 abnormalities respectively and 10 patients had translocations involving chromosome 11q23, though, in contrast to *de novo* AML/MDS, presence of specific abnormalities did not predict outcome. Twenty patients underwent allogeneic HSCT, 17 after induction therapy for tMN. Sixteen of these patients who underwent transplant (80%) achieved complete remission. Ten patients subsequently relapsed after transplant and only 1 of these patients achieved a sustained remission. Four patients died after transplant due to progressive disease (n=2) or transplant-related mortality (n=2). The remaining 13 patients died prior to transplant. Five-year overall survival (OS) was 24.2% (n=7) with median survival of 11 months. Five-year OS was 40% for those who underwent HSCT. Median survival was significantly longer in transplanted patients (20.8 months vs 5.2 months p=0.003).

Conclusion: We present one of the largest retrospective cohorts of tMN to date. Our findings are consistent with prior reports showing that HSCT is the only curative treatment for tMN. We aim to further elucidate associations in exposure and treatment that may reduce morbidity and mortality from tMN.

Poster # 86

CHARACTERISTICS & OUTCOME OF PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA FOLLOWING STEROID PRETREATMENT

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Background: Although survival rates for pediatric acute lymphoblastic leukemia (ALL) and T cell lymphoblastic lymphoma (T-NHL) approach 90%, one avoidable factor that may be associated with poor prognosis is corticosteroid exposure prior to diagnosis. Steroids may induce partial remission of undiagnosed ALL, thereby delaying diagnosis and increasing the risk of steroid resistance, as well as increasing the risk of clinically significant and unrecognized tumor lysis syndrome. The prevalence and outcome of steroid exposure prior to ALL diagnosis in pediatric patients is currently unknown.

Objectives: We sought to determine the prevalence, characteristics and outcome of children who received inadvertent systemic steroids prior to a diagnosis of ALL or T-NHL. This information may aid in the care of these children in several ways, first, in identifying children at risk and educating medical caregivers in order to avoid administration of steroids in these patients. Second, knowing the outcome of these children will allow for optimizing the oncology care of these children once the diagnosis is made.

Design/Method: From a database of 401 pediatric patients diagnosed with ALL or T-NHL between 1/1/2000 - 12/31/2020 we identified patients who received systemic steroids prior to diagnosis. We report the demographic and medical information of these patients, the circumstances of their steroid administration, and their short- and long-term outcomes.

Results: We identified 16 patients exposed to systemic steroids prior to a diagnosis of ALL. This cohort of patients consisted of 8 girls and 8 boys, the median age of whom was 9.5 years. Nine patients were diagnosed with B-ALL and seven with T-ALL. The most common indications for steroid prescription included joint pain and swelling, shortness of breath, and musculoskeletal pain. Of the 16 patients, one experienced a relapse and one died during induction.

Conclusion: Older patients and patients with T-ALL were overrepresented in the steroid pretreated group. These patients were more likely to present with atypical or uncommon symptoms, including joint pain and shortness of breath. In at least two cases, steroid pretreatment directly resulted in a delay in diagnosis of ALL. In this limited cohort, steroid pretreatment was not associated with worse long-term outcomes.

Poster # 87

VENETOCLAX FOR ACUTE MYELOID LEUKEMIA IN PEDIATRIC PATIENTS: THE MD ANDERSON EXPERIENCE

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Background: Although in recent clinical trials the 5-year event-free survival rates for childhood Acute Myeloid Leukemia (AML) ranges between 49% and 64%, bone marrow relapse still occurs in up to one-third of cases. The long-term outcome of this subset of patients continues to

be poor, with an overall survival under 40%. Novel drugs directed towards distinct pathways and new molecular targets are required to continue making progress in this aggressive hematological disease.

Venetoclax, a bcl-2 inhibitor, has recently shown improved overall and event-free survival in relapsed and refractory adult patients with AML. Its use in the pediatric population, however, has been limited and is still under investigation. We reviewed our institutional experience at MD Anderson Cancer Center with children and adolescents.

Objectives: To describe use of venetoclax and associated adverse events in pediatric patients with AML.

Design/Method: We performed a retrospective review of patients treated at MD Anderson Cancer Center prior to September 2020 with at least one cycle of venetoclax. Patients were included if between the ages of 1-21 years with a diagnosis of high grade myelodysplastic syndrome or refractory or relapsed AML. Minimal residual disease (MRD) was measured institutionally by flow-cytometric assay. Toxicities associated with Venetoclax administration were graded per the Common Terminology Criteria for Adverse Events version 5.0. Descriptive statistics were used to report efficacy and toxicity data.

Results: A total of 12 patients with relapsed or refractory AML received venetoclax as salvage therapy. The median age was 21 years (Range: 17-21). Of the patients included, 58% were female and 67% were Caucasian. The median number of therapies prior to venetoclax was two (Range, 0-7). Thirty-three percent of patients had four or more lines of therapy and 25% of patients had received a prior allogenic transplantation. Hematological and gastrointestinal adverse events were the most frequently observed. Most of the gastrointestinal adverse events were grade 1/2 and not severe enough to warrant stopping the medication. Common grade 3/4 adverse events included febrile neutropenia (75%), neutropenia (92%), anemia (33%), and thrombocytopenia (83%). No patients had to discontinue the medication as a result of adverse events. No clinical or laboratory events of tumor lysis were reported.

Conclusion: Venetoclax was well tolerated with a safety profile in pediatrics, similar to prior adult studies. Patients should be monitored closely for prolonged myelosuppression and febrile neutropenia. However, more studies are needed to establish an optimal dose in the pediatric population.

Poster # 88

DERANGED TRANSCRIPTION AND REPLICATION IN MYC-INDUCED B AND T CELL LEUKEMIAS

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Background: *MYC* is a key oncogene overexpressed by many cancers including acute lymphoblastic leukemia (ALL), the most common and second most lethal pediatric cancer. Much of MYC's oncogenicity has been attributed to its transcription factor function, but data suggest MYC also deregulates replication in transcription-independent fashion. We hypothesize that MYC dramatically alters both gene expression profiles (GEP) and replication timing [(RT) - non-random spatiotemporal process where part of the genome replicates early, and other late] in both types of ALL – B-ALL and T- ALL. Conceivably, MYC exerts oncogenic effects on ALL transcription and replication programs, with some changes shared by B- and T-ALL, and others unique to only one.

Objectives: We aim to address two novel questions not investigated before. First, in ALL, do the same genetic loci show aberrant RNA transcription ***and*** DNA replication? Second, how similar are the affected loci in two closely-related, yet distinct, ALL types driven by the same oncogene?

Design/Method: The basis of our project is a unique double-transgenic *rag2*:*hMYC, lck*:*GFP* zebrafish model we established – the only animal model proven to develop both B-ALL and T-ALL. This model is ideal to study human ALL as the GEP differentiating zebrafish B- and T-ALL also distinguish human B- and T-ALL. Here, B-ALL and T-ALL are induced by human MYC *(hMYC*) regulated by a *D. rerio rag2* promoter. Since B- and T-lymphoblasts both express *rag2*, both lineages over-express MYC, causing highly-penetrant B- and T-ALL. Differential activity of a *D. rerio lck* promoter causes B-cells to fluoresce dimly and T-cells to fluoresce brightly, allowing identification and purification of B-ALL and T-ALL by fluorescence-based methods.

Results: We have purified >20 zebrafish ALL (T-ALL and B-ALL) and isolated their RNA and DNA. We are comparing both ALL types to identify mRNA signatures that are unique to, or shared by, both types. We seek loci that shift DNA replication from early-to-late, or late-to-early, to define regions replicating at the same time in both ALL types, versus loci that vary by ALL type. We are interrogating these data to determine whether GEP and RT profiles correlate with each other, and with known MYC target genes. Our preliminary analyses show differences in the RT profiles between B-ALL and T-ALL.

Conclusion: Exploiting our expertise with the *hMYC* zebrafish model, we have established differences in GEP between B-ALL and T-ALL and have found that their RT profiles differ too. We continue to delineate how MYC alters transcription and replication.

Poster # 89

MYELODYSPLASTIC SYNDROMES IN PEDIATRICS: A RARE AND REFRACTIVE DIAGNOSIS

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Background: Myelodysplastic syndromes (MDS) is a group of clonal diseases of hematopoietic stem cells resulting from dysplasia of one or more cell lines that characterizes 4% of pediatric hematological malignancies. Given an incidence of 1.8-4 cases per 1 million children, this group of diseases has been historically difficult to study. Originally described as "preleukemia" or "smoldering leukemia," MDS shares similarities with other bone marrow diseases. Furthermore, the similarity of the hypocellular bone marrow pathology in pediatric MDS to other genetic diseases such as aplastic anemia make the identification of the disease itself a challenge. These difficulties have contributed to the limited breadth of literature published on pediatric MDS as compared to adult MDS.

Objectives: The aim of this work is to provide insights to the diagnosis, prognosis, and treatment of pediatric MDS research by presenting a summary of pediatric myelodysplastic syndromes at MD Anderson Cancer Center (MDACC).

Design/Method: An IRB-approved retrospective review of 22 patients with myelodysplastic syndrome who were diagnosed or treated at University of Texas MD Anderson Cancer Center from 1997 to 2019.

Results: The average age at the time of diagnosis of the 22 patients reviewed was 17.68 years. 73% (n = 16) of patients received chemotherapy, of which 44% (n = 7) went on to receive a stem cell transplant (SCT). Four other patients received SCT without prior chemotherapy regimens. A total of 50% (n = 11) of patients in the dataset received a SCT. One patient only received monoclonal antibody therapy with Daclizumab, and one patient died before receiving SCT. 59% (n = 13) of patients died, having lived on average of 1.76 years after the diagnosis was made. 18% (n = 4) of patients were lost to follow-up. 54% (n = 7) of the thirteen patients who died received chemotherapy only, while 23% (n = 3) received SCT only and the remaining 15% (n = 2) received both. Interestingly, about 23% (n = 5) of patients had cytogenetics positive for Monosomy 7; similarly, about 10-20% of adults with MDS have chromosome 7 abnormalities.

Conclusion: Myelodysplastic syndrome is a difficult disease to diagnose and treat, with a high mortality rate and short interval between diagnosis and death. This can complicate the choice of treatment regimen, and therefore, further research is needed to understand this disease process and elucidate the best treatment options for patients.

Poster # 90

A SINGLE INSTITUTION CASE SERIES EXPLORING INFANT LEUKEMIA AND HYPERLEUKOCYTOSIS

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Background: Infant leukemia (acute leukemia diagnosed prior to 1 year of age) is an uncommon disease with a reported incidence of 41 cases per million in the US. Hyperleukocytosis, defined as a white blood cell (WBC) count >100 000/microliter, occurs more frequently in patients

with infant leukemia than in older children and can be a poor prognostic factor. There is a paucity of data for the management of patients with infant leukemia with hyperleukocytosis.

Objectives: The purpose of this study is to report data from a single institution regarding disease presentation, initial management, and outcomes for patients with infant leukemia with hyperleukocytosis.

Design/Method: We performed a retrospective chart review to identify patients with a new diagnosis of infant leukemia with hyperleukocytosis between November 2018 – November 2020. We extracted data on presentation, management of hyperleukocytosis, chemotherapy, and outcomes, such as timing to minimal residual disease (MRD) negativity, bone marrow transplant (BMT) status, and survival.

Results: During a two-year timeframe, we identified 12 patients at our institution with a new diagnosis of infant leukemia, and six of these patients had hyperleukocytosis. Mean age at diagnosis was 4.7 months (range: 4 days – 9 months). Blast morphologies included: myeloid (1), B lymphocyte (2), and mixed-phenotype acute leukemia (3). All patients had CNS disease at diagnosis and five had a KMT2A rearrangement. All patients presented with hepatosplenomegaly and tumor lysis syndrome, and five had coagulopathy requiring blood product transfusion(s). No patients had a mediastinal mass or intracranial hemorrhage. Five patients received procedural WBC depletion by either automated leukapheresis or manual whole blood exchange transfusion. Receiving WBC depletion did not delay initiation of systemic chemotherapy. The four patients that are still alive became MRD-negative either by the end of induction (1) or after three total chemotherapy cycles (3). Three of these patients have sustained remissions (average follow-up = 18.7 months), including one post-BMT, and one patient has ongoing refractory disease. Of the two patients who died of disease, one died during induction and one died after post-BMT relapse (20 months after diagnosis).

Conclusion: In our cohort of 12 patients with infant leukemia, hyperleukocytosis was common (50%). Patients with hyperleukocytosis tolerated procedural WBC depletion well without delays to systemic chemotherapy. Half of our patients with hyperleukocytosis were able to sustain remissions to date. However, survival in patients with infant leukemia is abysmal compared to outcomes for older children with acute lymphoblastic leukemia, and further studies are needed to improve outcomes.

Poster # 91

CANCER-RELATED OUTCOMES AMONG AMERICAN INDIAN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Childhood cancer is the leading cause of disease-related death among children aged 5-19 years in the US. While there have been great successes in the treatment of cancer, little information is available on disparities in access to treatment and survival among underrepresented populations, especially American Indian (AI) children. No recent studies have conducted in-depth analysis of disparities among AI children with cancer. AI children who use Indian Health Service (IHS) or tribal health clinics may have unique challenges including the need to obtain referrals through the IHS system, and IHS funding limitations.

Objectives: We aimed to evaluate the relation between race and event-free survival among AI and non-Hispanic (NH) white children diagnosed with acute lymphoblastic leukemia (ALL) prior to age 20 from 1994-2019.

Design/Method: We partnered with a children's hospital at an academic medical center to abstract data from electronic medical records and the institution's cancer registry on cancer diagnosis, treatment, and outcomes for children with ALL. We used a Chi-Square Test to compare differences between covariates and race and an exact Chi-Square Test for variables with sparse data. We evaluated the difference in survival times from diagnosis to date of first recurrence, death, or end of the study period by race using Kaplan-Meier analysis with the log-rank test. We used the Cox Proportional Hazards Model for multivariable survival analyses. Analyses were conducted in SAS v. 9.4.

Results: We identified children with ALL who were AI (n=48, 15%) or NH white (n=283, 85%). Of these, 48% were female and the most common insurance types were Medicaid (51%) and private insurance (45%). The median age of ALL diagnosis was 5.4 years. We observed no difference in time from diagnosis to cancer recurrence or death using the log-rank test by race (p=0.47) and no difference between race and event-free survival in our multivariable analysis adjusted for year of diagnosis (Hazard Ratio: 1.05, 95% CI: 0.75, 1.48).

Conclusion: As a next step, we will obtain electronic medical record data from the other children's hospital in the state and link our dataset with the state cancer registry to allow for a more comprehensive, population-based evaluation of cancer disparities. This project will generate important preliminary data for future studies, which will evaluate strategies to improve care coordination and incorporate cultural factors important to AI families into pediatric oncology care by tribal health and oncology providers.

Poster # 92

A DECADE OF INDUCTION CHEMOTHERAPY PRACTICES AT A SMALL CHILDREN'S CANCER CENTER

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Background: Across the United States, children diagnosed with acute lymphoblastic leukemia (ALL) following Children's Oncology Group (COG) protocols undergo standard 3 or 4-drug

induction chemotherapy. However, length of stay (LOS) and antibiotic practices during induction chemotherapy vary by institution. Much less is known about hospital practices and outcomes during induction chemotherapy from small institutions similar to ours.

Objectives: To evaluate the influence of our hospital practices in relation to morbidity during induction chemotherapy within the last decade.

Design/Method: Retrospective chart review of 72 eligible patients between the age of 1 and 21 years with newly diagnosed ALL at our institution between May 1, 2010 and May 31, 2020. Exclusion criteria included infantile ALL, acute myeloid leukemia (AML), and Down's Syndrome. We categorized LOS into short LOS (≤11 days [d]), medium LOS (12-15 d), and long LOS (≥16 d). Evaluation of complications and readmission rates during induction chemotherapy were analyzed.

Results: Of the 72 patients, 14 (19%) patients had infectious complications during entirety of induction. Only 9 (13%) patients were readmitted for infectious complications or fever. Rates were similar when analyzed by the National Cancer Institute (NCI) risk group or 3-drug versus (vs.) 4-drug induction. The most common infectious complication found was methicillin-susceptible *Staphylococcus aureus* (MSSA) bacteremia (56%) followed by *Escherichia coli* (*E. coli*) (11%). No deaths were identified. There were significant differences in LOS. Twenty-two of the 40 patients (55%) who received 3-drug induction had short LOS (≤11 d) as compared to 5 (16%) of the 32 patients with 4-drug induction (P=0.0007). Contrary, 26 (81%) of these patients had long LOS (≥16 d) as compared to 10 (25%) patients who received 3-drug induction (P=<0.00001). Most of the few patients undergoing 4-drug induction with short LOS were readmitted. Interestingly, 7 (78%) patients <10 years of age were readmitted for infectious complications, in comparison to 2 (22%) patients ≥10 years of age (P=0.01732).

Conclusion: We found lower but comparable total rate of infectious complications during ALL induction chemotherapy as reported in the literature. However, our rate of readmission as well as rates of infectious complications or fever when readmitted, was much lower. Furthermore, when stratified by NCI risk group or 3-drug vs. 4-drug induction, we did not see a difference. We believe the practice of keeping standard risk patients until at least day 8 of induction and most of those receiving 4-drug induction past absolute neutrophil count nadir or LOS ≥16 days, may account for our favorable findings.

Poster # 93

IBRUTINIB+RICE/RVICI FOR R/R MATURE B-NHL IN CHILDREN/YOUNG ADULTS: SPARKLE TRIAL INTERIM ANALYSIS

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Background: Pediatric relapsed/refractory (R/R) mature B-cell non-Hodgkin lymphoma (B-NHL) has a poor survival rate of ≤30%. SPARKLE (NCT02703272) is a 2-part, open-label, randomized, controlled phase 3 trial assessing ibrutinib plus chemoimmunotherapy (rituximab, ifosfamide, carboplatin, etoposide [RICE], or rituximab, vincristine, idarubicin, carboplatin, ifosfamide [RVICI]; both included dexamethasone) versus chemoimmunotherapy alone in pediatric/young adult R/R mature B-NHL. The safety/pharmacokinetics run-in part 1 established preliminary efficacy, safety, and dosing for part 2.

Objectives: The preplanned interim analysis was to be performed after 30 event-free survival (EFS) events (death, disease progression, or no response after 3 cycles) to assess efficacy, futility, and safety in SPARKLE part 2.

Design/Method: Patients aged 1-30 years with confirmed R/R mature B-NHL (initial diagnosis <18 years) were randomized 2:1 to receive chemoimmunotherapy ± ibrutinib until completion of 3 cycles, stem-cell transplantation, disease progression, or unacceptable toxicity. Primary endpoint was independent review committee (IRC)-confirmed EFS.

Results: As of November 2020, 51 patients were randomized. In the ibrutinib plus chemoimmunotherapy (n=35) versus chemoimmunotherapy (n=16) arms, respectively: median age was 15 years; 48.6% versus 37.5% of patients had Burkitt lymphoma/leukemia; 34.3% versus 50.0% had diffuse large B-cell lymphoma; 17.1% versus 12.5% had primary mediastinal or other B-NHL; 5.7% versus 0 had second relapse. EFS hazard ratio (HR; ibrutinib plus chemoimmunotherapy vs chemoimmunotherapy) was 1.078 (90% confidence interval [CI], 0.585-1.984; p=0.42). In the ibrutinib plus chemoimmunotherapy versus chemoimmunotherapy arms, respectively: median EFS was 5.36 versus 6.97 months; median overall survival was 13.44 versus 11.07 months (HR 0.782 [90% CI, 0.402-1.520]; p=0.5414); IRC-confirmed overall response rate was 68.6% versus 81.3%; proportion of patients with investigator-assessed partial response or better to undergo transplantation was 34.3% versus 37.5%. The ibrutinib plus chemoimmunotherapy versus chemoimmunotherapy arms had comparable rates of grade ≥3 adverse events (AEs) (both 100%), serious AEs (71.4% vs 73.3%), and AEs leading to death (11.4% vs 13.3%). Among patients receiving ibrutinib plus chemoimmunotherapy, 51.4% experienced serious ibrutinib-related AEs; 2.9% had AEs leading to ibrutinib discontinuation. Major hemorrhage was higher with ibrutinib plus chemoimmunotherapy versus chemoimmunotherapy (17.1% vs 6.7%); infections were lower (51.4% vs 66.7%). Death occurred in 17 (48.6%) patients receiving ibrutinib plus chemoimmunotherapy and 10 (66.7%) receiving chemoimmunotherapy. Ibrutinib plasma concentrations at study dose were consistent with data in adults.

Conclusion: The primary endpoint, EFS, met the futility criteria (1-sided p≥0.341); enrollment ceased per independent data monitoring committee recommendation. No new/unexpected safety signals were observed with ibrutinib plus chemoimmunotherapy. Follow-up is ongoing.

(Burke, *Leukemia*, 2020)
Sponsored by Janssen.

Poster # 94

CELL-SPECIFIC GENE EXPRESSION AND CELLULAR SENESCENCE IN PEDIATRIC HODGKIN LYMPHOMA

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Background: Pathogenic mechanisms underlying Hodgkin lymphoma (HL) remain incompletely defined. Studies characterizing Hodgkin Reed-Sternberg (HRS) cell gene expression in pediatric HL have been challenging due to rare HRS (<1%) within HL tumors.

Objectives: To define transcriptomes of HRS cells and tumor-infiltrating lymphocytes to inform pathogenic mechanisms and identify potential therapeutic targets in pediatric HL.

Design/Method: Multi-parameter flow cytometry was used to sort HRS cells, CD4+/CD8+ T-cells, and CD20+/30+ B-cells from pediatric subjects' HL lesions and control tonsils. Gene expression profiles (GEPs) for all sorted cell types and HL cell lines were assessed using Affymetrix GeneChip HTA 2.0. Unsupervised hierarchical clustering and principal component analysis determined relatedness, and Cibersort confirmed the phenotype of the sorted cell types. GEPs of HL cells were compared to respective controls using a univariate t-test. Significance was determined using a multivariate permutation test to estimate false discovery. DEGs were analyzed through gene set enrichment analysis (GSEA) and ingenuity pathway analysis (IPA). Immunohistochemistry (IHC) was performed on HL lesions to confirm the presence of specific proteins based upon results of GSEA/IPA.

Results: GEPs were compared for HL samples: HRS vs. control CD20+/CD30+ (1934/3846 DEGs), HL CD4+ vs. control CD4+ (635 DEGs), HL CD8+ vs. control CD8+ (2 DEGs). HRS cells demonstrated a heterogeneous phenotype (Cibersort) that may reflect aberrant differentiation, and they over-expressed genes associated with T-cell pathways while clustering separately from T-cells, which may reflect an innate T-cell signature rather than T-cell rosetting and contamination. Comparing HRS vs. control CD30+ cells using transcriptomic analysis revealed that genes were upregulated in pathways related to cellular senescence, including G1/S Checkpoint Regulation (z-score=2.4, p=1.78E-06), G2/M DNA Damage Checkpoint Regulation (z-score=2.2, p=1.12E-05), and Cyclins and Cell Cycle Regulation (z-score=-3.0, p=3.16E-06). Upstream analysis of G2/M DNA Damage Checkpoint Regulation pathway demonstrated that P21 and GADD45, senescence markers, were upregulated in HRS cells (fold-change=2.27, p=3.1E-06; fold-change=2.9, p=1.13E-05, respectively), while Cyclin B1 and 2, proliferation markers, were downregulated in HRS cells (fold-change=0.09, p=1.28E-05; fold-change=0.06,

p<1E-07, respectively). Using IHC, HRS cells stained positively for senescence markers p21, p53, and senescence-associated beta-galactosidase, and negatively for Ki67.

Conclusion: Characterization of specific cell populations within HL tumors is feasible through flow-sorting viable tissue. HRS cells in this cohort expressed gene signature consistent with oncogene-induced senescence, which has not been previously associated with pediatric HL. These findings support further pre-clinical and clinical testing of novel therapeutic strategies that target pathologic senescence in pediatric HL.

Poster # 95

GREATER THAN 3 RELAPSES IN AYA WITH HODGKIN LYMPHOMA: MD ANDERSON CANCER CENTER'S 10 YEAR EXPERIENCE

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Background: Hodgkin lymphoma (HL) is one of the most common neoplasms among the Adolescent and Young Adult (AYA) population. Despite novel therapies, a select number of patients experience multiple relapses or are refractory to therapy. This also increases the risk of developing early and late-onset systemic toxicities due to repeated exposure to chemotherapy and radiation therapy.

Objectives: Due to the risks of multiple relapses in HL and the associated adverse effects, there is a need for more targeted epidemiological data to determine populations at risk of multiple relapses. We reviewed our 10-year institutional experience of AYA classical HL (cHL) patients at MD Anderson Cancer Center and present an evaluation of risk factors in patients with greater than 3 relapses.

Design/Method: This single center study included AYA patients with a diagnosis of cHL who were first seen at the University of Texas MD Anderson Cancer Center between January 1st, 2010 and May 1st, 2020 for either newly diagnosed cHL or relapsed/refractory (R/R) cHL. Patients between the ages of 15-39 years at diagnosis were included. Pathology was confirmed and analyzed at our institution. The range for continuous variables - such as age and lab measurements - and frequency counts and percentages for categorical variables - such as sex and response - were analyzed.

Results: Between 2010 and 2020, 2784 patients met the inclusion criteria of HL, and 448 were excluded for being NLPHL. From 2336 cHL patients, our preliminary data collection shows 106 (47%) had 3 or more relapses. 62 (58%) patients were male, and 44 (42%) patients were female. The median age of presentation for these patients was 28 years old. One of these patients was <15 (1%), 19 patients (18%) were between the ages of 15-21, 49 (46%) were between the ages of 22-30, and 41 (39%) were between the ages of 31-39. Follow-up duration ranged from 1 to 146 months, with a median duration of follow-up of 18 months. Treatment details were obtained, and

survival analysis was performed per age group and year of diagnosis.

Conclusion: AYA patients with more than 3 relapses of cHL have dismal outcomes. Our preliminary data shows that survival of this subset has improved over the years but the risk of relapse may have age and gender predilections. Further studies are needed to recognize specific populations at greater risk of relapse.

Poster # 96

DIAGNOSTIC EFFICACY OF EXCISIONAL VERSUS PERCUTANEOUS NEEDLE BIOPSIES IN PEDIATRIC LYMPHOMAS

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Background: Tumor biopsies are essential for lymphoma diagnosis and having accurate diagnostic tissue is necessary for initiating successful and timely treatment plans. The 2020 NCCN guidelines recommend excisional biopsy as the gold standard for diagnosis of lymphoma. However, Interventional radiology (IR) guided percutaneous fine needle aspiration (FNA) and core needle biopsies (CNB) are being utilized more frequently as an alternative due to their minimally invasive approach, with the potential risk of insufficient diagnostic tissue. Developing an institutional standard for diagnostic biopsies can improve patient care and outcomes.

Objectives: Evaluate and compare the diagnostic efficacy of surgical excisional biopsies versus IR guided FNA and CNB to determine a more standardized approach to diagnostic biopsy guidelines for lymphoma at our institution.

Design/Method: A retrospective chart review was conducted that included all patients over the last 5 years with a diagnosis of lymphoma treated at Riley Hospital for Children. Pathology reports and final diagnosis were reviewed for patients that underwent surgical or IR guided biopsies to determine whether adequate tissue was obtained to achieve an accurate diagnosis.

Results: One-hundred and thirty-one patient charts were reviewed which included 166 biopsies. Eighty-four were surgical excisional biopsies with 96.4% being diagnostic and 82 were IR guided with 85.4% being diagnostic (p= 0.013). Seventy-two primary biopsies were excisional with a 97.2% diagnostic yield and 79 were IR guided with an 84.8% diagnostic yield (p=0.009). Forty-six out of 46 (100%) primary surgical biopsies performed at Riley were diagnostic versus 64 out of 73 (87.7%) primary IR biopsies (p=0.013). At Riley, 98.2% of all surgical biopsies performed were diagnostic versus 88.2% of IR biopsies (p=0.031). There were 28 surgical and 6 IR biopsies performed outside Riley with a 92.9% and 50% diagnostic yield respectively (p=0.007). Fifteen repeat biopsies were performed for non-diagnostic samples with all but 2 being done at Riley; 12 surgical and 3 IR. Twelve out of the 15 biopsies were initially done as IR biopsies.

Conclusion: Both surgical and IR guided biopsies have a high diagnostic success rate for

lymphoma, however, surgical excisional biopsies yielded a statistically significant better diagnostic efficacy when compared to IR guided biopsies amongst patients treated at our institution. These significant findings provide support for making surgical excision biopsies our institutional standard approach to diagnosing lymphoma and reserving IR biopsies for those not amendable to surgical excision.

Poster # 97

AYA WITH MIXED CELLULARITY CLASSICAL HODGKIN LYMPHOMA:MD ANDERSON CANCER CENTER'S 20-YEAR EXPERIENCE

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Background: Mixed cellularity classical Hodgkin Lymphoma (MCCHL), a less common classical HL (cHL), is characterized by poorer outcomes compared to other types of cHL. It occurs more commonly in those with EBV positive histopathology. With improvement in chemotherapies and radiation therapy over the past few decades, patients are living longer in the setting of multiple relapses. However, they are at risk of morbidities related to the acute and late-onset systemic effects of these therapies.

Objectives: We reviewed our 20-year institutional experience of adolescent and young adult (AYA) patients with MCCHL to elucidate specific epidemiological data that may help target specific populations.

Design/Method: This single center study included AYA patients with a diagnosis of MCCHL who were first seen at the University of Texas MD Anderson Cancer Center between January 1st, 2000 and May 1st, 2020 for newly diagnosed or relapsed/refractory HL. Patients between the ages of 15-39 years at diagnosis were included. Pathology was confirmed and analyzed at our institution. EBV status, HIV infection and nutrition status was also collected. Range for continuous variables such as age, and lab measurements, and frequency counts and percentages for categorical variables such as race, gender, and response were analyzed.

Results: Between 2000 and 2020, 124 patients with MCCHL met all inclusion criteria. There were 39 patients (31%) that were female and 85 (69%) were male. The median age of presentation was 30 years old. Twenty-three patients (18%) were between the ages of 15-21, 43 (35%) were between the ages of 22-30, and 58 (47%) were between the ages of 31-39. The median duration that patients followed with a provider was 37 months. Thirty-six patients with MCCHL were noted to relapse at least once, comprising a relapse rate of 29%. In those that relapsed, 23 (64%) were male. The median age of relapse was 30.5 years of age with 50% of patients between the ages of 31-39. Clinical characteristics of this subset were studied. Treatment regimens included doxorubicin, bleomycin, vincristine, etoposide, prednisone, and cyclophosphamide (ABVE-PC), doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD) based therapy, brentuximab vedotin (BV) based therapy and checkpoint inhibitors (CPIs) based

therapy.

Conclusion: MCCHL is an infrequent variant of cHL with higher relapse rates and possible age and gender predilections. Further studies are needed to discover targeted chemotherapies for this subset of patients in order to increase survival rates, decrease systemic toxicities, decrease progression rates, and improve quality of life.

Poster # 98

AYA NODULAR LYMPHOCYTE PREDOMINANT HODGKIN LYMPHOMA: MD ANDERSON CANCER CENTER'S 20 YEAR EXPERIENCE

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Background: Hodgkin Lymphoma (HL) represents one of the most common cancers observed in the adolescent and young adult (AYA) population. HL is divided into two categories, classical HL (cHL) and non-classical HL represented by a rare subtype, nodular lymphocyte predominant HL (NLPHL). NLPHL is defined by CD-20 expression and is associated with survival rates greater than 90% with a low risk of progression. In patients that do relapse, salvage therapy includes systemic chemotherapy, CD-20 targeted drugs, or autologous stem cell transplant, options that carry systemic toxicities.

Objectives: Due to the rare nature of NLPHL, epidemiological data is limited. We reviewed our 20-year institutional experience of adolescent and young adult (AYA) patients with HL to elucidate specific epidemiological data in patients with NLPHL. This may help target specific populations with therapy options.

Design/Method: This single center study included AYA patients with a diagnosis of HL who were seen at the MD Anderson Cancer Center between January 1st, 2000 and May 1st, 2020 for either newly diagnosed or relapsed/refractory HL. Patients between the ages of 15-39 years at diagnosis were included. Pathology was confirmed and analyzed at our institution. Range for continuous variables such as age, and percentages for categorical variables such as race, gender, and response were analyzed.

Results: Between 2000 and 2020, 2784 patients met the inclusion criteria of HL. Among them, 448 (16%) were diagnosed with NLPHL. There were 197 (44%) female patients and 251 (56%) male patients. Median age of presentation was 28 years old. Eighty-nine (20%) patients were between the ages of 15-21, 194 (43%) were between the ages of 22-30, and 165 (37%) were between the ages of 31-39. The median duration of follow up with a provider was 51 months. Forty-two patients with NLPHL had at least one relapse, comprising a relapse rate of 9%. The median age of those that relapsed was 31 years old with 29 (69%) patients being male. Front-line management included surveillance, doxorubicin, bleomycin, vincristine, etoposide, prednisone, and cyclophosphamide (ABVE-PC), doxorubicin, bleomycin, vinblastine and dacarbazine

(ABVD) based therapy, Rituximab only, Rituximab, cyclophosphamide, Doxorubicin, Vincristine, and Prednisone (R-CHOP), and radiation therapy.

Conclusion: Our data supports and adds to the literature that NLPHL has a male predominance, possible age predilection, and lower incidence compared to cHL. Despite the rarity of NLPHL, studies are needed to discover targeted chemotherapies that decrease systemic toxicity and rate of relapse and improve quality of life, especially as patients live longer.

Poster # 99

IMPACT OF BODY MASS INDEX ON OVERALL RELAPSE OF HODGKIN LYMPHOMA

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Background: Hodgkin lymphoma (HL) is a common neoplasm among adolescents and young adults in the US. Nutrition has been noted to impact survival in this subset of patients.

Objectives: We reviewed our 20-year institutional experience of adolescent and young adult (AYA) patients with HL and analyzed nutrition status as measured by body mass index (BMI) and its impact on progression free survival (PFS), and overall survival (OS).

Design/Method: This single center retrospective study included AYA patients ages 15-39 with newly diagnosed HL or relapsed/refractory (R/R) HL seen at MD Anderson Cancer Center between January 1st, 2000 and May 1st, 2020. Pathology was analyzed and confirmed at our institution. BMI was calculated by kg/m^2, and then stratified according to Centers for Disease Control and Prevention (CDC) definitions. For patients less than 18 years, stratification was based on BMI percentile: less than 5^{th} was underweight, 5^{th} to 85^{th} was normal weight, 85^{th} to 95^{th} was overweight and greater than the 95^{th} was obese. For patients greater than 18 years, stratification was based on BMI numerical value: less than 18.5 was underweight, 18.5 to 24.99 was normal, 25–29.99 was overweight, and 30 and higher was obese. Standard statistical analysis methods were applied to both continuous and categorial variables using a confidence interval (CI) of 95%.

Results: Between 2010 and 2020, 2784 patients met the inclusion criteria.1421 (51%) patients were female. 1362 (49%) patients were male. Median age at diagnosis was 28. 471 patients (20%) were 15-21 years of age, 978 patients (42%) were 22-30 years of age, and 887 (38%) were 31-39 years of age at diagnosis. Follow up ranged from to 1 to 241 months. Medium follow up was 37 months. Front-line treatments varied among age groups and year of diagnosis: doxorubicin, bleomycin, vincristine, etoposide, prednisone, and cyclophosphamide (ABVE-PC), doxorubicin, bleomycin, vinblastine and dacarbazine (ABVD) based therapy, brentuximab vedotin (BV) based therapy and checkpoint inhibitors (CPIs) based therapy. 1145 patients (49%) relapsed and underwent Autologous Stem Cell Transplant. This group was subdivided based on

BMI. Our preliminary data collection results reveal that 30.8% of overweight and 34.6% of obese patients relapsed once or more.

Conclusion: This retrospective study aims to discover a relationship between BMI at the time of diagnosis in relation to PFS and OS of HL. Our preliminary data shows a strong association between weight gain and relapse. Further studies need to obtained to clarify this association.

Poster # 100

POST-HSCT OUTCOMES AFTER EMAPALUMAB TREATMENT IN PRIMARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

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Background: The treatment goal of primary hemophagocytic lymphohistiocytosis (pHLH) is to stabilize the disease by controlling the associated hyperinflammation to bring patients to hematopoietic stem cell transplantation (HSCT), the only curative therapy.

Objectives: Report the post-HSCT outcomes of an extended cohort of patients with active pHLH who received emapalumab, a fully human, anti-IFNy monoclonal antibody, in the pivotal study (NCT01818492) and its ongoing extension study (NCT02069899).

Design/Method: Patients aged $\leq$18 years received an initial intravenous dose of emapalumab 1mg/kg every 3-4 days. Subsequent doses could be increased up to 10mg/kg if required, based on predefined laboratory and clinical response parameters. Planned treatment duration was up to 8 weeks, with possible shortening to a minimum 4 weeks, or extension up to HSCT if needed. Emapalumab was administered on a background of dexamethasone 5-10mg/m^2. Analysis was performed on 45 patients in two groups: second line (34 patients previously treated with conventional HLH therapies) and all treated (34 second-line plus 7 treatment-naïve patients).

Results: As of 31 January 2019, 37 of 45 patients had entered the long-term extension trial: 18 had completed the long-term follow-up for 1 year; 7 were ongoing (5 in the post-HSCT long-term follow-up, 1 receiving HSCT conditioning, and 1 still receiving emapalumab); and 12 had withdrawn prematurely (death, adverse event, consent withdrawal, lost to follow-up, or other). Overall, 23/34 (67.6%) of the second-line and 29/45 (64.4%) of the all-treated groups proceeded to HSCT with a median time to transplant of 84 (95% CI 65-135) and 101 (95% CI 82-156) days, respectively. Donor type included mismatched unrelated (n=8), matched unrelated (n=13), haploidentical (n=5) and matched sibling (n=2). Stem cell source was bone marrow (n=18), cord blood (n=1) and peripheral blood (n=9). Preparative regimens varied but included melphalan- (reduced intensity) and busulfan- (myeloablative) based regimens. Engraftment occurred in 21/23 (91.3%) and 24/29 (82.8%) of the second-line and all-treated groups, respectively. In the

all-treated group, 4/5 patients who failed to engraft received haploidentical transplantation, and 1 patient received cord blood from a mismatched unrelated donor. Seven patients (all in second-line group) developed GvHD, with 3 of these patients experiencing grade 3 or 4 GvHD. Post-HSCT survival probability estimates up to 1 year were 91% (95% CI 68.3-97.6) and 82% (95% CI 62.1-92.1) in the second-line and all-treated groups, respectively.

Conclusion: IFNy neutralization with emapalumab permitted most patients with active pHLH to proceed to HSCT, and was associated with a favorable rate of engraftment, GvHD, and survival estimates.

Poster # 101

MYPART RARE TUMOR NETWORK: EARLY RESULTS AND INTERIM ANALYSIS OF CHORDOMA AND ACC PATIENT COHORTS

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Background: Pediatric rare solid tumors are understudied and detailed knowledge of their biology, genomics, and clinical course is lacking. The Cancer Moonshot-funded **M**y **P**ediatric and **A**dult **R**are **T**umor (MyPART) network (cancer.gov/mypart) in the NCI Pediatric Oncology Branch launched a longitudinal natural history protocol (NCT03739827) including standardized comprehensive clinical, patient reported outcomes (PROs) and biospecimen analysis of pediatric, adolescent, and young adult (AYA) patients with rare solid tumors with the goal of translating these findings to improve care and treatment. Sub-protocols for chordoma (NCT0391046) and adrenocortical carcinoma (ACC) (NCT04447014) collect tumor-specific data.

Objectives: Comprehensive study of the natural history and treatment development of rare pediatric and adult solid tumors.

Design/Method: Patients of any age with a rare solid tumor (<15 cases per 100,000 people per year) are eligible. Patients can participate from home or visit the NIH for annual evaluations. Participants complete individual medical history, family history, PROs, and provide saliva for DNA. Tumors are analyzed using a 500+ gene panel (TruSight500, Illumina), discussed in a molecular tumor board, and undergo comprehensive genomic and epigenomic analyses, with single cell sequencing if feasible. Data are entered into a central database. Participants invited to NIH undergo clinical evaluation, genetic counseling, blood collection (standard clinical labs, germline DNA/RNA, immune phenotypes, cytokines, exosomes), and imaging studies, as indicated. Patients with chordoma or ACC have disease-specific evaluations including PROs volumetric image analysis, and cognitive assessment in a subset of patients.

Results: Protocol NCT03739827 has enrolled 250 patients since January 2019, 107 enrolled remotely during the COVID pandemic. Eighty-one patients are ≤ 39, with 27 ≤ 18 years old. Most frequent diagnoses include ACC, neuroendocrine tumor, chordoma, and succinate dehydrogenase-deficient gastrointestinal stromal tumor. Twenty-six patients (15 AYA) are enrolled on the chordoma sub-protocol. For these 15 patients, chordoma subtypes are: poorly differentiated (N=3), conventional transformed to dedifferentiated (N=1), and conventional (N=11). Disease status at enrollment: metastatic disease (N=6), recurrent disease (N=5), disease-free after recurrence (N=2), no evidence of disease (N=8). For the ACC sub-protocol, 47 patients (11 AYA) have enrolled. Of these 11 patients, 7 have recurrent and metastatic disease and 4 have no evidence of disease. Tumor tissue was obtained on all patients.

Conclusion: Protocol NCT03739827 has successfully enrolled patients with a variety of rare solid tumors who have undergone comprehensive data collection. Remote enrollment allows participation from any location. Data analysis is ongoing and will enable better clinical, immunologic, and genomic/epigenomic characterization of these tumors.

Poster # 102

DRUG SCREEN IN ZEBRAFISH ANGIOSARCOMA MODELS CREATED FROM A NOVEL GRAFTING TECHNIQUE

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Background: Angiosarcoma is a clinically aggressive tumor with a high rate of mortality, especially in the pediatric population. It can arise in vascular or lymphatic tissues, involve any part of the body, and aggressively spread locally or metastasize. Due to the rarity of angiosarcoma, molecular drivers and optimal treatment strategies are lacking. Also, a considerable barrier to studying new treatment options for angiosarcoma is the lack of suitable cell lines and few appropriate mammalian animal models. Furthermore, when previous tumor transplant methods in zebrafish of single cell injection were used, angiosarcoma cells did not efficiently engraft due to loss of viability. Our solution was to create a novel technique to engraft angiosarcoma into live animal models, which then allowed us to proceed with a screen of pharmacologically active compounds to find better treatments for this devasting disease.

Objectives: We hypothesize that the diffuclty with transplantation of angiosarcoma is due to the loss of the microenvironment of the angiosarcoma tumor. To overcome this obstacle, a novel transplant method was developed, which maintains the microenvironment of the tumor. This results in quick and efficient engraftment of the angiosarcoma tumor when compared to previously published methods. We then used this angiosarcoma model for an in vivo drug screen, which evaluates for both treatment and toxicity, to find better treatment options for patients with angiosarcoma.

Design/Method: To create an angiosarcoma zebrafish model, GFP+ CG1 tp53del/del zebrafish were utilized. These zebrafish spontaneously develop angiosarcomas that are molecularly and histologically like humans. Tumor pieces were transplanted into syngeneic non-GFP CG1 zebrafish. These angiosarcoma burdened zebrafish were dosed with select compounds of varying actions from the LOPAC small molecule library for 6 hours daily during 7 days in a 3D printed housing system that enables a reduction in drug quantity and water volume.

Results: The new transplant method had 92.8% engraftment rate compared to 23.8% for the previous method. In our ongoing drug screen, we found that over 7 days our DMSO control fish grew on average about 200% and previously published treatments of Paxitacil, Sunitinib, and Rapamycin had significant decreased growth. We've had varying preliminary results of both small and large effects and others being toxic. Overall, we've had encouraging results in certain drug classes.

Conclusion: Our preliminary data has shown the feasibility of a drug screen using a novel zebrafish angiosarcoma model, which has already revealed possible new therapeutic options for these patients.

Poster # 103

A PHASE 1 STUDY OF TALIMOGENE LAHERPAREPVEC (T-VEC) IN PEDIATRIC PATIENTS WITH ADVANCED SOLID TUMORS

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Background: Immunotherapies that recruit immune cells into the tumor microenvironment are appealing therapeutics for the immunologically inert pediatric solid tumors. T-VEC is a genetically modified, oncolytic herpes simplex virus (HSV)-1 designed to selectively replicate within tumors and produce GM-CSF to enhance systemic antitumor immunity. T-VEC was approved for the treatment of advanced adult melanoma and was observed to increase tumor-infiltrating lymphocytes.

Objectives: Here, we report preliminary safety and efficacy from a phase 1, multicenter, open-label, dose de-escalation study (NCT02756845) of T-VEC in pediatric patients with advanced non-CNS, non-lymphoma tumors that can be directly injected. The primary objective was to assess safety via incidence of DLTs. Secondary objectives included overall response rate.

Design/Method: Patients with tumors for which no standard therapy is available were enrolled into 2 cohorts (A1: 12 to ≤21 years, B1: 2 to <12 years). T-VEC was administered at the adult dose: 10^6 plaque-forming unit (PFU)/mL followed by 10^8 PFU/mL 21 days later and q14d thereafter (all ≤4 mL). Dose de-escalation was planned for 10^6 PFU/mL following the same schedule. The dose-limiting toxicity (DLT) evaluation period was 35 days from initial T-VEC administration. DLT was evaluated per the 3+3 design. Patients were DLT evaluable if they

received 2 doses of T-VEC within the 35-day window unless DLT occurred after the first dose before the end of the 35-day window.

Results: Overall, 11 patients (10 in A1, 1 in B1) were enrolled. As of July 26, 2020, 4 patients remained on study. Median age was 14 years, 7 patients (64%) were male, 7 (64%) had HSV-1 positive serostatus, 10 (91%) had metastatic disease, and 10 (91%) had prior anticancer therapy. Tumor types included soft-tissue sarcoma (n=5), bone sarcoma (n=3), neuroblastoma (n=1), nasopharyngeal carcinoma (n=1), and melanoma (n=1). The most common treatment-related adverse events (TRAEs) were grades 1-2 pyrexia (55%), grades 1-2 fatigue (27%), and grade 1 vomiting (27%). Two patients (18%) had grade ≥3 TRAEs (asthenia, pulmonary embolism; n=1 each) which occurred outside of the DLT window. The DLT analysis set included 9 patients; no DLTs were observed. No patients had herpetic events. No objective response was noted. Nine patients were assessed for best overall responses: 4 (44%) had progressive disease, 3 (33%) had stable disease (2 soft-tissue sarcoma, 1 melanoma), and 2 (22%) were unevaluable.

Conclusion: T-VEC is thus far tolerable in pediatric non-CNS solid tumors with no DLTs reported. Enrollment is ongoing in the US and EU.
Study supported by Amgen Inc.

Poster # 104

TUMORS OF THE RIBS DIAGNOSED AT A REFERRAL CENTER IN CENTRAL CALIFORNIA

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Background: Chest wall primary bone tumors account for only 5-8% of all skeletal masses. Ewing sarcoma (EWS) is the most common diagnosis, while osteosarcoma and other types of sarcomas are much more rare. Disseminated Coccidioidomycosis, although infrequent, can affect almost any organ system with up to 50% having skeletal involvement. Coccidioidomycosis has been labeled “the great imitator” as it can mimic many diseases, including neoplastic processes.

Objectives: To describe the clinical spectrum of rib lesions and/or masses diagnosed at the largest referral center in Central California.

Design/Method: Retrospective chart review from January 2002 to December 2019 of pediatric patients with rib lesion and/or mass diagnosed at Valley Children's Hospital, the largest referral pediatric cancer center in the San Joaquin Valley. Demographics, clinical findings, laboratory and radiographic data were collected.

Results: Over the 17 year period, we encountered 18 patients with rib lesions. Male:Female ratio was 11:7. Age ranged from 2 – 17 years (median= 12). We found 14 neoplastic tumors and 4 *Coccidioides* infection related rib masses. Of the neoplastic processes, the majority were EWS (N=10), followed by Langerhans cell histiocytosis (N=2), osteosarcoma (N= 1), and

chondrosarcoma (N=1). All patients presented with rib pain or mass. Fever was the most common presentation in *Coccidioides* infection compared to EWS (75% vs 25%). Our data demonstrates significant overlap in terms of symptoms and laboratory findings for neoplastic rib tumors vs coccidioidomycosis. Patients with neoplastic tumors and coccidioidomycosis both demonstrated elevated LDH and ESR. However, ESR was elevated in the range of 34 – 66 mm/h (median 38 mm/h) in the neoplastic tumors group vs. 61 – 120 mm/h (median 66 mm/h) in the coccidioidomycosis group. There were no characteristic trends with regards to WBC, ANC, ALC, Hb, or platelets. Imaging studies demonstrated overlapping features. On MRI, both neoplastic and coccidioidomycosis lesions demonstrated T1 hypointense and T2 hyperintense signal abnormalities, some with extraosseous extension or cortical bone destruction. The ultimate diagnosis was performed with histopathological examination and *Coccidioides* infection was confirmed with cultures and serology results.

Conclusion: As expected, the most common malignant tumor of the ribs is EWS, with other sarcomas and histiocytosis seen with less frequency. *Coccidioides* infection should be considered in the differential diagnosis of rib lesion and/or mass in endemic areas such as the San Joaquin Valley of California. In such areas, the diagnostic work up should include fungal cultures and serology in addition to histopathological examination.

Poster # 105

NEUROBLASTOMA RESPONSE CORRELATES WITH ALTERATIONS IN NK CELL AND TREGS FOLLOWING DINUTUXIMAB

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Background: Despite improvement in outcomes for patients with relapsed or refractory high-risk neuroblastoma (R/R HR-NBL) with dinutuximab in combination with irinotecan, temozolomide, and granulocyte macrophage colony-stimulating factory (I/T/DIN/GM-CSF) outcomes remain poor. Response to dinutuximab, in large part, requires natural killer (NK) cells to mediate antibody-dependent cellular cytotoxicity (ADCC). However, other immune cells, including T conventional and regulatory T cells (Tregs), also play critical roles.

Objectives: To characterize the immune landscape in patients with R/R HR-NBL treated with I/T/DIN/GM-CSF and to correlate these findings with disease-specific outcomes.

Design/Method: Peripheral blood mononuclear cells were isolated from patients using density gradient centrifugation and immediately cryopreserved. T-, B-, and NK cell subtypes were analyzed with respect to markers of differentiation, activation, and exhaustion using a 21 color multiparameter flow cytometry panel. Spectral analysis of the panel was validated using samples from control patients. Fresh and cryopreserved samples were tested either immediately following thawing or after being rested for 18 hours at $37^{o}/5\%CO_2$. Rested samples led to superior results that closely reflected those in matched fresh samples.

Results: Seventeen samples from 5 individual patients with R/R HR-NBL who were treated with I/T/DIN/GM-CSF have been analyzed. Patients had an increase in the percentage of Tregs following cycle 1 that was sustained throughout the remainder of therapy. The mean percentage of Tregs prior to therapy was 1% (+/- 0.5) compared to 6.1% (+/- 2.4) post-therapy (*p-value* 0.006). Concurrently, there was a progressive decrease in cytotoxic NK cells in patients post-treatment of 34.5% (+/- 35) down to 5% (+/- 3.7) (*p-value* 0.009). Cytotoxic NK cells in patients who achieved a complete remission (CR) or developed stable disease (SD) were 10.4% (+/- 4.3) compared to 2.13% (+/- 1.4) in patients who developed progressive disease (PD) (*p-value* 0.004). Additionally, compared to patients with CR or SD, those with PD developed evidence of cytotoxic NK cell exhaustion with increased expression of the immune checkpoint proteins TIGIT and TIM-3.

Conclusion: Treatment with I/T/DIN/GM-CSF was associated with a decreasing percentage of cytotoxic NK cells and increasing percentage of Tregs in patients with R/R HR-NBL. Favorable response following treatment with I/T/ DIN/GM-CSF correlated with higher levels of non-exhausted cytotoxic NK cells. Additional patients and samples are needed to further verify predictive biomarkers of treatment success or failure and to identify potential therapeutic opportunities to enhance the efficacy of dinutuximab.

Poster # 106

USP7 IS A PROMISING THERAPEUTIC TARGET FOR NEUROBLASTOMA

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Background: The ubiquitin-proteasome system plays an essential role in post-translational modification to maintain proteostasis. Ubiquitination of a target protein is coordinated by different enzymes, which add and link ubiquitin in specific ways that determine the fate of the protein. Ubiquitination is further regulated by deubiquitinases, which remove ubiquitin and rescue the target protein from being degraded. Dysregulation of the ubiquitin-proteasome system has been linked many human diseases, including cancer. Ubiquitin-specific protease 7 (USP7) is a deubiquitinase that plays a critical role in immune response, tumor suppression and DNA repair. Overexpression of USP7 has been associated with tumor aggressiveness in a variety of tumors, including in neuroblastoma. Therefore, USP7 is a potential therapeutic target for neuroblastoma. Almac4 is a highly potent and selective small molecule inhibitor of USP7 that has demonstrated significant antitumor activity in preclinical models of adult cancer. We hypothesize that inhibition of USP7 will be effective against neuroblastoma tumor growth.

Objectives: To evaluate the efficacy of USP7 inhibition with Almac4 against neuroblastoma tumor growth.

Design/Method: Neuroblastoma cell lines were treated with increasing concentrations of Almac4 alone and in combination with chemotherapy. Cell proliferation was measured using continuous live cell imaging. Cell viability was measured using AlamarBlue assay. Apoptosis

was measured by caspase cleavage using Caspase 3/7 apoptosis assay as well as by PARP cleavage seen by Western Blotting. Changes in various protein were measured by Western blotting.

Results: Pharmacologic inhibition of USP7 resulted in significant decreases in both cell proliferation and cell viability *in vitro* only in *TP53* wild-type neuroblastoma cell lines. There was no correlation seen between *MYCN* amplification status and treatment response. USP7 inhibition induced apoptosis with dose-dependent increase in both caspase and PARP cleavage. Treatment with Almac4 led to increased protein expression of p53 in all sensitive cell lines tested and increased protein expression of MYCN in *MYCN*-amplified cell lines. In addition, the combination of Almac4 with chemotherapy commonly used in neuroblastoma showed enhanced efficacy.

Conclusion: Our data suggests that USP7 inhibition may be a promising therapeutic strategy for children with high-risk and relapsed neuroblastoma.

Poster # 107

THE ROLE OF GALNT14 IN CHEMORESISTANT AND METASTATIC OSTEOSARCOMA

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Background: Osteosarcoma is the most common bone tumor in children and adolescents. Many patients have disease progression through standard chemotherapy regimens of methotrexate, cisplatin, and doxorubicin. Presently, there are no salvage therapies that have added significant survival benefits, leaving minimal options for relapsed and resistant disease. Additionally, there are no clinically significant biomarkers for this disease that would predict treatment failures. *N-acetylgalactosyltransferase 14* (*GALNT14*) is an enzyme that initiates O-linked glycosylation to outer membrane-bound and extracellular proteins. Using transcriptomic analyses, we identified *GALNT14* overexpression correlated with poor tumor necrosis and survival outcomes. Therefore, we hypothesize that *GALNT14* contributes to metastatic and chemoresistant phenotypes in pediatric osteosarcoma.

Objectives: We aim to evaluate *GALNT14* expression as a prognostic biomarker in pediatric osteosarcoma.

Design/Method: Transcriptomic data from the Therapeutically Applicable Research for Generating Effective Treatments (TARGET) database and RNA-sequencing of institutional patient-derived xenografts (PDXs) revealed that overexpression of *GALNT14* correlated to poor necrosis rates. Gene Set Enrichment Analysis (GSEA) also identified upregulation of glycosylation pathways. Aberrant expression of *GALNT14* was confirmed using quantitative polymerase chain reaction (qPCR) and Western blot analyses in various osteosarcoma cell lines.

Transient *GALNT14* knockdown and overexpression were then analyzed for effects on proliferation, invasion, migration, and chemotherapy response *in vitro*. Kaplan-Meier curves demonstrating overall survival (OS) and event-free survival (EFS) were established using data from the TARGET database.

Results: *GALNT14* expression was higher in both commercial and PDX cell lines that were known to be more prone for chemoresistance and invasiveness. The highest quartile of patients based on *GALNT14* overexpression had 40% OS and 25% EFS, compared to 80% ($p=0.002$) and 75% ($p<0.001$) for the lowest quartile of expression, respectively.

Conclusion: *GALNT14* shows promise as a predictive marker of chemoresistance and metastasis for pediatric osteosarcoma. Future functional genomic studies through gain and loss-of-function studies will evaluate the role of GALNT14 in osteosarcoma chemoresistance and metastatic potential.

Poster # 108

GENETICALLY DETERMINED HEIGHT, BIRTHWEIGHT, AND PUBERTY TIMING AND RISK OF OSTEOSARCOMA.

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Background: Osteosarcoma is the most common malignant primary bone tumor in children. Known risk factors for osteosarcoma include radiation, chemotherapy, and some cancer predisposition syndromes. Although evidence is not consistent, several studies have also linked increased osteosarcoma risk with tall stature, high birthweight, rapid adolescent growth, and early puberty.

Objectives: To evaluate the risk of osteosarcoma associated with genetically inferred height, puberty timing, and birthweight by constructing genetic risk scores (GRS) using previously established genetic loci for these traits.

Design/Method: Genotype data from two genome-wide association studies (GWAS) of European ancestry were used to construct GRS (GWAS 1: N=968 cases, 2927 controls; GWAS 2: N=71 cases, 212 controls). Five GRS were created using previously published SNPs for height (N=3,305), pubertal height growth (N=10), birthweight (N=211), and puberty timing [i.e., female age at menarche (N=389), and male age at voice breaking (N=76)]. Each GRS was created by multiplying the number of alleles by its reported weight and summing across all SNPs. Each GRS was evaluated as a continuous variable and categorized into quartiles. Association analyses were conducted using logistic regression for each study overall and, for the larger study,

stratified by age at diagnosis (i.e., during puberty vs. outside puberty peak), metastasis, tumor location (i.e., appendicular vs. axial), and histology. Results from the two studies were combined using a fixed-effects meta-analysis.

Results: There were significant associations ($p<0.05$) between osteosarcoma and genetically determined birthweight. In the combined analysis, higher genetically determined birthweight was associated with an increased risk of osteosarcoma ($OR_{\text{per Z-score standard deviation}}$ =1.65, 95% CI 1.11-2.45, p=0.01). Compared to the lowest quartile of birthweight GRS, the highest quartile was associated with 1.31-fold elevated risk (95% CI 1.07-1.61, p=0.01). The association was stronger for males ($OR_{\text{per Z-score standard deviation}}$ =1.85, 95% CI 1.12-3.06, p=0.02), age of diagnosis outside of the puberty peak (OR=1.90, 95% CI 1.12-3.21, p=0.02), no metastatic disease at diagnosis (OR=2.55, 95% CI 1.5-4.32, p=0.0005), conventional histology (OR=2.68, 95% CI 1.56-4.59, p=0.0004), and appendicular tumor location (OR=1.69, 95% CI 1.11-2.56, p=0.01).

There were no statistically significant associations between osteosarcoma and GRS for tall stature, pubertal height growth, age of menarche, or male puberty timing.

Conclusion: A genetic propensity to higher birthweight was associated with increased osteosarcoma risk, suggesting that biological pathways that affect birthweight may contribute to osteosarcoma pathogenesis and osteosarcoma may have an in-utero origin. Further studies are needed.

Poster # 109

YAP1 IS A KEY REGULATOR OF G2/M TRANSIT IN FUSION-POSITIVE RHABDOMYOSARCOMA

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Background: Fusion-positive rhabdomyosarcoma (FP-RMS), driven by the fusion oncogene PAX3-FOXO1 (P3F), is among the most difficult to treat pediatric cancers. P3F is believed to promote G2/M "checkpoint adaptation" - cell cycle progression despite unrepaired DNA. While checkpoint adaptation may contribute to therapy resistance in FP-RMS, the underlying mechanisms responsible for this process are poorly understood. Since P3F is not currently pharmacologically targetable, we sought to identify therapeutically tractable co-activators. We hypothesized YAP1, a transcriptional co-activator and major effector of the Hippo signaling pathway, is required for G2/M transit and mediates G2/M checkpoint adaptation.

Objectives: To investigate the requirement for YAP1 on G2/M cell cycle progression; to evaluate whether YAP1 may contribute to resistance mechanisms for FP-RMS therapies targeting the G2/M checkpoint.

Design/Method: In human FP-RMS cell lines, YAP1 gain- and loss-of-function was achieved using vectors expressing control, wild-type YAP1, constitutively active mutant YAP1 (S127A), and shRNA or CRISPR/Cas9 knockdown. mRNA and protein-level expression of YAP1 and P3F were evaluated with qRT-PCR and immunoblot. Cell cycle analysis using propidium iodide staining with flow cytometry was used to determine the functional requirement for YAP1 in promoting G2/M progression. Co-immunoprecipitation-coupled mass spectroscopy (IP-MS) was used to identify G2/M regulatory proteins that physically associate with YAP1. RNA-Seq and quantitative tandem-mass tag mass spectrometry (TMT-MS) were used to determine the impact of YAP1 suppression on the cyclins and kinases involved in cell cycle regulation. Pharmacologic inhibition of YAP1 activity was tested in murine xenograft studies using verteporfin (VP) and with VP in combination with vincristine (VCR).

Results: YAP1 promotes G2/M transit and is able to partially rescue FP-RMS cells from a G2 arrest caused by either VCR or siRNA suppression of P3F. IP-MS revealed that YAP1 physically associates with regulatory proteins involved in the G2/M checkpoint. Further, RNA-Seq and TMT-MS demonstrated that YAP1 is required for the differential expression of proteins involved in G2/M transit, and that YAP loss leads to upregulation of proteins involved in TP53 signaling. YAP1 mRNA expression is upregulated in VCR-resistant FP-RMS cells. Additionally, FP-RMS expressing YAPS127A are more resistant to VCR. In xenografts, combining VP with VCR is more efficacious than either agent alone.

Conclusion: YAP regulates the G2/M checkpoint and is required for G2/M progression in FP-RMS. YAP1 may contribute to checkpoint adaptation and acquired VCR resistance. Thus, YAP1 is a promising therapeutic target in FP-RMS. Although additional studies are required, combining YAP inhibition with current FP-RMS antitubulin agents may prevent therapy resistance.

Poster # 110

OSTEOSARCOMA: A SURVEILLANCE, EPIDEMIOLOGY, AND END RESULTS PROGRAM ANALYSIS FROM 1975 TO 2017

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Background: Osteosarcoma is the most common primary bone tumor in children, and peak incidence occurs during the adolescent growth spurt. Recent studies have reported that the youngest cases (aged <10 years) have the highest frequency of pathogenic germline genetic variants in established cancer susceptibility genes, potentially suggesting their genetic etiology is different than adolescent or adult onset cases. However, studies have historically grouped all children and young adult cases together due to small sample sizes, which limits understanding of the unique epidemiologic factors for more specific age groups and the youngest cases of osteosarcoma. The National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program offers a unique opportunity to perform detailed incidence and survival analyses

of rare neoplasms, covering up to 34% of the US population.

Objectives: To perform a detailed analysis of osteosarcoma incidence and survival patterns to better understand the epidemiologic differences by specific age groups, particularly for the youngest cases.

Design/Method: Incidence and survival rates for 2,694 children and adolescents with osteosarcoma from SEER (1975-2017) were analyzed by age (0-9 and 10-24 years), race, histologic subtype, stage, and tumor location using SEER*Stat software.

Results: For the youngest cases (0-9 years), incidence of primary osteosarcoma increased significantly throughout the study period (annual percent change=1.1, $p<0.05$); was greatest in Blacks; and, approximately equal between sexes. The 5-year relative survival (RS) for these young cases has steadily increased from 25% in the 1970s to 80% in the most recent decade. Survival was highest for Hispanics (73%), and similar by sex. For the 10-24 age group, incidence was greatest in Blacks and males. The 5-year RS was 66% in the most recent decade, significantly increased from the 1970s and 1980s ($p<0.05$) but decreased from the 1990s. Survival was higher for females versus males, and Whites had the highest survival rate by race (69%). For all cases aged 0-24 years, the incidence of secondary osteosarcoma increased 3-fold since the 2000s. The 5-year RS for metastatic disease in all cases aged 0-24 was 36%.

Conclusion: This is the most comprehensive population-based analysis of osteosarcoma incidence and survival in children and adolescents to date. We identified important differences in osteosarcoma incidence and survival for the youngest cases compared to the adolescents. Overall, the incidence of secondary osteosarcoma is rising, likely reflecting an increased number of young childhood cancer survivors. Our study illustrates the importance of analyzing specific age groups to better understand their unique epidemiology and underlying biology.

Poster # 111

EFFECT OF LEROCICLIB ON PEDIATRIC SARCOMAS

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Background: Cyclin-dependent kinases 4 and 6 (CDK4/6) are responsible for regulating cell cycle progression from G1 to S phase. Once activated, CDK4/6 phosphorylates retinoblastoma (Rb) protein, deactivating its tumor suppressor function. Dysregulation of the cell cycle through upregulation of CDK4 is common in many cancers, including osteosarcoma and synovial sarcoma. CDK4/6 inhibitors are approved for use in estrogen receptor positive breast cancer. An improved CDK4/6 inhibitor leading to less neutropenia, lerociclib, has yet to be evaluated in pediatric malignancies, including osteosarcoma and synovial sarcoma.

Objectives: To evaluate the effects of lerociclib on osteosarcoma and synovial sarcoma cells *in vitro*.

Design/Method: We investigated two established osteosarcoma cell lines (U2-OS and MG-63) and two patient-derived xenograft lines (COA54 – osteosarcoma, COA79 – synovial sarcoma). Cells were treated with increasing doses of lerociclib. Western blotting evaluated the effect of lerociclib on phosphorylated Rb (pRb), and expression of total Rb, CDK4 and CDK6. Cell proliferation and viability were examined using CellTiter96® and alamarBlue® assays, respectively. Motility was evaluated with modified Boyden chamber and wound healing assays. Cell cycle was assessed with flow cytometry.

Results: Immunoblotting demonstrated CDK4 and CDK6 were expressed in all cell lines, and increasing concentrations of lerociclib led to decreased phosphorylated Rb. In U2-OS cells treated with lerocicib (5μM), proliferation was decreased by 58% ($p \leq 0.01$), and viability was decreased by 55% ($p \leq 0.01$). At the same dose, MG-63 cells had a decrease in proliferation by 43% ($p \leq 0.05$) and viability by 72% ($p \leq 0.01$). In COA54 cells, proliferation was reduced by 84% ($p \leq 0.05$) and viability by 87% ($p \leq 0.05$) with lerociclib (4μM). Similarly, COA79 cells demonstrated a decrease in proliferation by 73% ($p \leq 0.01$). Viability was reduced by 69% ($p \leq 0.05$). U2-OS cells treated with 2.5 μM of lerociclib showed cell cycle arrest with increased percentage of cells in G1 phase and decreased percentage of cells in S phase. Lerociclib decreased migration (by 55 ±0.04%, $p \leq 0.01$) and invasion (by 55 ± 0.12%, $p \leq 0.05$) in U2-OS cells. Similarly, motility of MG-63 cells was significantly reduced following lerociclib treatment ($p \leq 0.01$).

Conclusion: Lerociclib treatment led to decreased cell proliferation, viability, migration and invasion and a halt in cell cycle progression in osteosarcoma and synovial sarcoma cells. These findings suggest lerociclib may be a promising therapeutic option for these difficult to treat tumors.

Poster # 112

USE OF QUANTITATIVE ULTRASOUND IN PEDIATRIC OSTEOSARCOMA AND EWING SARCOMA: A NEW SCREENING TOOL?

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Background: Studies have identified adverse effects on bone mineral density (BMD) in childhood cancer survivors[1], with up to 2/3 of survivors of bone sarcoma being affected[2]. Treatment in the majority of bone sarcomas occurs in adolescents, thus during a critical period in the development of bone density. Survivors are potentially left at long-term increased risk of fractures and osteoporotic complications.[3]
Dual-radiograph absorptiometry (DXA) is the standard for evaluating BMD. Other tools such as Quantitative Computed Tomography (QCT) and Quantitative Ultrasound (QUS) continue to be evaluated. The use of QUS eliminates exposure to ionizing radiation, costs less than DXA, and

does not require sedation even in young children. Calcaneal QUS has been used a screening tool for osteoporosis,[4] and normal values for calcaneal QUS in healthy children have been established. A pilot study in children with leukemia demonstrated that QUS calcaneal measurements correlated with whole-body, lumbar, and femoral neck DXA measurements.[5]

Objectives: To prospectively evaluate BMD changes in newly diagnosed pediatric patients with OS and ES during and after treatment and to investigate the use of calcaneal QUS as a novel screening tool for the assessment of BMD in this patient population.

Design/Method: Prospective evaluation of BMD via DXA scan and bilateral calcaneal QUS of 10-12 patients with OS or ES at 5 time points: at diagnosis, after competition of induction chemotherapy but before local control, at completion of therapy, and 6-12 months after completion of therapy.

Results: 9 patients were enrolled after surgical resection, and only 2/9 enrolled prior to end of therapy. BMD reported by DXA and QUS were not highly correlative, showing a 40-60% difference. QUS reported more osteopenia and did not miss any osteopenia found by DXA. There was a significant difference in z-scores from both measurements in affected versus unaffected limbs for all 9 patients, that persisted over the follow-up period. 3/9 patients who enrolled before or close to end of therapy date showed improving BMD z-scores over time, and 6/9 patients who enrolled at least 3 months after therapy showed BMD z-scores that were decreased but stable over time.

Conclusion: QUS cannot reliably be used as a diagnostic tool to diagnose osteopenia, but can be used as a cost-effective, non-irradiating tool to pre-screen bone density in this patient population. Our study was limited by difficulty enrolling patients in the challenging time period of new diagnosis.

Poster # 113

SHAVE BIOPSY OF PEDIATRIC MELANOCYTIC TUMORS COMPROMISES STAGING AND THERAPY PLANNING

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Background: Melanoma is the primary skin cancer of pediatric patients, and accounts for 1-3% of pediatric malignancies. The prognosis for both adults and children with melanoma correlates with stage at diagnosis, with initial Breslow depth being a critical component. Kaplan-Meier melanoma-specific survival curves show survival rates ranging from 98% (T1a) to 75% (T4b) at 10 years for adult patients with stage I and II disease at diagnosis. Pediatric patients are known to present with thicker primary melanomas as compared to their adult counterparts. The preferred biopsy method by the American Academy is Dermatology for melanoma is excisional, however a partial biopsy by shave method is most frequently performed in children given its simplicity,

efficiency, and often low clinical suspicion for cutaneous malignancy. Despite the ease of biopsy technique, shave biopsy has a high rate of base transection, reducing accuracy of microstaging, which is crucial for appropriate therapy planning.

Objectives: Describe the effect of biopsy method on accurate staging, surgical recommendations, and treatment approach for pediatric patients with melanocytic tumors.

Design/Method: Retrospective chart review.

Results: Data was available for 91 pediatric patients with a spectrum of melanocytic tumors ranging from atypical with unknown malignant potential, to melanoma. Patient characteristics including gender, age at biopsy, biopsy method, status of biopsy margins, recommendations for re-excision, sentinel lymph node biopsy, and treatment plan were collected and analyzed. There were 48 females and 43 males with age range 1—22 years (mean, 10 years). Sixty-eight of 91 (75%) tumors had a positive margin on diagnostic biopsy, 52/68 (76.5%) were via shave method. Of all shave biopsies, 86% had positive biopsy margin as opposed to only 16% using alternative biopsy methods. In 10/91 (11%) patients, surgical recommendations were changed based on inaccurate microstaging due to positive biopsy margins, 9/10 (90%) of these patients had undergone shave biopsy. Most (8/10) patients had melanoma, the remaining 2/10 had highly atypical spitzoid tumors in which melanoma could not be ruled out.

Conclusion: Pediatric patients with melanocytic tumors at our institution most commonly underwent shave biopsy as the initial diagnostic biopsy method. This method of biopsy was associated with higher incidence of positive margins at diagnosis and more aggressive definitive surgical management. These findings suggest that more routine use of excisional biopsy in pediatric patients with lesions being evaluated for malignancy could lead to decreased incidence of positive margins and reduce the need for more aggressive definitive surgical management.

Poster # 114

PATIENT-DERIVED HEPATOBLASTOMA TUMOROIDS DEPEND ON BOTH RTK SIGNALING AND WNT ACTIVATION

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Background: Hepatoblastoma is the most common primary liver malignancy in children, with rising incidence, but progress in developing targeted and less toxic treatments has been hindered by the disease's rarity and a relative lack of robust experimental models.

Objectives: The goal of this study was to obtain primary patient-derived 3D cultures of hepatoblastoma for genomic and functional studies.

Design/Method: We adapted previously published protocols for 3D culture of primary hepatocytes and adult liver cancer cells to obtain 3D cultures of primary hepatoblastoma tumor cells, termed "tumoroids". We characterized gene expression in early passage tumoroids using bulk quantitative RT-PCR as well as single cell RNA sequencing with the 10x Genomics platform. We further investigated the requirement of specific growth factors on tumoroid colony formation.

Results: We successfully obtained primary 3D tumoroids from five patients with hepatoblastoma treated at LPCH and UCSF. These patient-derived tumoroids all had heterozygous mutations involving exon 3 of the *CTNNB1* gene, known to result in constitutive activation of the Wnt pathway. The tumoroids expressed known markers of hepatoblastoma, including *AFP* and *DLK1*, as well as Wnt targets, *AXIN2*, *DKK1*, and *TBX3*. In addition to expression of hepatocyte markers, hepatoblastoma tumoroids also maintained high expression of cholangiocyte markers, suggestive of an early progenitor stage in hepatoblast differentiation. Three of the hepatoblastoma tumoroid cell lines required exogenous growth factors acting through receptor tyrosine kinase pathways via MEK in order to form colonies from single cells. Interestingly, one of the hepatoblastoma tumoroid cell lines formed colonies without requiring the addition of exogenous growth factors. Using single cell RNA sequencing analyses, we identified in this tumoroid cell line a unique subset of tumor cells expressing FGF19, which we hypothesize acts in a paracrine fashion to drive tumor proliferation.

Conclusion: Our results support the hypothesis that hepatoblastoma depends on receptor tyrosine kinase signaling through MEK, in addition to constitutive Wnt pathway activation, for cell cycle progression and proliferation. We identify paracrine FGF19 signaling as a potential mechanism by which a subset of hepatoblastomas may fuel their own growth.

Poster # 115

LOW GRADE NEUROEPITHELIAL TUMORS: SINGLE INSTITUTIONAL 20 YEARS EXPERIENCE

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Background: Low grade neuroepithelial tumor (LGNET) including ganglioglioma and dysembreyoplastic neuroepithelial tumor (DNET) are low grade brain tumor in children frequently associated with seizure. It has benign nature of course with excellent survival outcome. When non-surgical treatment is needed, it has been treated similar to other low grade glioma (LGG) and rarely described the outcome separately. With the advanced knowledge of molecular study showing the distinct features of LGNET from other LGG, it leaves the question if LGNET should be treated same as other LGGs.

Objectives: Identify treatment approach of LGNET and its response for tumor control and seizure control.

Design/Method: Retrospective chart review and review of literature.

Results: Our cohort included 26 patients with mean age at diagnosis of 9 years (range: 1 to 17 years). Nine patients had DNET and seventeen patients were diagnosed with ganglioglioma. Most common clinical presentation was seizure (8/9 for DNET, 6/17 for ganglioglioma) and one ganglioglioma patient was found to have seizure after diagnosis. Molecular analysis was performed on ten patients and revealed FGFR1 duplication in 1/2 patient with DNET and BRAF V600E mutation in 7/8 patients with ganglioglioma. Overall survival for the entire cohort was 100% with the median follow up time of 63 months. Twelve patients who had gross total resection did not require adjuvant therapy or had relapse at their last follow up. Among the rest of 14 patients with residual disease after the first surgery, 12 patients were observed with serial MRIs, one patient received upfront chemotherapy and one patient received radiation therapy. Seven patients developed disease progression/relapse for which three underwent second surgery, three received chemotherapy, and one had radiation. None of DNET patients received chemotherapy or radiation. The combination of vincristine and carboplatin was the most frequent (3/4) used first line chemotherapy and two patients received BRAF molecular targeted therapy due to further relapse. Majority of patients (6/8 for DNET and 7/7 for ganglioglioma) remain on antiepileptics at the last follow up and two DNET patients who had gross total resection came off from antiepileptics.

Conclusion: While patients with gross total resection have an excellent tumor outcome, those with residual disease are at risk of disease progression. Disease progression/relapse was frequent when ganglioglioma was treated with conventional chemotherapy LGG protocol. With the knowledge of molecular features, this group may benefit with a different approach including upfront molecular target therapy. Long term follow up is warranted for seizure control even with gross total resection.

Poster # 116

STUDY OF CJOC42 DERIVATIVES ALONE & IN COMBINATION WITH CHEMOTHERAPY FOR TREATMENT OF LIVER CANCER

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Background: Gankyrin is an established oncoprotein that is overexpressed in pediatric liver cancer. This member of the ubiquitin proteasome system leads to degradation of tumor suppressor proteins which allows for uncontrolled proliferation and has been linked to chemoresistance in several other solid tumors. Cjoc42 is a small molecule inhibitor of Gankyrin which has shown anti-proliferative effects in cell culture. Second generation Gankyrin inhibitors, known as cjoc42 derivatives, have since been developed with better affinity to and inhibition of Gankyrin.

Objectives: The goal of this study was to determine the anti-proliferative activity and downstream biological effects of three cjoc42 derivatives (AFM-1-2, DK-1-7, and JA-1-38) in established pediatric liver cancer cell lines.

Design/Method: All studies were done in HepG2 (human hepatoblastoma) and Hep3B (pediatric hepatocellular carcinoma) cell lines. Proliferation assays were performed to identify IC50 dosing for each compound. Quantitation of tumor suppressor proteins and cell cycle markers were measured by Western blotting and QRT-PCR. To evaluate for apoptosis, flow cytometry and an apotracker green dye fluorescence assay were performed. We also measured drug synergy to cisplatin and doxorubicin using Combenefit software.

Results: The IC50 for cjoc42 derivatives ranged from 17-46 uM in HepG2 cells and 20-26 uM in Hep3B cells. IC50 for cjoc42 was > 50 uM in both cell lines. All cjoc42 derivatives demonstrated an increase in several tumor suppressor proteins. Interestingly, while Gankyrin works on a protein level, we also found a consistent decrease in mRNA expression of tumor suppressors treated with cjoc42 derivatives. HepG2 and Hep3B cells demonstrated increased apoptosis after treatment with cjoc42 inhibitors. Drug synergy was identified between cjoc42 derivatives and doxorubicin in both cell lines. No synergy was detected with cisplatin in HepG2 cells, but antagonism was identified. In Hep3B cells, synergy was seen at lower concentrations and antagonism at higher concentrations.

Conclusion: Cjoc42 derivates demonstrate good Gankyrin inhibition with reduction in proliferation, rescue of tumor suppressor proteins, and increased apoptosis. While the IC50 concentration is less than cjoc42, it is still too high to be clinically relevant as a single agent. In combination with doxorubicin, however, there was significant drug synergy identified, which may be an effective therapeutic strategy in chemoresistant tumors. Further *in vivo* work is needed next to study safety, confirm efficacy, and understand mechanisms of drug synergy.

Poster # 117

GEMCITABINE-OXALIPLATIN-LENVATANIB FOR UNRESECTABLE/REFRACTORY FIBROLAMELLAR CARCINOMA: 12 PATIENTS

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Background: Fibrolamellar carcinoma (FLC), an extremely rare primary liver cancer of children and young adults with no underlying liver disease, that often presents at an advanced stage with minor and non-specific symptoms. There are no proven systemic therapies for the treatment of FLC, and surgery remains the only potentially curative option. There is a need for effective systemic treatments. We describe 12 patients, most of whom had multiple prior surgeries and systemic therapies, who were judged unresectable. We chose gemcitabine-oxaliplatin (GEMOX) as a backbone based on case reports of GEMOX efficacy in FLC, combined with the oral antiangiogenic/multi-kinase inhibitor lenvatanib (LEN), based on hepatocellular carcinoma (HCC) data and similarity to the GEMOX- sorafenib approach in the current COG trial

AHEP1531, but with expected less toxicity and more efficacy then sorafenib, as previously reported for HCC.

Objectives: The purpose of this study was to evaluate a combination systemic chemotherapy consisting of gemcitabine (1000mg/m^2 day 1), oxaliplatin (100mg/m2 day 1) and lenvatanib (8mg <60Kg, 12mg > 60kg po daily) [GEMOX-LEN] repeated every 14 days, for the treatment of refractory, relapsed, metastatic, or unresectable FLC.

Design/Method: Data from all patients receiving GEMOX-LEN between April 15, 2019 and January 10, 2021 were reviewed. All were assessed for toxicity. Those having received at least 6 cycles with follow up imaging obtained at least two months after initiation were assessed based for objective response based on RECIST 1.1, progression and survival.

Results: During the study period, 12 patients were treated with GEMOX-LEN, 10 of whom were evaluable based on inclusion criteria. The median age was 16 (7-33, 5M/7F), with a median of 9 cycles (2-18). Median progression-free survival (PFS) was 7 months (2-14). By RECIST 1.1 criteria, one patient achieved clinical remission, 5 had a partial response, 4 had stable disease. The overall objective response (clinical remission + partial response) was 60%, and tumor control rate (clinical remission + partial response + stable disease) was 100%. Five unresectable patients, became resectable and were able to have aggressive resections. No one stopped due to toxicity, but 4 patient had dose reduction due to side effects attributable to oxaliplatin (neuropathy, allergy, neutropenia). There were no deaths.

Conclusion: This is preliminary, in controlled data. However, we believe gemcitabine-oxaliplatin-lenvatanib to be a promising option in FLC and make some patients surgical candidates, giving them a chance at cure. This regimen has been well-tolerated and can be administered in the outpatient setting. Research on GEMOX-Len is ongoing.

Poster # 118

CLINICAL, PATHOLOGIC AND MOLECULAR CHARACTERISTICS OF THYROID CANCERS IN PEDIATRIC CANCER SURVIVORS

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Background: The survival rate for childhood cancer has increased from 1970 to the present, with 5-year survival rates now approaching 80%. Secondary neoplasms are among the most serious long-term adverse health conditions in childhood cancer survivors. Radiotherapy was found to be associated with increased risk for development of secondary thyroid cancer (STC) in childhood cancer survivors.

Objectives: The aim of this study was to characterize clinical and pathological profiles and examine genomic alterations in patients with STCs.

Design/Method: This study consisted of a retrospective analysis of medical records from childhood cancers survivors seen at National Capital Consortium (NCC) for management of thyroid cancer. Formalin-fixed paraffin-embedded samples from STCs were used for extraction of nucleic acids and detection of BRAF, RAS, RET mutations/fusions. Microfluidic Digital PCRs were performed using QIAcuity Digital PCR System.

Results: Analysis of data from 620 thyroid cancer patients seen during 2010-2020 at the NCC revealed that 5 patients with history of pediatric malignancy. There were 2 men and 3 women; average age at diagnosis of primary malignancy was 8 ± 7 years. For the treatment of first malignancy chemotherapy was performed in all cases, and radiotherapy in 4/5 cases. All patients were in remission at the time of thyroid cancer diagnosis. The average age at the time of diagnosis of STC was 17.8 ± 10.9 years. The latency period between the diagnosis of first and second malignancy was 9.7 ± 5.8 years. STCs were discovered during routine follow up for primary malignancy. Total thyroidectomy was performed in all cases and histopathology revealed classical papillary thyroid cancers (CPTC) in 1 case, CPTC with areas of de-differentiation in 1 case; follicular variant PTC (FVPTC) in 2 case and solid variant PTC in 1 case. Extra thyroidal invasion into the strap muscle was found in 1 case. In 3/5 cases nucleic acids were of sufficient quality for genotyping. BRAFV600E mutations were detected in 1/3 cases. Treatment with radio-active iodine (RAI) was performed in 2 cases. Complete responses to the treatment were documented in 2 cases.

Conclusion: In survivors of pediatric malignancy STC develop within 10 years post-initial diagnosis. Subset of these tumors demonstrate aggressive morphology and harbor BRAFV600E mutations. Our data suggest that implementation of molecular-based techniques for the early detection of STC could be useful in patients with history of pediatric malignancy.

Poster # 119

COMBINATION OF 5-FLUOROURACIL, INTERFERON, AND NIVOLUMAB IN THE TREATMENT OF FIBROLAMELLAR CARCINOMA

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Background: Fibrolamellar carcinoma (FLC), an extremely rare primary liver cancer of children and young adults with no underlying liver disease, often presents at an advanced stage with minor and non-specific symptoms. There are no proven systemic therapies for the treatment of FLC, and surgery remains the only potentially curative option.

Objectives: The purpose of this study was to evaluate a combination systemic immunochemotherapy consisting of 5-fluorouracil (5-FU), interferon (IFN), and nivolumab for the treatment of refractory, relapsed, metastatic, or unresectable FLC.

Design/Method: Data from all patients receiving 5-FU, IFN, and nivolumab between May 2018 and January 2021 were reviewed. Those meeting the criteria of having received at least six

cycles of this immunochemotherapy with follow up imaging obtained at least two months after initiation were assessed based on objective response, survival, and toxicities.

Results: Twenty-seven total patients were treated with the combination of 5-FU, IFN, and nivolumab, 19 of whom were evaluable based on inclusion criteria. The median age at time of treatment was 24 (11-38). Patients received a median of 18 cycles (8-47). At time of analysis, the median progression-free survival (PFS) was 9.5 months (4.5-29), which was 52% longer than prior to initiating this immunochemotherapy. Eight patients achieved clinical remission during the study period, ten were stable or improving, and one progressed. The overall objective response (clinical remission + partial response) was 58%, and tumor control rate (clinical remission + partial response + stable disease) was 95%. Two patients stopped treatment due to side effects.

Conclusion: We believe combination immunochemotherapy with 5-FU, IFN, and nivolumab to be a promising treatment option to slow disease progression and prolong survival in patients with refractory, relapsed, metastatic, or unresectable FLC. This regimen has been well-tolerated and can be easily administered in the outpatient setting, contributing to a stronger quality of life. We continue to administer this combination therapy and obtain relevant data to confirm outcomes.

Poster # 120

MULTI-INSTITUTIONAL STUDY OF THE INCIDENCE AND OUTCOME OF PEDIATRIC IDH-MUTANT GLIOMA

Kee Kiat Yeo, Jennifer Cotter, Sanda Alexandrescu, Jayne Vogelzang, Jessica Clymer, Tom Rosenberg, Christine Chordas, Mary Ann Zimmerman, Kristina Cole, Marilyn Li, Emily Owens, Amy Smith, Stewart Goldman, Kristiyana Kaneva, Emily Burton, Kellie Nazemi, Susan Chi, Katherine Warren, Ashley Margol, Karen Wright

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Background: *IDH1/2* mutation have traditionally been thought to be rare in pediatric glioma with unclear incidence. In contrast, *IDH1/2* mutations are common in adult gliomas and associated with gliomagenesis and malignant transformation. It is unknown if the biology and prognosis of pediatric IDH-mutant gliomas are similar to adults. This is challenging, as the treatment approaches by pediatric and adult providers vary significantly.

Objectives: We aimed to describe the incidence, treatment approaches and outcomes of pediatric IDH-mutant glioma.

Design/Method: Incidence: Using next-generation sequencing (NGS) data of patients with pediatric (age:0-21) glioma (excluding ependymoma) sequenced at DFCI/BCH (2013-2019) and CHLA (2017-2019), we identified all patients with *IDH1/2* mutations and compared these to the number of gliomas sequenced during the respective timeframe.

Outcome: We performed a retrospective review of pediatric patients with *IDH1/2*-mutant gliomas treated at seven children's hospitals, analyzing clinico-genomic features, treatment approaches and survival outcomes.

Results: Incidence: We identified 425 patients with pediatric glioma diagnosed at DFCI/BCH and CHLA who underwent NGS. Of these, 42 (10.1%) were *IDH1/2* mutant. Among patients 0-9 and 10-21 years old, 2/186 (1.1%) and 40/237 (16.9%) had *IDH1/2*-mutant tumors, respectively. Among LGGs, 31/286 (10.8%) were IDH1/2 mutant, with 20 astrocytomas and 11 oligodendrogliomas. Among high-grade gliomas, 11/139 (7.9%) were IDH1/2 mutant, with one anaplastic oligodendroglioma and ten anaplastic astrocytoma/GBM. Most common co-occurring genetic alterations for astrocytomas were *TP53* and *ATRX* mutations.

Outcome: Fifty-two patients with IDH1/2-mutant glioma from seven collaborating sites were evaluable for outcomes with median follow-up of 4.7 years. Forty-one patients had astrocytic histology, while 11 patients had oligodendroglial histology. Eighty-five percent of patients with low-grade histology were managed observantly following surgery without additional therapy. For low-grade astrocytoma, 5-year progression-free survival (PFS) was 53% with a median PFS of 6.8 years (range:0.8-8.1). Among patients who experienced disease progression, 54% had histologic malignant transformation. Despite excellent short-term overall survival (OS; 10-year OS 85.7), numerous deaths after year ten were reported (15-year OS 34.2%). Patients with IDH-mutant high-grade astrocytoma had a 5-year PFS and OS of 32.1% and 80.5%, respectively.

For patients with oligodendroglioma, ten were grade II and one grade III histologically. Five- and 10-year PFS were 59.4% and 44.4% respectively, with no reported deaths (median followup:4.5 years; range:1.5-33.8).

Conclusion: A significant proportion of pediatric gliomas are characterized by *IDH1/2* mutations, substantially higher among adolescents. Findings suggest that the natural history is similar to those of adult IDH-mutant gliomas, supporting consideration for adopting/incorporating adult treatment approaches.

Poster # 121

OUTCOMES FOR CHILDREN WITH RECURRENT ATYPICAL TERATOID RHABDOID TUMOR: A SINGLE INSTITUTION STUDY

Steven Carey, Jie Huang, Sahaja Acharya, Brent Orr, Arzu Onar-Thomas, Layna Michalik, Paul Klimo, Jr., Frederick Boop, Thomas Merchant, David Ellison, Giles Robinson, Amar Gajjar, Santhosh Upadhyaya

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Background: Atypical teratoid rhabdoid tumor (ATRT) is an aggressive pediatric central nervous system malignancy associated with very poor outcomes despite the administration of multimodality therapy. However, data on survival and salvage therapies for patients who have

not been cured by frontline therapy are limited.

Objectives: To define progression-free survival (PFS) and overall survival (OS) for children with recurrent or progressive ATRT as determined from the time of recurrence to the date of subsequent progression or death.

Design/Method: We conducted a single-institution retrospective study of children <21 years old with ATRT that was recurrent or progressive disease (PD), and were treated and followed at St. Jude Children's Research Hospital, Memphis, United States, from 2000 to 2020. Demographic data, clinicopathologic features, and treatment details were collected for the 68 eligible patients, and outcome distributions were estimated by Kaplan–Meier analysis.

Results: Tumors from all 68 eligible patients had the typical histopathologic characteristics of ATRT. Tissue was available to confirm nuclear loss of INI1 by immunohistochemistry in 63 of 68 (93%). Median age at initial diagnosis was 1.5 years (range: 0–17.1 years) and at PD was 1.9 years (range: 0.3–17.9 years). Median time from initial diagnosis to PD was 5.2 months (range: 0.5–125.6 months), and median number of relapses was 2 (range: 1–9). PD was predominantly metastatic (*n*=33, 49%) or combined (*n*=22, 32%). Overall, 60 patients died from their disease after a median time of 4.2 months from PD (range: 0.2–55 months). Consequently, at a median follow-up of 0.4 years (range: 0.0–18.1 years) from PD, the 2- and 5-year PFS and OS for the cohort were 4.5% (±2.2%)/3.5% (±2.1%) and 21.1% (±4.8%)/9.3% (±3.9%), respectively. Of the patients without events after initial PD (*n*=3), the median follow-up time from PD was 14.1 years (range: 0.2–16.1 years). Seven patients are alive, with no evidence of disease (*n*=5), stable disease (*n*=1), or PD (*n*=1), and one was lost to follow-up. Salvage therapy in the 7 survivors included chemotherapy (*n*=7), re-resection (*n*=4), craniospinal radiation (*n*=4), focal radiation therapy (*n*=3), and targeted therapy (*n*=5).

Conclusion: We found a <4% 5-yr PFS and <10% 5-yr OS for children with recurrent ATRT. A few patients benefit from salvage therapies, including radiation or chemotherapy. Novel therapies are urgently needed for affected children. Molecular grouping and germline analysis of the study cohort are ongoing.

Poster # 122/Early Career Award Recipient

VIROIMMUNOTHERAPY FOR DIFFUSE INTRINSIC PONTINE GLIOMAS

Sumit Gupta, Virginia Laspidea, Juan Fueyo, Oren Becher, Teresa Nguyen, Dong Ho Shin, Hong Jiang, Sagar Sohoni, Xuejun Fan, Yanhua Yi, Joy Gumin, Frederick Lang, Candelaria Gomez-Manzano, Marta Alonso

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Background: Diffuse Intrinsic Pontine Glioma (DIPG) is a pediatric brain tumor with a 2-year survival of approximately 7%. The standard of care treatment, radiation, prolongs the survival by few months. We are exploring a new modality of treatment for DIPG using oncolytic adenoviruses. Currently, our group leads a phase I trial in naïve DIPGs using the oncolytic

adenovirus Delta-24-RGD (NCT03178032). In the work reported here, we aimed to examine the the anti-tumor efficacy of Delta-24-RGD combined with T cell activators in pediatric gliomas.

Objectives: Characterize the infectivity and oncolytic properties of Delta-24-GREAT and Delta-24-RGDOX in human DIPG cells and the anti-tumor efficacy in immunocompetent murine models of DIPG.

Design/Method: We used the NP53 and XFM, and TP54 and TP83, murine and human DIPG lines, respectively. Infectivity was analyzed using an Ad-RGD-GFP (replication incompetent expressing GFP protein). Infection with oncolytic adenoviruses expressing OX40L (Delta-24-RGDOX) and GITRL (Delta-24-GITRL) resulted in the expression of the costimulatory ligands GITRL and OX-40L in more than 50% of the culture. In vivo experiments were performed by implanting murine DIPG cells in the pons of the murine brainstems, followed by intratumoral injection of the armed-oncolytic adenoviruses, in accordance with institutional regulations. Study of immune populations within the tumors after viral administration was analyzed by flow cytometry.

Results: We detected the expression of ectopic GFP in more then 80 percent of the cells in NP53 (50 MOIs), XFM (15MOIs), TP54 (30 MOIs), and TP83 (80 MOIs). The viral hexon protein was detected in the infecting cells by western blot analysis, indicating a semipermissive status for viral replication. Accordingly, flow cytometry and western blot analyses demonstrated the overexpression of GITRL and OX-40L in the adenovirally-infected DIPG cells. In vivo studies showed a dose-dependent effect and the generation of immune memory.

Conclusion: Delta-24-GREAT and Delta-24-RGDOX maintain their infectivity and replication properties, and induce expression of the positive immunocheckpoints GITRL and OX-40L, respectively, in murine and human DIPG cells lines, providing an enhanced form of viroimmunotherapy for pediatric brain tumors.

Poster # 123

INTEGRATION OF PALLIATIVE CARE INTO PEDIATRIC BRAIN TUMOR POPULATION: ASSESSING PERSPECTIVES

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Background: Pediatric oncology is a field of medicine that requires complex treatment approaches and multidisciplinary care. While historically used interchangeably with hospice care, palliative care offers an additional layer of support and benefit to the patients and their families that is not exclusive to end-of-life treatment. Despite prognosis, there is evidence that early integration of palliative care services leads to improved quality of life and symptom management. Currently, the Melodies Center for Childhood Cancer and Blood Disorders at Albany Medical Center does not have an established protocol for integration of palliative care services in the pediatric oncology population. Utilizing the Journey's Palliative Care team,

integration of palliative care services will begin at initial diagnosis in all pediatric brain tumor patients.

Objectives: The purpose of this quality improvement study is to assess patient and family perceptions of palliative care and assess impact of palliative care on quality of life.

Design/Method: The study includes brain tumor patients, age 0-21, newly diagnosed or currently undergoing treatment, selected by the Pediatric Neurooncolgy team and Journeys Palliative care team. A 10-minute survey will be administered to assess patient perceptions of palliative care, and symptoms management; rating prevalence and severity. The survey will be administered at 4-month intervals (months 0, 4, 8, and 12)

Results: To date, we have enrolled 10 patients. The majority of surveys have been completed by parents. 66.67% respondents had heard of the term palliative care prior to study enrollment The majority associated palliative care with quality of life, comfort care, symptom management and emotional support; however, 2 respondents associated palliative care with end of life and discontinuation of treatment, and only 1 patient associated it with hospice. Nausea/vomiting was the most common symptom identified. We have identified 15 additional patients to enroll in this study.

Conclusion: Further patient data is needed to understand the potential benefits of palliative care integration in the pediatric brain tumor population at our institution. Based on the preliminary data, patients do not necessarily associate palliative care with end-of-life care, which may be advantageous in integrating palliative care services. Additionally, nausea/vomiting was identified as the most common symptom, which provides room for intervention in symptom management to improve quality of life.

Poster # 124

INTRATHECAL LIMITED CHEMOTHERAPY REGIMEN TO TREAT CHILDREN WITH NODULAR/DESMOPLASTIC MEDULLOBLASTOMA

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Background: Therapy for medulloblastoma in patients < 4 years old generally omits radiotherapy due to risk of neurocognitive deficits. The German Pediatric Brain Tumor Study Group described a chemotherapy regimen (HIT-SKK' 92 and HIT-SKK 2000) without radiation which yielded a five-year progression-free survival (PFS) rate of 85% in children with nodular/desmoplastic medulloblastoma (NDMB) and medulloblastoma with extensive nodularity (MBEN).

Objectives: We modified the HIT-SKK regimen to reduce the number of intrathecal methotrexate doses and report the outcomes of five patients treated with this approach.

Design/Method: IT MTX was eliminated on weeks when high-dose intravenous methotrexate was administered. On weeks when no systemic methotrexate was administered, a single dose of lumbar-administered IT MTX was substituted in place of multiple intra-Ommaya doses. These changes reduced IT MTX from 12 to 2 doses/cycle. Following chemotherapy, patients were monitored with interval imaging and observation for acute and late effects.

Results: Four children remained in remission 3, 5, 9, and 10 years post-treatment respectively. One child had recurrent tumor with metastases six months post-treatment. She failed the attempted salvage regimen and continued to deteriorate, dying of disease at 3 years old.

Conclusion: While this report is limited by the small number of children treated, we believe there is encouraging evidence that our approach warrants further evaluation in a larger population of young children with NDMB and MBEN.

Poster # 125

ATYPICAL TERATOID RHABDOID TUMOR: SINGLE INSTITUTIONAL 20 YEARS EXPERIENCE

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Background: Atypical teratoid rhabdoid tumors (ATRT) is a rare, aggressive central nervous system tumor primary occurring in early childhood. It accounts for 1-2% of all pediatric CNS tumors and 10-20% of tumors in children under the age of 3 years. ATRT is associated with somatic and germline mutation of SMARCB1 and SMARCA4 which are tumor suppressor genes. Historically, patients with ATRT have been treated in heterogonous manner and the poor outcome are associated with germline mutation, younger age, metastatic disease and subtotal resection. Most recently, Children Oncology Group reported outcomes for ACNS0333 trial demonstrated four-year event free survival (EFS) and overall survival (OS) for the entire cohort was 37% and 43% improved from historical outcomes. We performed comprehensive analysis of our institutional experience and data to identify factors associated with survival outcome and long-term morbidities

Objectives: Describe the outcome of ATRT at Children's Wisconsin and review the published data to identify key factors to make the outcome differences

Design/Method: Retrospective chart review and literature review. Kaplan Meier survival analysis, chi-square analysis was applied to identify factors associated with treatment outcome.

Results: Our cohort of 15 patients had median age at diagnosis of 18 months (range: 2 months to 23 years). Two of the patients received major part of the treatment at different institutions. Two patients died without pursuing curative therapy at the time of diagnosis. Of the remaining 11 patients treated at Children's Wisconsin, all received multimodality therapy including surgery, radiation, and chemotherapy. First line therapy included COG ACNS0333 (n=6), Dana-Farber

Cancer Institute (n=3) and Medical University of Vienna (MUV) (n=2) protocols. With the median follow up time of 36 months, there are nine patients (81.8%) alive at the last follow up. Although the sample size is small to be powered with statistical significance, combined group of patients treated by Dana-Farber and MUV protocols had four-year EFS of 100% where 50% for ACNS0333. Metastatic disease, radiation field and age appear not be associated with the survival outcome. For long-term morbidities, out of 9 patients currently alive, five developed severe hearing loss, two patients have hypothyroidism requiring treatment, and two patients developed growth hormone deficiency. Two patients required prophylaxis for seizures and two patients underwent hemispherectomy for seizure control.

Conclusion: Despite the historically poor outcomes, our data suggests that the outcome of ATRT can improve by multimodality therapy. Long-term follow up for treatment associated morbidities and second cancer for patients with rhabdoid tumor syndrome are needed.

Poster # 126

THE PREVALENCE OF CRANIAL NERVE PALSIES AS PRESENTATION OF INFRATENTORIAL OR CERVICAL CORD TUMOR

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Background: Common symptoms that cause providers to suspect brain tumors are raised intracranial pressure, seizures, focal deficits, or papilledema. The prevalence of cranial nerve palsies in the literature ranges from 16-51 %. Cranial nerve palsies as the only symptom at presentation is rare, and the incidence is not known. We analyzed the prevalence of cranial nerve palsies as the only symptom at presentation, as well as an accompanying symptom in patients with brain tumors, focusing on infratentorial and cervical cord tumors.

Objectives: The goal of this study is to analyze how frequently patients with infratentorial and cervical spinal cord tumors present with cranial nerve palsies either alone or with other symptoms. Duration and outcome of cranial nerve palsies will also be investigated.

Design/Method: A retrospective chart review was performed of patients who were diagnosed with infratentorial or cervical spinal cord tumors between 1990 and 2020. The patient's medical record was reviewed for initial presenting symptoms and physical exam, as well as the duration of symptoms prior to presentation. Nineteen different diagnoses were found in patients ranging in age from 3 months to 25 years old at diagnosis.

Results: The electronic medical record of 170 patients was reviewed. Cranial nerve palsies were present in 17% (total 29) of patients at presentation. Of those presenting with cranial nerve palsies, 7% of them had cranial nerve palsy as the only symptom. Cranial nerve 6 palsy, presenting as esotropia, was the most common at presentation. Patients with cranial nerve palsy tend to have a longer duration of symptoms compared to other presenting symptoms. Symptoms of increased intracranial pressure including headache and vomiting were the most common

associated symptom. Multiple cranial nerve palsies were identified including cranial nerve 3 (14%), 5 (3%), 6 (38%), 7 (34%), 8 (3%), and 12 (3%).

Conclusion: Cranial nerve palsies at presentation of infratentorial or cervical spinal cord tumors is rare (17%) compared to symptoms of headache (49%), vomiting (46%), and ataxia (38%). Though rare, we found that cranial nerve palsy can be the only symptom of brain or spinal cord tumors. Cases with prolonged history of cranial nerve palsy suggest that identifying cranial nerve palsy could lead to earlier detection of infratentorial or cervical cord tumors.

Poster # 127

POST-TRAUMATIC STRESS SYMPTOMS IN PEDIATRIC HODGKIN LYMPHOMA SURVIVORS: A REPORT FROM COG AHOD0031

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Background: With a 5-survival rate of Hodgkin Lymphoma (HL) that exceeds 95%, survivors are at risk for adverse medical and psychological health outcomes. The intrusive thoughts of cancer treatments, re-experiencing, and avoidance associated with post-traumatic stress symptoms (PTSS) can have detrimental effects on HL survivors' quality of life.

Objectives: This study investigates the associations between experiences and beliefs (treatment received, relapse, secondary medical conditions, health behaviors, activity limitations, and future concerns) and PTSS among pediatric and adolescent survivors of intermediate risk HL treated on the Children's Oncology Group (COG) AHOD0031 study.

Design/Method: Participants enrolled in COG AHOD0031 from September 2002 through July 2009 completed self-report questionnaires following the end of therapy concerning secondary medical conditions, activity limitations, fatigue, future concerns, health behaviors, and PTSS. Participants (n=1110) completed the first questionnaire at a median of 6.7 months post diagnosis (Quartiles: 5.3 - 11.5 months) and 736 participants completed a second questionnaire at a median of 12.4 (10.1 - 17.6) months since the first one. For PTSS, a sum score of 5 questions tallied how often participants experienced symptoms of avoidance, intrusive thoughts, or feelings of nervousness. Ordinal regression analyses using proportional odds models estimated the association between covariates and PTSS.

Results: Among participants who completed the first questionnaire, increased fatigue (OR=1.15 (95% CI: 1.11-1.18), $p<0.01$), increased concerns for the future (OR=1.13 (95% CI: 1.09-1.16), $p<0.01$), increased limitations in daily living and activities (OR=1.06 (95% CI: 1.02-1.09), $p<0.01$), and history of relapse (OR=2.15 (95% CI: 1.19-3.90), $p=0.01$) were associated with higher PTSS scores. Longer time since diagnosis (years) (OR=0.84 (95% CI: 0.75-0.94), $p<0.01$) was associated with lower PTSS scores. Among participants who completed another follow-up questionnaire, increased fatigue (OR= 1.16 (95% CI: 1.12-1.21), $p<0.01$), increased concerns for

the future (OR=1.14 (95% CI: 1.10-1.19), p<0.01), increased limitations in daily living and activities (OR=1.05 (95% CI: 1.00-1.1), p=0.044), and higher PTSS scores on the first questionnaire (OR=1.19 (95% CI: 1.16-1.23), p<0.01) were associated with higher PTSS scores. Time since diagnosis and PTSS were negatively associated (OR=0.84 (95% CI: 0.76-0.93), p<0.01). Age, sex, race, stage, response to therapy and secondary medical conditions were not associated with PTSS.

Conclusion: These findings suggest that fatigue, limitations in daily living, and future health concerns among pediatric survivors of HL are associated with PTSS. Future research should examine how long PTSS persist and focus on interventions targeted to risk factors to allow for improved quality of life and subsequently healthier outcomes among this population.

Poster # 128

USE OF VOLUMETRIC DOSIMETRY TO SCREEN CHILDHOOD CANCER SURVIVORS FOR RADIATION-RELATED LATE EFFECTS

Sally Cohen-Cutler, Arthur Olch, Kenneth Wong, Jemily Malvar, Richard Sposto, Pierre Kobierski, Louis Constine, David Freyer

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Background: Radiation-related late effects screening guidelines for survivors of childhood cancer currently use irradiated regions (IR). However, contemporary radiotherapy techniques utilize volumetric dosimetry (VD), which is more organ-specific. In a recent proof-of-principle study, we showed use of VD decreased mean number of recommended diagnostic imaging studies and procedures by -37.0% per patient (p<0.001), with approximately 60% fewer patients flagged for surveillance of cochlear and cardiac-related late effects.[1] Here we have incorporated chemotherapy exposures to determine if the greater precision of VD is preserved.

Objectives: Determine impact of VD versus IR to apply late effect surveillance guidelines for childhood cancer survivors, with focus on diagnostic imaging and procedures

Design/Method: This was a cross-sectional cohort study of patients treated for cancer using computerized tomography-planned irradiation at Children's Hospital Los Angeles from 2000-2016. For each patient, both VD and IR were applied to compare radiation exposure to the cochlea, heart, lung, breast, and colon; chemotherapy exposures relevant to these organs (busulfan, carmustine, lomustine, bleomycin, carboplatin, cisplatin, anthracyclines) were summarized. Under each method, Children's Oncology Group (COG) Long-Term Follow-Up Guidelines were applied to determine chemotherapy- and radiation-related potential late effects and their correlative screening practices. Organs of interest flagged for surveillance were compared between the two methods.

Results: In this cohort (n=132), median age at end of treatment was 10.6 years (range, 1.4-20.4). Brain tumor was the most common diagnosis (45%) and head/brain the most common irradiated region (61%). At least one relevant chemotherapy was received by 71% of patients. With use of

VD and accounting for chemotherapy, significantly fewer patients were flagged for screening for cochlear (-18%) and cardiac-related (-22.5%) late effects, and significantly more for lung-related late effects (+29.1%). Incorporation of relevant chemotherapy diminished the previously reported impact of use of VD by 41% and 44.4% for cochlear- and cardiac-related late effects, and 65.4% for lung-related late effects.

Conclusion: Use of VD rather than IR enhances precision of guideline-based screening for radiation-related late effects in long-term childhood cancer survivors even when chemotherapy-related recommendations are considered. Future directions will include incorporation of chemotherapy and VD dose thresholds informed by data from Pediatric Normal Tissue Effects in the Clinic (PENTEC) to compare number of recommended diagnostic imaging studies and procedures over patients' lifetimes.

1. Cohen-Cutler et al, Cancer Medicine, 2020

Poster # 129

LOW RATES OF HPV VACCINATION IN ONCOLOGY SURVIVORS AND PATIENTS WITH SICKLE CELL DISEASE

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Background: Human papilloma virus (HPV) vaccination prevents the development of HPV-associated malignancies. Despite HPV vaccination being preventative, the HPV vaccination rate remains lower than that of other vaccinations. Children with chronic medical conditions are at an increased risk for HPV infections and suboptimal health outcomes. Adolescent and young adult (AYA) survivors of childhood cancers and patients with sickle cell disease (SCD) are two populations of vulnerable patients who would significantly benefit from HPV Vaccination.

Objectives: We aim to determine the HPV vaccination rate amongst the AYA SCD and oncology survivorship populations at a comprehensive pediatric childrens' hospital.

Design/Method: We performed a retrospective chart review for patients aged 11-26 years who were seen in our comprehensive SCD and oncology survivorship clinics from January 2019 through December 2019. Vaccination records for this study were reviewed through Indiana's online vaccination database. Patients were considered up to date (UTD) if their age matched their expected vaccine status based on ACIP and AAP guidelines for HPV, as well as Tdap and meningitis vaccinations. Special considerations were made for when childhood cancer survivors could re-start vaccinations.

Results: Of the 70 patients with SCD, only 33 (37.1%) of the patients were UTD on HPV vaccination. This is in stark contrast to the 91.4% (64 patients) rate of Tdap vaccination. Of the 37 patients who were not UTD on HPV Vaccination, 31 patients (84%) had received Tdap vaccination. Amongst the oncology survivorship population, only 74 (41.8%) of the 177 patients

eligible were UTD on HPV vaccination. When comparing to other age-appropriate vaccinations, 153 patients (86.4%) were UTD for Tdap and meningococcal vaccines. Of the 103 patients not UTD with HPV vaccination, 79% received Tdap vaccination and 78% were vaccinated against meningitis.

Conclusion: Our data reveals a notable difference between the rate of HPV vaccination and other age-appropriate vaccinations, indicating substantial missed opportunities. Additionally, this is one of the first studies to demonstrate HPV vaccination rates in AYA with sickle cell disease. This data demonstrates the need for improved vaccination counseling and promotion in our vulnerable patient population. Patients with chronic medical conditions often receive care from both their primary care provider and their subspecialist. This complicates which provider may be comfortable with vaccination counseling, either due to the chronic medical condition or due to lack of familiarity with vaccination schedules. Given our preliminary findings, we have expanded this project to explore system-level barriers, patient/parent vaccine hesitancy, and subspecialty provider beliefs regarding HPV vaccination.

Poster # 130

ACHIEVING WELLNESS AFTER ILLNESS FOR TEENS (AWAIT): AN APP-BASED HOPE INTERVENTION

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Background: Childhood cancer survivors (CCS) are at increased risk of morbidity and mortality due to treatment-related chronic conditions, which may be augmented by unhealthy lifestyles. Hope, a positive psychological concept focused on goal-directed thinking, has been associated with engaging in health-promoting behaviors. Achieving Wellness After Illness for Teens (AWAIT) is a behavioral intervention focused on increasing hope in order to improve quality of life (QoL) and health-promoting behaviors in adolescent CCS.

Objectives: To test the feasibility and acceptability of the AWAIT intervention in adolescent CCS.

Design/Method: CCS aged 13-17 years and >3 months from therapy completion were randomized 2:1 to the AWAIT intervention or attention control, stratified by diagnosis and time since therapy completion (<3 years or ≥3 years). Those randomized to the 8-week AWAIT intervention received access to weekly coaching calls to discuss progress towards patient-selected goals and a mobile app with weekly video modules, practice exercises and behavioral and mood tracking. Participants completed a modified Children's Hope Scale, PedsQL v4.0, and assessments of diet and physical activity at baseline and 2 months. Intervention acceptability was measured at the end of intervention. Differences between groups were assessed using Fisher's exact and Wilcoxon Rank Sum tests. Changes within the groups were evaluated using

McNemar's and paired t-tests.

Results: Overall participants (n=48) were median age 15 years, 54% male and 42% leukemia/lymphoma CCS with no differences between the groups. Twenty participants (63%) completed intervention activities in at least 7 of 8 weeks (prior to COVID19 pandemic 20/28 [71%], after pandemic 0/4 [0%]). Thirty-seven participants (77%; AWAIT 24/32 [75%], Control 13/16 [81%]) completed the 2-month evaluation. Compared to baseline, there was no change in hope or overall QoL in either arm; however, AWAIT participants reported improvements in specific goal-directed thinking arenas (ability to think of many ways to get important things in life, p=0.025; finding ways to solve problems without quitting, p=0.059). Additionally, there was a trend toward decreased hours of television (p=0.08) and other screen time (p=0.1) as well as increased physical activity (p=0.1) in the AWAIT participants. Most participants (72%) were very/quite satisfied with the intervention; 92% would recommend it to another CCS; 75% felt the information was very/quite relevant; and 88% felt the coaching calls were very/quite helpful.

Conclusion: Implementation of the AWAIT intervention is feasible and adolescent CCS found it acceptable. Future analyses will evaluate the sustainability of findings at 4 months and the ideal time from completion of therapy for AWAIT participation.

Poster # 131

EARLY PARENTAL KNOWLEDGE OF RISKS OF LATE EFFECTS IN CHILDREN WITH CANCER

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Background: Despite the pervasiveness of late effects in childhood cancer survivors, communicating late effect risks has proved challenging. Previous work has shown that parents want early information about late effects, in part to support treatment decision-making, yet many parents feel inadequately informed about their child's risks.

Objectives: We aimed to examine parental knowledge of risks of late effects during treatment, predictors of increased awareness of risks, and how knowledge differs between specific late effects.

Design/Method: 96 parents of children with cancer receiving treatment at Dana-Farber/Boston Children's Cancer and Blood Disorders Center between November 2016 and June 2018 completed a survey which asked whether their children were at risk of 8 late effects (infertility, neurocognitive impairment, cardiac toxicity, second malignancy, ototoxicity, pulmonary toxicity, osteonecrosis, renal toxicity). Actual risk was determined by comparing treatment data extracted by chart review with the Children's Oncology Group's Long-Term Follow-Up Guidelines v5. Parents were considered knowledgeable about a given late effect if they correctly identified their child as being either at risk or not at risk for the specified late effect. A knowledge score was

calculated by assigning one point for each correctly identified late effect and tabulating the percentage of the 8 late effects about which the parent was knowledgeable. Descriptive statistics were used to summarize knowledge scores by patient and parent characteristics. Ordinal logistic regression was used to identify predictors of higher knowledge scores.

Results: The mean knowledge score was 68.10% (SD=18.75%); 11.46% (n/N=11/96) of parents correctly identified all of their child's risks for the 8 late effects evaluated. Among 21 parents whose children were at risk for ototoxicity, 95% correctly identified this risk. In contrast, parents were less knowledgeable about risk of secondary malignancy (63% correct identification; N=94 at risk), cardiac toxicity (61%; N=71), neurocognitive impairment (56%; N=63), and infertility (28%; N=61). Ordinal logistic regression analysis reported no significant differences in parental knowledge of late effects risks by parent education, income, worry about late effects, receipt of late effects information, or child's cancer diagnosis.

Conclusion: Parental knowledge deficits of late effects of childhood cancer treatment are apparent early in a child's care and parents are more knowledgeable about some late effects, such as ototoxicity, than others, such as infertility. This may suggest inadequate initial communication about late effects risks. As no child- or parent-specific factors were associated with increased knowledge of late effects risks, interventions must be applied broadly.

Poster # 132

BARRIERS TO ADHERENCE IN CHILDHOOD CANCER SURVIVORS

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Background: Childhood Cancer Survivors (CCS) are at high risk for chronic illness and premature death due to late complications associated with cancer treatment. Adherence to screening recommendations is relatively poor in this high-risk population. Identifying specific barriers to adherence can lead to interventions to address them.

Objectives: The aims of this study are to (i) Characterize barriers to adherence to general medical care and specific screening procedures among adult CCS in long-term follow-up care; (ii) Identify sociodemographic and medical correlates of barriers to adherence; and (iii) Examine whether barriers to adherence relate to quality of life domains.

Design/Method: Adult CCS from the Survivors Facing Forward program, a lifelong follow-up program for CCS at Cohen Children's Medical Center, were anonymously surveyed using the Barriers to Care Questionnaire (BCQ) for general medical care and for specific screening tests, and the Quality of Life Scale–Cancer Survivor (QOL-CS). Demographic data was also collected. The survey was distributed through REDCap®.

Results: 150 CCS started the survey, and 84 completed all 4 sections (BCQ, Specific Recommendations Barrier Survey, QOL-CS and demographics). Of the 84 who completed the entire survey, the median age was 25y (IQR:21-31), median age at completion of therapy was 13y (IQR:8-16) and the median time off-therapy was 14y (IQR10-19). 64% were female, 70% white, 7% black, and 9.5% Asian/Pacific Islanders. 8% identified as Hispanic. The median BCQ total score was 88.5 (IQR:78.4-95.7), with the lowest scores (greatest barriers) reported in the Skills and Pragmatism subscales (88.4 and 84.7 respectively). These sections include questions on the ease of navigating the health care system (Skills – facility in navigating referrals, communication between patient and physician…) and practical barriers (Pragmatism – cost, insurance, transportation…). There was no correlation between the BCQ scores and any demographic variable (p's>.05). There was a statistically significant correlation between the BCQ Total score and the QOL-CS Total score (r_s=0.47, p<0.0001), as well as between the BCQ Total score and all QOL-CS subscales, except the spiritual well-being subscale.

Conclusion: Barriers to screening for CCS are mostly health system related, including costs, access to insurance and practical barriers such as transportation. The significant association between the BCS and QOL-CS suggests that lower quality-of-life among CCS is associated with a perception of greater barriers to care. Adherence to screening recommendations among CCS can be improved by refining access to and usability of the health care system, and by addressing and improving the quality-of-life for CCS.

Poster # 133

PERCEIVED CHILD VULNERABILITY AND PSYCHOLOGICAL DISTRESS IN PARENTS OF CHILDHOOD CANCER SURVIVORS

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Background: Our past work found high rates of parents perceiving their childhood cancer survivor (CCS) as medically vulnerable many years post-treatment, independent of the survivor's current age, elapsed time since treatment, socioeconomic factors, or medical complications. The role of parental psychological distress, however, was not examined.

Objectives: To determine whether parental psychological distress is a significant contributor to perception of child vulnerability (CV).

Design/Method: This is a cross-sectional study of parents/legal guardians of CCS currently <18 years old, >1 year post-treatment, and in remission. Parents accompanying their child to survivorship clinic (1/28/2019-3/9/2020) completed the Child Vulnerability Scale, Patient Reported Outcome Measurement Information System (PROMIS) Anxiety and Depression short form scales, the Posttraumatic Stress Disorder Checklist 5, and a demographic survey including mental health history. Instrument cutoffs were used to determine the presence of the measured construct. Patient characteristics were abstracted from medical records. Multivariable logistic

regression examined the association between parental psychological distress and CV adjusted for CCS individual and treatment factors significant at $p<0.1$ in univariate analyses, in addition to parent sex, education, and age.

Results: Sixty-seven parents (75% mothers) with a mean age of 48.5 (SD=8.2) years completed the study (participation rate = 95%). Survivors were 39% female, had a mean current age of 15.0 (SD=5.9) years and mean time since diagnosis of 9.5 (SD=5.5) years. Twenty-five percent of parents perceived their child as vulnerable. Forty-two percent of parents (N=28) reported psychological distress: depression (N=3), anxiety (N=8), post-traumatic stress symptoms (N=9), or past/current counseling and/or medication (N=19). In univariate analyses, younger age at diagnosis was significantly associated with perceived vulnerability (OR=1.32, 95% CI: 1.06, 1.64). In multivariable regression, adjusting for parent sex, educational status, and age, young survivor age at diagnosis remained significant (OR=1.39, 95% CI: 1.09, 1.79). Psychological distress was not associated with CV.

Conclusion: Similar to previous studies**,** 25% of parents of CCS perceive their child as vulnerable. Younger age at diagnosis was associated with increased odds of perceived CV, a finding not demonstrated in our precursor study. There was no association between parental psychological distress and perceived CV. These results suggest the need to better support parents of CCS, particularly those with younger children at diagnosis, and to optimize ongoing communication about health risks.

Poster # 134

MANAGEMENT OF CHILDHOOD CANCER SURVIVORS AT RISK FOR THYROID FUNCTION ABNORMALITIES: A DELPHI STUDY

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Background: Thyroid function abnormalities are associated with some childhood cancer therapies. Consensus guidelines recommend screening childhood cancer survivors (CCS) at risk for thyroid dysfunction, but evidence and recommendations for management of asymptomatic CCS are lacking.

Objectives: To systematically develop physician-expert consensus recommendations and identify areas of clinical disagreement on management of CCS at risk for thyroid dysfunction using Delphi methodology.

Design/Method: A panel of 40 expert-physicians from USA and Canada, representing pediatric oncology, radiation oncology, adult endocrinology, pediatric endocrinology, and adult primary-care with a median of 15 years in practice and 100 CCS clinical visits per year was recruited to participate in a Delphi study using three rounds of anonymous, iterative questionnaires formatted as clinical scenarios including patients who have normal thyroid stimulating hormone [TSH]

with declining free T4 [FT4]; normal TSH with low FT4; low TSH with low FT4; persistently elevated TSH with normal FT4; and suppressed TSH with normal FT4. Consensus defined as ≥90% agreement. Participation was 100% for all rounds.

Results: Panelists reached consensus that CCS treated with radiation fields including neck, total body, whole brain, partial brain (including hypothalamic-pituitary axis [HPA]), and therapeutic MIBG (97-100% agreement) should have annual, lifelong (98%), screening for thyroid dysfunction using TSH and FT4 (98%) starting within one year off-treatment (98%). Panelists agreed that conventional chemotherapy, diagnostic MIBG, and brain radiation not including HPA were not indications to screen (90-97% agreement). Consensus was not reached on continuing to screen CCS for thyroid dysfunction after immunotherapy associated with acute thyroid-injury including immune checkpoint inhibitors (50%), tyrosine kinase inhibitors (35%), and cytokines (31%). Consensus was achieved for endocrinology referral and treatment with levothyroxine for central hypothyroidism (low FT4 and normal or low TSH) (93-100%) and referral to endocrinologist for patients with normal FT4/suppressed TSH (90%). Management decisions that did not reach consensus include the role of brain imaging for CCS at risk for central hypothyroidism (57-83%) and thyroid ultrasound for primary hypothyroidism (50%); additional screening tests to assess HPA (46-86%) in the setting of central hypothyroidism; and TSH threshold to initiate treatment of subclinical hypothyroidism (>= 10 mU/L, 35%; >= 7 mU/L, 25%; >= 5 mU/L, 40%).

Conclusion: Despite lack of evidence, physician-experts who care for CCS at risk for treatment-related thyroid dysfunction reached consensus on most recommendations for screening and management. Areas of disagreement for further investigation include screening after completion of immunotherapies and initiation of levothyroxine in subclinical primary hypothyroidism.

Poster # 135

PREDICTORS OF SUBOPTIMAL FOLLOW UP IN SURVIVORS OF CHILDHOOD CANCER IN WEST VIRGINIA

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Background: Children's Oncology Group recommends long-term risk-based follow-up care for childhood cancer survivors. However, despite these guidelines, attendance to follow up care continues to be suboptimal.

Objectives: Our study aimed to identify the reasons behind poor adherence to recommended follow-up care in childhood cancer survivors at a large tertiary care center.

Design/Method: We reviewed an internal institutional database maintained by pediatric oncologists at Charleston Area Medical Center/ West Virginia University- Physicians of

Charleston. A cohort of pediatric cancer patients from 2004 to 2017 was analyzed. Inclusion Criteria were: (1) cancer survivors diagnosed at age 0-18 years with a neoplasm and completion of any treatment two years before the start of the study. (2) No evidence of disease at last visit to hospital/clinic. Exclusion criteria were patients in the active treatment/follow up group and death due to any cause.

Results: About 103 patients were eligible for the study and were administered the survey questionnaires out of which thirty patients (29.1%) responded to the survey. More than half of the respondents(53.3%) reported no follow-up care. Patients who were lost to follow-up had more years elapsed since the diagnosis (11.0 ± 3.4;$p<0.02$). Age, gender, race, and insurance status did not associate with follow-up status ($p>1$). Patients had more solid tumors in both groups (43.85% in lost to follow up vs 35.7% in active follow up; $p=1.00$). Additionally, treatment modality did not differ between cohorts ($p=0.94$), with surgery being the most common modality. Patients who received bone marrow transplant had 100% follow up rate($p=0.09$). Most common reasons for not receiving follow-up care included lack of knowledge regarding cancer follow up (n=11, 68%) relocation to a new state (n=2), transfer of care to a different oncologist (n=1), other reasons (n=2). Financial reasons were not found to be a reported determinant of poor follow up.

Conclusion: Follow-up care by childhood cancer survivors is an understudied area. In the surveyed childhood cancer survivors subgroup, knowledge deficits rather than financial reasons or other sociodemographic factors were reported to be a cause of poor follow-up care. This information can help oncology centers to develop future interventions targeted towards this patient population, thus promoting guideline-driven, long-term cancer survivorship care.

Limitations:
This study was completed during the COVID-19 pandemic and the response rate was lower than anticipated. As a result, survey results may have been underpowered. Secondly, West Virginia has a racially homogenous population so our sample population results cannot be generalized across the United States.

Poster # 136

DAILY PAIN AND PSYCHOLOGICAL CO-MORBIDITIES IN SURVIVORS OF CHILDHOOD CANCER

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Background: Pain is commonly experienced by youth following active childhood cancer treatment. In other pediatric conditions, pain tends to co-occur with fatigue and symptoms of anxiety and depression. These factors have been minimally examined in pediatric cancer.

Objectives: The current pilot study examined associations among pain, fatigue, and negative

affect (anxiety, depression) in survivors of childhood cancer (e.g., leukemia, brain tumor, solid tumor), using baseline questionnaires and a 14-day diary.

Design/Method: The sample included 17 patients (M_{age}=12.76 years, *SD*=2.76; 41.2% female; 64.7% White) who were at least one year from any type of cancer diagnosis. Parents completed a baseline demographics questionnaire and children completed the Children's Pain Questionnaire, Pediatric PROMIS-25 Profile, and Pediatric Quality of Life Inventory. Children then reported on daily pain severity, fatigue, anxiety, and sadness (proxy for depression) at bedtime for up to 14 days (average 12 diary days) using a hand-held Palm OS-based personal digital assistance (*n*=8) or paper diary (*n*=9), depending upon family preference. Correlations and t-tests were conducted in SPSS 26.0. Multilevel modeling (MLM) for repeated daily diary data was conducted in LISREL 8.71.

Results: On questionnaires, children reported a median pain frequency of 2-3 times per week (range=none to daily pain), average pain severity of 5.63 of 10 (*SD*=2.16), and median pain duration of a few hours per episode (range=less than 1 hour to all day). More frequent baseline pain was correlated with greater baseline anxiety (r=0.501, p<0.05) and depression (r=0.670, p<0.01). Higher baseline pain severity was correlated with greater baseline depression (r=0.61, p=0.02) and fatigue (r=0.64, p=0.01), and lower quality of life ($r_{(16)}$ =-0.52, p<0.05). Across all diary days, White children reported significantly higher daily pain severity than their minority race counterparts [t(195)=4.87, p<0.05]. On pain days, children with other cancer diagnoses had significantly higher pain severity than children with leukemia [t(51)=8.17, p<0.001]. Older children (13-16 years) also reported higher pain severity than younger children (8-12 years) [t(51)=2.62, p=0.01]. Controlling for race, MLM revealed that greater daily anxiety was significantly associated with higher daily pain severity (β-hat=0.46, z=2.48, p=0.01). Greater daily sadness was marginally associated with higher daily pain severity (β-hat=0.32, z=1.88, p=0.06).

Conclusion: These results are consistent with the broader pediatric pain literature and suggest that symptoms of negative affect (anxiety, depression) are associated with higher pain severity on a daily basis in survivors of childhood cancer. Early screening and intervention for pain and co-morbid negative affect are needed for survivors of childhood cancer.

Poster # 137

DISTRESS DURING A PANDEMIC: HOW ARE CAREGIVERS OF CHILDREN WITH BLOOD AND CANCER DISORDERS AFFECTED

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Background: Distress for caregivers of children with chronic diseases, including blood and cancer disorders, has been well-documented. The impact of the SARS-CoV2 pandemic has the potential to increase distress in this caregiver population.

Objectives: To understand the impact of the COVID-19 pandemic on distress for caregivers of children with chronic blood or cancer diagnoses.

Design/Method: We conducted a cross-sectional survey of caregivers of children diagnosed with cancer, sickle cell disease (SCD), or hemophilia at Riley Hospital prior to March 2020. We utilized the CEFIS (COVID-19 Exposure and Family Impact Scale) survey, which measures the impact of the pandemic on families of children with pediatric health conditions.

Results: Thirty-two caregivers completed the survey; 24 had children with cancer, 6 with SCD, and 2 with hemophilia. 82% of caregivers self-identified as female. Median age was 38.5 years (range 25-53). The majority self-identified as white (76%) and non-Hispanic/Latino (96%). The most common annual household income categories included under $25,000 (21%) and $50,000 to $74,999 (25%). The majority (54%) had a high school education or GED; 42% had a college or graduate degree.

The majority (89%) of caregivers had a stay-at-home order at the time of the survey, 84% of whom also had schools/child care centers closed. 61% felt their child/ren's education was disrupted.

Over 70% had a family member who was considered essential personnel or a frontline worker, and 61% reported a family member had to reduce work hours or became unemployed due to the pandemic.

Only 2 respondents reported difficulty accessing medications or healthcare for their child during this time. However, 54% said the pandemic made caring for their child with a blood disorder or cancer "A little worse' or "A lot worse". 93% reported their anxiety and/or mood being "A little worse" or "A lot worse". On an overall distress scale of 1 (no distress) to 10 (extreme distress), the median reported score for caregivers was 7. This was the same when caregivers answered this question in regards to their child.

Conclusion: Our results indicate the pandemic has caused significant distress among caregivers of children with blood and cancer disorders which may not be related to accessing healthcare, but rather socioeconomic consequences of the pandemic. This has the potential to impact caregivers' well-being, as well as that of their child's. Additional long-term evaluation and qualitative interviews will be conducted as part of future endeavors to inform how best to support caregivers during and after the pandemic.

Poster # 138

INITIAL IMPACT OF COVID-19 PANDEMIC ON PEDIATRIC ONCOLOGY CARE AND OVERALL EXPERIENCES

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Background: The COVID-19 pandemic led to unprecedented change in healthcare delivery. In pediatric oncology, patients and providers were challenged to adapt to evolving circumstances while balancing adherence to well-established oncology treatment and monitoring plans in order to decrease exposure and prevent serious infections in this potentially immunosuppressed population. These changes may have affected healthcare behaviors.

Objectives: To evaluate the impact of the first 4 months of the COVID-19 pandemic on the timing of oncologic care and the overall experiences of pediatric oncology patients and families.

Design/Method: Caregivers of patients aged under 18 or patients over 18 seen for active treatment or follow-up in the oncology clinic between January 1, 2019 and June 30, 2020 were eligible to participate. An anonymous, encrypted electronic survey was created and distributed. Responses were collected from July to December 2020.

Results: There were 78 partial or complete responses to the survey. Of these, 24 were on active therapy with 8.4% reporting delay in therapy. About 17.9% respondents reported a delay in getting surveillance scans. About 24.2% reported a delay in scheduled appointments. No patients surveyed chose to delay treatments against provider's recommendations.

About 15.9% used our electronic medical record platform to send messages, and 59.4% had video visits with positive feedback overall. Only 5% participants reported difficulty getting in touch with the oncology team.

Nearly a quarter (22.4%) of participants endorsed fear about going to the emergency department for care. About 89.7% responders felt the institution's visitor policy helped keep them safe, and 93.2% felt it helped keep others safe.

About 17.6% families reported exposure to COVID-19, and 10.3% indicated a household member had symptoms or diagnosis of COVID-19. Of college students, 36.4% planned to defer classes. Over a third of households (35.8%) had someone stop working due to the risk of exposure.

The majority of participants reported using a government website as their source for information about COVID-19, but participants relied more on their healthcare providers for cancer-specific information. The majority of participants reported following the appropriate guidelines for mask-wearing and social distancing during the pandemic.

Conclusion: Adherence to therapy and access to the oncology team was largely maintained. Given the frequency of interruptions to education and/or work, screening for social stressors and increased social work involvement is warranted. Continuing education for providers with up-to-date information is critical as patients rely predominantly on their healthcare providers for cancer-specific recommendations related to COVID-19.

Poster # 139

THE ROLE OF CHILDREN IN THE TRANSMISSION OF SARS-CoV-2 IN HOUSEHOLDS OF IMMUNOCOMPROMISED PERSONS

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Background: The Severe Acute Viral Respiratory Syndrome 2 (SARS-CoV-2), that causes COVID-19 (Coronavirus Disease 2019) has swept the planet with unprecedented force and speed disrupting economies and societies. Epidemiologic studies in China reported that 75-85% of transmission was driven by family clusters where secondary household attack rates were as high as 15% early in the epidemic in healthy individuals. However, the role children play in the spread and transmission of COVID-19 disease is unknown, and this uncertainty surrounding this issue has fueled school closures. Additionally, data has shown that immunocompromised patients have a low rate of contracting COVID-19 but a much higher rate of morbidity and mortality than their healthy counterparts.

Objectives: To assess the risk of household viral transmission to immunocompromised participants across households with and without children.

Design/Method: A prospective, longitudinal cohort study of immunocompromised participants living in households with and without children. All participants and household members were enrolled in this 6-month study. At the baseline visit and at 6 months blood is collected for SAR-CoV-2 serology (IgG, IgM, IgA) and mid-turbinate swabs for RT-PCR. In addition, all participants collect nasal swabs and complete symptom questionnaires every two weeks. Additional testing is performed if participants or household members become symptomatic or are found to have COVID. Clinical data including demographics, risk factors, clinical symptoms, household/communal exposure are collected.

Results: Since July 2020, we have recruited 28 family cohorts with a total of 90 participants including immunocompromised participants and their household members. Of the 28 adult immunocompromised participants, 16 (57%) are male,16 (57%) are non-Hispanic whites, and 9 (32%) are Hispanic or Latino, and 11 (39%) immunocompromised adult participants are living with children under 7 years old. No immunocompromised children have been enrolled to-date. All participants were SARS CoV2 seronegative at enrollment. To date, we identified six SARS-CoV-2 infections cases from two family cohorts. In the first family cohort without children, the index case was a household member who became infected at work followed by transmission to the immunocompromised participant. In the second family cohort including two adults and one adolescent child were infected and symptomatic. The immunocompromised participant exhibiting symptoms first and all family members have remained RT-PCR positive for >20 days.

Conclusion: To date, we have observed SARS-CoV-2 infections in two families, one with a child and one without. In both family cohorts, the infected immunocompromised participants had a mild clinical course. Updated results will be presented at the conference.

Poster # 140

COVID-19 INFECTION IN PEDIATRIC HEMATOLOGY ONCOLOGY PATIENTS IN LOUISIANA

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Background: The majority of documented SARS-CoV2 infections in children have been mild illnesses. The highest frequency of infection is documented in children between the ages of 5 - 17 years; with the incidence of SARS-CoV2 being the highest in adolescents aged 12-17 years. Severe respiratory complications and a multi-system inflammatory syndrome (MIS-C) have been documented in pediatrics. There is very limited information about pediatric hematology and oncology patients in the United States, actively undergoing therapy, and how SARS-CoV2 affects them. Louisiana was an early "hotspot" for SARS-CoV2 with its first documented infection on March 9, 2020. We present our institutional experience with SARS-CoV2 and pediatric hematology-oncology patients.

Objectives: Our objectives were to examine pediatric hematology-oncology patients who had a positive SARS-CoV2 test between March 9, 2020, till December 15, 2020. The goal was to characterize demographics and signs and symptoms of pediatric hematology-oncology patients undergoing active treatment at Children's Hospital of New Orleans.

Design/Method: A retrospective chart review was performed on all pediatric hematology-oncology patients who were actively being treated at Children's Hospital of New Orleans between March 9, 2020, through December 15, 2020. Any patient who had a positive SARS-CoV2 test was included in the chart review. Information including demographics, signs, and symptoms at the time of testing, hospitalization, medications, diagnosis, and treatment was obtained. The institutional review board at Louisiana State University Health Sciences Center and Children's Hospital of New Orleans approved this study.

Results: Between March 9, 2020, and December 15, 2020, 582 children tested positive for SARS-CoV2 at Children's Hospital of New Orleans. Fourteen of those children had a pediatric hematological or oncological diagnosis. The mean age of the pediatric hematology-oncology patients was 9.2 years, and 57.1% were female. Twenty-eight percent of the patients identified as Hispanic. Of the 14, seven children (50%) had a diagnosis of acute lymphoblastic leukemia or T cell Lymphoblastic Lymphoma and all were actively undergoing chemotherapy. One of the children had undergone a bone marrow transplant. Five (35.7%) were hospitalized; 2 (14.3%) with severe infections requiring PICU admission and 3 (21.4%) patients were treated for MIS-C with SARS-CoV2 specific therapy including Remdesivir, steroids, and Tocilizumab. One of our patients died from SARS-CoV2 related complications.

Conclusion: Pediatric hematology-oncology patients are a heterogeneous group of

patients. There are very limited studies on how SARS-CoV2 affects our patients. Interestingly, the majority of our patients noted to have been infected with SARS-CoV2 had a diagnosis of leukemia or lymphoma.

Poster # 141

RACE AND ETHNICITY ON ACCESS, TIMING, AND DISPARITIES IN PEDIATRIC PALLIATIVE CARE

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Background: Pediatric palliative care (PPC) can improve quality of life for children and adolescents with cancer. Little is known about disparities in the frequency and timing of PPC referrals by different race and ethnicity groups. We previously showed that our integrated pediatric palliative oncology (PPO) clinic improved access and timing of PPC. Early PPC generally reduces physical and emotional stress, lessens intensive end-of-life care, and decreases caregiver distress.

Objectives: Evaluate the impact of race and ethnicity on the frequency and timing of PPC referral after initiation of an embedded PPO clinic.

Design/Method: Patients with cancer between 0 to 25 years at diagnosis treated at Children's Healthcare of Atlanta who experienced a high-risk event (death, relapse/progression, Phase I/II enrollment) between July 2015 and June 2018 were eligible. Demographic, disease, and PPC information were obtained. Descriptive statistics and logistic regression were used to assess likelihood of receiving PPC services by race/ethnicity.

Results: Of 426 patients who experienced a high-risk event, 48% were non-Hispanic white (NHW), 31% were non-Hispanic black (NHB), 15% were Hispanic of any race, and 4% were non-Hispanic Asian (NHA). The median ages at diagnosis and at death were 8.0 years (Range: 0 – 23) and 13.0 years (Range: 0.3 – 26.7 years). Diagnoses were relatively evenly distributed amongst leukemia/lymphoma, solid tumors and brain tumors. Half the cohort was deceased. No significant differences were found between race/ethnicity and age at diagnosis and death, sex, and diagnosis. Phase I/II clinical trial enrollment (p=0.01) and PPC consultation (p=0.03) differed significantly by race with NHB patients (16%, 21/133) enrolling on clinical trials less often than NHA (39%, 7/18) or NHW (31% - 64/209) patients. NHB patients were 1.7 times more likely than NHW patients to receive PPC after adjusting for age at diagnosis, diagnosis type, and vital status (p=0.01). NHB (8.0) and Hispanic patients (8.0) had twice the median PPC encounters compared to NHW patients (4.0). NHW patients spent less time in the hospital in the last 90 days of life compared to NHB, NHA, and Hispanic patients (Median 3 days vs. 8, 12.5, and 14 days, p=0.009).

Conclusion: Significant race and ethnicity disparities exist in patients receiving pediatric oncology and PPC services. Clinical trial enrollment and end-of-life outcomes remain discrepant. Cultural tendencies as well as unconscious and cultural biases may affect PPC referral by race/ethnicity. Better understanding of tendencies and biases may improve end-of-life outcomes for children and young adults with cancer.

Poster # 142/Advanced Practice Professional Award

IMPROVING WEEKEND CLINIC HANDOFF, A SINGLE INSTITUTION QUALITY IMPROVEMENT EFFORT

Erin Harper, Allison Ast, Lauren Jerkins, Lonnesha Wilkins, Melissa Joyner, Casey Long, Vanice Page, Delaine Johnson, Charles Coe, Jamie Flerlage, Anna Vinitsky, Kenneth Pettit Jr, Liza-Marie Johnson, Jitsuda Sitthi-Amorn

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Background: Effective communication is crucial for quality patient care. Our institution runs a weekend clinic staffed by pediatric hematology/oncology hospitalist physicians, advanced practice providers (APPs), and registered nurses (RNs) who are not part of the primary team and not as familiar with the patient's medical history. In 2018, a staff survey identified the handoff from primary clinics to weekend providers as an improvement opportunity. Recognizing communication failure due to inadequate handoff as one of the most common causes of medical errors, a quality improvement (QI) project was initiated.

Objectives: To improve communication between primary and weekend clinics, as measured by the satisfaction of weekend clinic providers with communication received, from a baseline of 79% (physicians/APPs) and 68 % (RNs) to 90% in 1 year.

Design/Method: From January 2018 to September 2020, weekend provider surveys were collected on randomly selected weekend visits using data from January 2018 to March 2019 to establish baseline. The survey collected data on reason for visit, missing information in the electronic medical record (EMR), and weekend provider satisfaction with the handoff information provided. Incomplete surveys were included if a provider's satisfaction section was completed. Utilizing QI methodologies, per the Institute of Healthcare Improvement model, key drivers of adequate handoff were identified. Mean weekend providers' satisfaction with handoff quality were tracked on control charts. Centerlines were shifted based on established statistical control process rules for signal detection in the context of interventions.

Results: Data were collected on 618 weekend visits from 286 (46%) physicians/APPs and 332 (54%) RNs. Common reasons for weekend encounters were assessment of transfusion needs, hydration, and electrolytes status. Frequently omitted information from clinical documentation were transfusion parameters, need for transfusion pre-medications, and contingency plans for IV fluids. Interventions included: (1) developing a required prompt in EMR documenting purpose of weekend visits, (2) standardization of blood product pre-medication needs documentation, and (3) direct provider coaching with primary teams. After implementation of these three

interventions, satisfaction with handoff improved for physicians/APPs from 79% to 93% and RNs from 68% to 88%.

Conclusion: Following QI methodologies, we improved weekend provider satisfaction with handoff communication from primary clinics, which can potentially lower the risk of medical error and improve patient care. A hospital-wide effort is ongoing to further increase weekend provider satisfaction with handoff communication to goal, by standardizing the documentation of key information in outpatient clinic notes.

Poster # 143

PIVOTING A SICKLE CELL DISEASE PROJECT ECHO TO EDUCATE PEDIATRIC HEMATOLOGISTS ABOUT COVID-19

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Background: Project ECHO (Extension for Community Healthcare Outcomes) is a telementoring model that rapidly disseminates education to providers. The Sickle Treatment and Outcomes Research in the Midwest (STORM) regional sickle cell provider network has successfully utilized Project ECHO for monthly, virtual evidence-based management of pediatric and adult sickle cell disease (SCD) education since 2016. In response to COVID-19, the program pivoted to COVID-19 based topics and open forums for discussion among providers.

Objectives: To describe ulitizing Project ECHO to effectively and rapidly disseminate education o pediatric hematologists during a global pandemic.

Design/Method: STORM quickly expanded to a weekly COVID-19 and SCD ECHO beginning on March 19, 2020 to assess changing clinical practices and address concerns about patients with SCD. The first two sessions were open forums and subsequent didactic presentations included: telemedicine, SCDAA patient and provider advisories, SCD COVID-19 surveillance registry, blood safety and transfusion practices, multi-inflammatory syndrome in children, sickle cell trait and COVID-19, serology and more. Participants received Continuing Medical Education credits and Maintenance of Certification (Part II) credits.

Results: During 13 COVID-19 sessions, the program saw a 148% increase in attendance from the average monthly attendance prior to COVID-19 with pediatric hematology practice providers accounting for over 75% of the overall attendance. Over 145 providers attended at least one session, with nearly 50% of participants being new to STORM TeleECHO. On average, pediatric hematologists attended 5 COVID ECHO sessions and 89% attended at least 1 session.

Conclusion: STORM TeleECHO is an innovative learning and networking strategy to virtually connect providers to education about the evidence-based management of SCD. The STORM COVID-19 and SCD TeleECHO session participants have been highly satisfied with this educational forum for emerging issues with coronavirus, particularly how it impacts children and

adults living with SCD.

Pediatric hematologists have been instrumental as teaching faculty for STORM TeleECHO: presenting didactic lectures and COVID-19 and SCD case-presentations, and providing care recommendations. Moreover, pediatric hematologists reported increasing their own knowledge by participating in STORM TeleECHO. The increase in participants sustained for COVID-19 ECHO's demonstrated a desire and need to have a forum to share unprecedented practice changes including challenges implementing telemedicine, emerging clinical protocols, rapid need for patient education and other pandemic resources for pediatric hematology practices. COVID-specific sessions are scheduled to continue throughout the vaccination phase.

Poster # 144

CRITICAL STATUS AT DIAGNOSIS IMPACTS CLINICAL TRIAL ENROLLMENT & OUTCOME IN PATIENTS WITH T-ALL/LLY

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Background: Patients with T-cell acute lymphoblastic leukemia and lymphoma (T-ALL/LLy) more commonly present with critical features such as hyperleukocytosis and mediastinal mass which complicates the ability to complete a diagnostic and staging workup. The effect this has on clinical trial enrollment and outcome has not been evaluated.

Objectives: Describe the frequency of critical features at presentation in patients with T-ALL/LLy and assess the effect this has on clinical trial enrollment and outcome.

Design/Method: Consecutive patients newly diagnosed with T-ALL/LLy from 1999-2019 at the Children's Hospital of Philadelphia were analyzed for PICU admission, presence of hyperleukocytosis (WBC>100,000uL), mediastinal mass, tumor lysis syndrome (TLS) and need for dialysis; as well as clinical trial enrollment and outcome. Medical non-enrollers were defined as patients requiring emergent therapy precluding them from trial enrollment.

Results: We identified 153 patients diagnosed with T-ALL (103) and T-LLy (50). Fifty-three (35%) required PICU level care within 24 hours of admission and 73 (48%) within 7 days. Forty-four (29%) presented with hyperleukocytosis, 17 (11%) underwent apheresis (for WBC>300,000uL), and 102 (67%) had a mediastinal mass. Of 105 patients diagnosed when a trial was open 31 (30%) did not enroll; 19 medical non-enrollers, 11 parental refusal, 1 unknown. Non-PICU patients had a 79.4% enrollment rate versus PICU 56.1% enrollment rate (p=0.016). Patients enrolled on trial had a 16.2% relapse rate versus 25.8% of non-enrollers (p=0.282). In the total cohort, 18% of patients relapsed (10% with T-LLy, 22% with T-ALL). If admitted to the PICU within 24 hours, 26% relapsed vs. 14% of non-PICU patients (p=0.079). If enrolled on a clinical trial the PICU cohort relapse rate was 21% versus 33% for those who did not enroll (p=0.4). Forty-four patients with T-ALL presented with hyperleukocytosis of which 30% relapsed versus 17% without (p=0.158). Almost half of the patients who underwent apheresis for

hyperleukocytosis (8/17) relapsed versus 18% without (p=0.022). In a univariate analysis presence of mediastinal mass, TLS, or dialysis did not affect relapse risk.

Conclusion: Surprisingly almost half of T-ALL/LLy patients required PICU-level care within the first week of diagnosis, making enrollment on clinical trials challenging and significantly less likely. For patients requiring PICU-level care, enrollment on a clinical trial predicted better outcome. Physicians should attempt to balance maintaining eligibility with safety to offer patients trial options. As well, eligiblity requirements limiting T-ALL/LLy patients' ability to enroll on trials, potentially containing new agents, should be reviewed for necessity.

Poster # 145

A SURVEY OF HEALTHCARE PROVIDERS TO ASSESS CARE CHALLANGES AND KNOWLEDGE ABOUT SICKLE CELL DISEASE

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Background: Sickle cell disease (SCD) is a multifaceted disorder affecting approximately 1 in 500 African-Americans and over 100,000 Americans. Because many complications begin during childhood, treatment for patients is complex and requires comprehensive care including preventive interventions, pain management, disease-modifying medications, and blood transfusions. A trained hematologist ideally should provide patient care; however, as most pediatric patients transition to adulthood the likelihood of care from a hematologist is slim. Currently in Indiana, nearly 1,500 individuals live with SCD. Of Indiana's 92 counties, pediatric hematology care is located in five; adult hematology care is available in one. Limited hematology access leads to patients receiving care from primary care providers who commonly lack the knowledge needed to care for patients with SCD.

Objectives: Assess primary health care provider knowledge about SCD, disease modifying therapies, and challenges related to treatment.

Design/Method: Initially designed as a QI project to survey Indiana health care providers about their experience and challenges related to caring for patients with SCD, the 9 question survey conducted by mail (October 2018 to May 2020), was sent to 2357 health care providers. Survey questions were developed to identify provides caring for patients with SCD. Questions included provider demographics, years caring for patients with SCD, number of current patients, challenges in providing care to patients with SCD, and topics of interest for education.

Results: We received 175 completed surveys (7.4% response rate). Seventy-nine percent of respondents identified as a MD/DO. Nearly half (47%) work in Family Medicine. Of the 107 providers who reported at least one patient with SCD in their care, 58 had more than 5 years of care experience. The most common care challenges identified were patient medication adherence, patient or parent knowledge, lack of knowledge about disease-modifying treatments and lack of community resources.

Conclusion: Patients with SCD in Indiana receive care from providers with more primary care training than hematology training. Challenges related to the patients and parents are similar among providers caring despite years of experience. Some providers lack knowledge about disease-modifying medications, which can limit access to these treatments in their care. In an effort to address these barriers to care, our next steps will be to schedule in-person education sessions or mail printed material to the survey respondents and distribute a post- survey to assess improved knowledge about SCD and disease modifying therapies and rate their comfort level in providing care for patients with SCD.

Poster # 146

DIFFERENCES IN PALLIATIVE OPPORTUNITIES ACROSS DIAGNOSIS GROUPS IN CHILDREN WITH CANCER

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Background: Children with cancer experience significant morbidity during the course of their disease, often resulting in physical and emotional stress. During these times, patients and families could benefit from palliative care (PC) to improve symptom burden, enhance family-centered goals of care, and improve overall quality of life.

Objectives: We defined and evaluated "palliative opportunities" and compared them across three main disease categories within pediatric oncology: leukemia/lymphoma (LL), solid tumors (ST), and central nervous system (CNS) tumors.

Design/Method: *A priori*, nine palliative opportunity categories were defined: disease progression or relapse, bone marrow transplant or chimeric antigen receptor T-cell therapy, phase 1 trial enrollment, admission for severe symptoms, social concerns or end-of-life (EOL) care, intensive care admission, do-not-resuscitate (DNR) status, and hospice enrollment. A single-center retrospective review was completed on patients with cancer aged 0-18 years at diagnosis who died from 1/1/12-11/30/17. Demographic, disease, and treatment data were collected. Descriptive statistics were performed. Opportunities were evaluated over time quartiles from date of diagnosis to death. Timing and reasoning for consultation to a subspecialty PC service were examined. These variables were compared across disease groups.

Results: Included patients (n=296) had diagnoses of LL (n=87), ST (n=114), and CNS tumors (n=95). Palliative opportunities were more frequent in patients with ST (median 8, range 1-21) and CNS tumors (median 7, range 0-31) versus LL (median 5, range 0-21, p=0.001). Patients with ST and CNS tumors had more admissions for severe symptoms (p=0.0002). While patients with ST had more progression/relapse-related opportunities (p<0.0001), patients with CNS tumors had more EOL-related opportunities (P<0.0001), specifically DNR status and hospice enrollment, compared to LL and ST. Palliative opportunities increased towards the EOL in all

diseases. PC was consulted in 108 (36%) patients overall: LL (48%), ST (34%), and CNS (32%, p=0.02). Prior to death, patients with CNS tumors, when compared to LL and ST, had earlier PC consultation (63 vs. 51.5 and 48 days), DNR status (18 vs. 3 and 3 days), and hospice enrollment (45 vs. 31 and 23 days).

Conclusion: Pediatric patients with cancer incur many events during their disease course that warrant PC support, regardless of underlying diagnosis. Patients with ST and CNS tumors had more palliative opportunities than patients with LL yet received subspecialty PC less often. Understanding the type and timing of palliative opportunities within each disease can guide utilization of PC consultation to ease patient and family stress and symptoms during the cancer course.

Poster # 147

MANAGEMENT OF ASPARAGINASE-ASSOCIATED COAGULOPATHY AMONG PEDIATRIC ONCOLOGY PROVIDERS

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Background: Coagulopathy and thrombosis are well-described complications of asparaginase therapy. Over one third of pediatric patients undergoing asparaginase therapy experience thrombotic events; however, the majority are undiagnosed because they are clinically asymptomatic. Proposed strategies for managing hemostatic derangements include repletion of deficient proteins (e.g., fibrinogen, antithrombin) and/or administration of pharmacologic anticoagulation; however, evidence-based guidelines for pediatric patients are lacking.

Objectives: To assess current management practices for asparaginase-related coagulopathy by pediatric hematology oncology (PHO) providers.

Design/Method: Email survey of 2,327 PHO providers, primarily practicing in the United States. Descriptive statistics were used to describe and summarize survey findings.

Results: Two hundred and eighty five (12.2%) attending physicians completed the survey. Only 4.6% (n=13/285) routinely prescribe prophylactic anticoagulation during induction chemotherapy for leukemia with asparaginase. Slightly more than half (n=145/250, 50.9%) of all providers perform baseline coagulation studies. Among those who order coagulation labs routinely, 41% (n=59/144) repeat testing only if abnormal, 19.4% (n=28/144) order labs prior to invasive procedures such as lumbar punctures, and 11.1% (n=16/144) repeat labs once a week following asparaginase. Commonly ordered baseline laboratory studies include a complete blood count (n=90/145, 62.1%), PT (n=86/145, 59.3%), aPTT (n=85/145, 58.6%), fibrinogen (n=84/145, 57.9%), and antithrombin (n=24/145, 16.6%). Most that were surveyed (n= 185/285, 64.9%) only replete coagulant factors if the patient experiences bleeding or increased bruising. One hundred and thirty (n = 130/285, 45.6%) physicians replace low fibrinogen at a median cutoff level of 100 mg/dL (range: 40-200) with the median target of 100 (range: 50-200). The

most common replacement products include cryoprecipitate (n=110/130, 84.6%), fresh frozen plasma (n=37/130, 28.5%) and fibrinogen concentrate (n=21,16.2%). A minority of physicians (n=39/250, 13.7%) of physicians replace low antithrombin with the most common products being antithrombin concentrate (91.5%) and FFP (2.6%). The median cutoff activity level for antithrombin replacement is 60% (range 40-100) with a median target of 75% (range: 40-125).

Conclusion: There is a large variation in PHO provider practices for monitoring and management of asparaginase-associated hemostatic derangements. This observation highlights the need for evidence-based guidelines to standardize practices.

Poster # 148

TELEHEALTH ACCEPTABILITY BY PEDIATRIC HEMATOLOGY/ONCOLOGY CAREGIVERS AND PATIENTS IN AN URBAN CLINIC

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Background: Due to restrictions imposed by the COVID-19 pandemic, telehealth has become a necessary part of healthcare. Our pediatric hematology/oncology (PHO) urban clinic supports a predominantly Black community with a medium to low income level. For our families the direct and indirect costs of in-person clinic visits for chronic illness are a burden, worsened by the potential for infectious exposure. Given the heightened socioeconomic burdens in the midst of the pandemic we sought the perspectives of our families in regards to use of telehealth as an alternative to in-person visits.

Objectives: This study aims to assess patients and families' opinions on telehealth and whether insurance status, race or education has an effect on patients and families' acceptability of telehealth in the setting of an urban PHO clinic.

Design/Method: In this cross-sectional study, parents of PHO patients or patients (if older than 18years) who had a telehealth visit in the past year completed a demographic questionnaire and the "Telehealth Acceptability Instrument" – a 30-question 5-domain Likert-scale survey assessing Ease of Use, Feasibility as a Healthcare Tool, Reliability, Satisfaction, and Telehealth Role during COVID-19 pandemic. Interviews were led by phone, data was managed using REDCap. Microsoft Excel was used for descriptive statistics and T-test analyses.

Results: Out of 66 eligible subjects 59% completed our survey. Of the 39 participants 51% were black, 59% had some college education or more, 79% had Medicaid or no insurance and 69% participated in hematology encounters. Overall participants favored telehealth visits, and those with concerns regarding COVID felt at ease using a Telehealth approach. 77% of participants agreed that telehealth saves them money and 92% agreed telehealth saves them time. We did not find a difference in acceptability based on education level of participants or between families accessing oncology versus hematology services. There was a trend towards significance for Black families who were more likely to favor telehealth services compared to their non-Black

counterparts (p 0.07). Similarly families with private insurance favored aspects of telehealth more than families with Medicaid or no insurance (p 0.07).

Conclusion: Our study provides insight into the perspectives of families from an urban community accessing PHO services using Telehealth technology. Overall patients and their families are satisfied receiving PHO care via Telehealth, found the interface easy to manage and were happy with the interaction with their provider. In addition Telehealth visits saved families time and money.

Poster # 149

PILOT PODCAST IMPROVES RESILIENCE AND REDUCES DISTRESS IN ADOLESCENTS WITH CANCER & THEIR CAREGIVERS

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Background: During cancer therapy, adolescent and young adult (AYA) patients experience considerable stress and anxiety, as do their parents and caregivers. Resilience-promoting interventions have been introduced for AYAs and their caregivers separately, but few have examined interventions that might enrich their relationship and help them cope together.

Objectives: To determine whether AYAs and their caregivers might benefit from a joint intervention, we conducted a series of guided parent-child conversations and measured (a) resilience and (b) psychological distress both before and after the intervention.

Design/Method: For this pilot intervention, English- or Spanish-speaking AYAs (ages 10 – 25 years [y]) with cancer and their caregivers were invited to participate in a podcast series (*CHONYCorps*) during which they would they would receive a list of suggested questions and interview each other for approximately 40 minutes about what was important to them. Within a week of the interview, a 5-minute clip would be published as a podcast episode. Primary outcomes were (1) resilience and (2) psychological distress, measured both before and after the intervention using the *10-item Connor-Davidson Resilience Scale* and the *Kessler-6 Scale*, respectively. Pre- and post-intervention data were analyzed using paired t-tests, and results are reported on a point scale with 95% confidence intervals (CI). P-values <0.05 indicate a significant difference between pre- and post-intervention measures.

Results: Between October and December 2020, eight pairs of AYAs (ages 10 – 18y, median 15y) undergoing cancer treatment at NewYork-Presbyterian / Columbia University Irving Medical Center and their parents consented to participate and completed both pre- and post-intervention assessments. For the patients, participation in *CHONYCorps* resulted in statistically significantly improved resilience (+3.25 points; 95% confidence interval [CI], 1.42 – 5.08, p=0.004) and psychological distress (+2.13 points; 95% CI, 0.06 – 4.19, p=0.046). In the caregivers, participation was also associated with improved resilience (+4.38 points; 95% CI, -

0.047-8.80, p=0.052) and psychological distress (+2.25 points; 95% CI, -0.46-5.0, p=0.090), though these did not meet statistical significance. All pairs reported that they enjoyed participating in the interview and would recommend the experience to others.

Conclusion: These pilot data suggest that for AYAs with cancer, participation in guided, meaning-making conversations with their parents is an acceptable intervention that improves both resilience and psychological distress. Recruitment is ongoing and will expand to include patients with sickle cell disease and recipients of bone marrow transplants in the future.
To listen to an episode, visit anchor.fm/chonycorps.

Poster # 150

SEDATION PRACTICES FOR LUMBAR PUNCTURES IN PATIENTS WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Lumbar punctures (LPs) are frequently performed in pediatric patients with acute lymphoblastic leukemia (ALL) for diagnostic and therapeutic purposes. Sedation is often used to reduce pain, anxiety, and fear associated with these procedures and is generally considered safe. However, there is a potential for negative long-term effects on neurodevelopment and cognition with repeat sedative exposures in young children.

Objectives: The purpose of this study is to determine the practice habits regarding sedation for LPs in pediatric patients with ALL among multiple institutions.

Design/Method: This is a retrospective study using data from 48 pediatric hospitals in the Pediatric Health Information Systems (PHIS) between October 2015 and December 2019. Children aged 1-18 years old with ALL who received chemotherapy into the CNS in an outpatient setting were included. Patients with Down syndrome or developmental delay were excluded. Encounters that combined LPs with non-LP procedures which commonly utilize sedation, such as bone marrow biopsies and line placements, were excluded to avoid confounding. We analyzed the prevalence of anesthesia usage and the types of anesthetics used.

Results: There were 18,531 unique encounters with pediatric ALL patients who had therapeutic LPs performed in a total of 3,178 unique patients. Of the 16,785 encounters with documented use of anesthetic medications, general anesthetics were used in 16,486 (98.2%) and local anesthetics alone in 299 (1.8%). The most commonly used medications used for general sedation were propofol (*n*=13,279; 79.1%), followed by midazolam (*n*=4,228; 25.2%), inhaled fluranes (*n*=3,169; 18.9%) and ketamine (*n*=2,100; 12.5%). Among encounters with local anesthesia only, lidocaine (*n*=278; 93.0%), lidocaine prilocaine (*n*=15; 5.0%), or bupivacaine (*n*=14; 4.7%) were utilized. In the LPs encounter which used local anesthesia only, patients were older on average (8.1 years vs 6.5 years; p<0.0001).

Conclusion: The majority of children's hospitals in the United States use general anesthetics for routine therapeutic LPs in pediatric patients with ALL. Propofol is one of the most common medications used for sedation. Attention should be paid to the sedation practices for routine LPs in patients with ALL given the potential neurocognitive effects of repeat general anesthesia exposures in young children.

Poster # 151

SURVEY OF PEDIATRIC ONCOLOGISTS REGARDING PALLIATIVE CARE INVOLVEMENT IN PEDIATRIC ONCOLOGY PATIENTS

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Background: Both the World Health Organization and American Academy of Pediatrics note that palliative care involvement is recommended for children with cancer at the time of diagnosis, irrespective of prognosis. Palliative care services offer numerous benefits such as psychosocial support, improved pain and symptom management, improved care coordination, fewer deaths in the intensive care unit, and improved patient and family quality of care. Despite this, barriers to involvement in pediatric cancer patients exist.

Objectives: We sought to describe palliative care services available to children with cancer along with pediatric oncologists' current and ideal practices of palliative care involvement in children with cancer.

Design/Method: A novel survey tool was administered via REDCap to attending pediatric oncologists in the United States. Multiple choice items were developed to assess demographics, checkbox items to assess palliative care team structure and situations in which the palliative care team is most helpful, Likert scale items to assess institutional and ideal standards regarding consulting palliative care. We performed conventional descriptive analysis of all survey items.

Results: A total of 265 survey responses were evaluated. Almost all respondents (96.2%) reported having some palliative care services available. The palliative care team structure was variable but approximately 75% had at least one medical provider and at least one psychosocial provider including social workers, child life specialists, psychologists, and pastoral care. Most respondents endorsed that palliative care *should* "always" be consulted for the following scenarios: advanced metastatic disease (53%), uncontrolled symptoms (65%), bone marrow transplant (55%), and relapsed/refractory disease (73%). For those same scenarios, the majority noted the *current standard* was to "sometimes" or "usually" consult**.** Most respondents (92.6%) felt that palliative care should be consulted more frequently than their current institutional standard. There were no significant differences in mean Likert scale responses for ideal practice based on years of experience, percentage of time spent in clinical care, oncology program size, and team composition.

Conclusion: The results from this survey revealed that pediatric oncologists believe palliative care should be consulted more frequently than the current institutional standard for a number of scenarios. Barriers to palliative care consultation have been described in the literature, however, how to address these barriers and exploration of the barriers specific to oncologists who are in favor of palliative care consultation in their patient population is lacking. It is crucial to learn more about these barriers in order to facilitate the integration of palliative care into the care of pediatric oncology patients.

Poster # 152

OUTPATIENT MANAGEMENT OF NON-NEUTROPENIC FEVER IN PEDIATRIC ONCOLOGY PATIENTS: MSK KIDS EXPERIENCE

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Background: Serious bacterial infections are a significant cause of morbidity and mortality in pediatric oncology patients, often heralded by a fever. Neutropenic patients with fever are empirically managed with rapid administration of broad-spectrum antibiotics. However, the management of non-neutropenic patients with fever varies: some institutions give antibiotics empirically, while others observe. A 3-10% incidence of bacteremia has been reported in patients with non-neutropenic fever, and patients with infections generally present with objective signs of illness.

Objectives: Characterize the clinical presentation, management, outcomes, and rate of bacteremia in pediatric oncology patients with central venous access presenting with non-neutropenic fever at a major oncology center.

Design/Method: Retrospective review of patients treated at MSK Kids receiving cancer-directed therapy with central venous access presenting to the Pediatric Ambulatory Care Center with fever (reported/recorded temperature ≥38.0ºC) and found to be non-neutropenic (ANC >0.5K/mcL) between 1/1/2019 – 6/30/2019. Patients who received allogeneic hematopoietic stem cell transplantation were excluded. Data points extracted include: demographics, diagnosis, current therapy, vital signs and labs on presentation, outcome of visit including disposition, and results of infectious evaluation. Descriptive statistics were used for analysis.

Results: 284 visits met inclusion criteria. Median age was 5.85 years (0.5 – 34.1), and 45.1% (n=128) of visits were female patients. Underlying diagnosis most commonly included neuroblastoma (54.2%, n=154), hematologic malignancy (19.7%, n=56), and sarcoma (18.3%, n=52); 47.2% (n=134) had relapsed disease. The majority had most recently received conventional chemotherapy (38.7%, n=110) or treatment with the anti-GD2 antibody naxitamab alone (34.9%, n=99). Based on hospital practice and clinician judgment, 94.4% (n=268) of visits received parenteral antibiotics, most commonly ceftriaxone (94.0% of antibiotics administered,

n=252). Blood cultures were positive in 1.8% of visits (5 encounters, 4 unique patients), primarily with gram positive organisms (80%, n=4); antibiotics had been empirically administered in 4 of these visits (80%). Three positive cultures (2 unique patients) occurred in patients with an underlying diagnosis of sarcoma and 2 occurred in patients with neuroblastoma. The majority (80%, n=4) were described as "well-appearing" on presentation, and none had focal infection. One patient was admitted at initial presentation due to clinical concern; 4 were admitted after blood culture resulted positive, and none required admission to the intensive care unit. No deaths from infection occurred.

Conclusion: Our experience reveals a lower rate of bacteremia than previously reported, suggesting that even in heavily pre-treated pediatric oncology patients with non-neutropenic fever, antibiotics can be safely avoided in well-appearing patients. Further prospective work is needed.

Poster # 153

PEDIATRIC AND ADULT JOINT HEMOGLOBINOPATHY CLINIC: AN EXPERIENCE OF SEAMLESS TRANSITION OF CARE

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Background: With improved survival of children with transfusion-dependent thalassemia (TDT) and sickle cell disease (SCD), transition of care (ToC) to adult care providers is of utmost importance. Due to several barriers to effective ToC (e.g. lack of formalized processes, limited access to knowledgeable providers and importantly, patients' fears of leaving familiar care facilities and providers, and uncertainties regarding new providers), loss to follow up (LTFU) is a major challenge. To mitigate these challenges and provide a smooth ToC, the McMaster Joint Hemoglobinopathy Clinic (MJHC) was established in 2013 to support lifelong care for a growing number of patients with SCD and other hemoglobinopathies in the Hamilton-Wentworth area in Ontario, Canada (population 747,000 people).

Objectives: To evaluate the prevalence of LTFU at MJHC after ToC from pediatric to adult caregiver. LTFU was defined as a lack of attendance at clinical visits for at least 2 years, for unknown reasons.

Design/Method: The MJHC is the first co-located pediatric and adult hemoglobinopathy clinic in Canada which caters for patients of all ages under one roof to provide comprehensive care across the entire age spectrum. The clinic runs one day a week and consists of a pediatric hematologist, an adult hematologist, one nurse coordinator, and a social worker. Predefined ToC process starts with 12-13 year-old patients and includes development of age-appropriate autonomy with self-care, medication management, transition preparedness questionnaire and discussions with the health care providers. While still in the pediatric clinic, patients meet with the adult physician several times. The last formal pediatric visit before transition to adult care is

structured as a joint visit with both the pediatric and adult physicians. Clinic database was evaluated for patient demography, disease type, timing of ToC and post-transition of follow up and care.

Results: From 2013 to 2018, a total 22 patients were transitioned to adult care; 11 with thalassemia of whom 6 had TDT. Of the 11 patients with SCD, 8 had HbSS and 3 HbSC disease. One patient with HbSC disease out of 22 patients (4.55%; 95%CI 0.12-22.8) was LTFU. One patient, unfortunately died within the first year after transition due to SCD-related complications.

Conclusion: DEspite the small sample size, we have documented ~95% successful ToC. The MJHC model introduces a novel ToC method especially suitable for medium size centers and may act as a template for future programs for hemoglobinopathy and other chronic diseases in Canada or elsewhere with universal health coverage.

Poster # 154

"YOUR CHILD HAS CANCER": PERSPECTIVES OF PEDIATRIC ONCOLOGISTS REGARDING NEW DIAGNOSIS DISCUSSIONS

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Background: Each year approximately 15,000 children are diagnosed with cancer, and the lives of these children and their families are forever changed. This pivotal moment is shaped by how the oncologist delivers the life-altering news, and the environment in which it is delivered. While physician-family communication is foundational to pediatric oncology practice, there is a paucity of literature regarding how oncologists conduct new diagnosis discussions with families.

Objectives: Conduct and analyze qualitative interviews with pediatric oncologists to determine their perspectives regarding the general approach, logistics and informational content for new diagnosis discussions.

Design/Method: Interviews for this IRB-approved qualitative study were conducted between July 2017 and March 2019 at a single institution in the Southeastern United States. Twenty pediatric oncology physicians (17 faculty, 3 fellows) participated. A trained research team member conducted the interviews. Standards for reporting qualitative research guidelines were followed. Content analysis methodology guided the process.

Results: Four major themes that defined physician approach to the new cancer diagnosis discussion emerged: i) *Staged Approach to Information Delivery; ii) Participants; iii) Preparation;* and iv) *Prognosis and Uncertainties. Staged Approach to Information Delivery* encompassed the concept that the new oncology diagnosis discussion is actually a series of discussions (i.e., concern for cancer; confirmation of the cancer diagnosis; and treatment

plan/consent), with oncologists entering the discussions at different stages based on cancer type. *Preparation* included the importance of finding an optimal location for the discussions that prioritized privacy, as well as physician preparation for leading the discussions (i.e., reviewing medical literature and treatment protocols, preparing for the emotional impact [on family and physician] of conveying a child's cancer diagnosis). *Participants* focused on determining which adults to include in the discussions (e.g., parents, extended family, healthcare team members), and factors relevant to inclusion of the child (e.g., maturity, parental preference). Finally, *Prognosis and Uncertainties* incorporated the "balancing act" of conveying prognosis honestly while taking into account parental preferences for receiving information, and the importance of conveying hope even in situations where the disease carried a dismal outlook.

Conclusion: Findings from this study provide insight regarding how pediatric oncologists conduct new diagnosis discussions with families using a staged approach, typically over multiple days to allow families to process new information as it becomes available. These findings can inform the training of pediatric hematology/oncology fellows who are learning to conduct diagnostic discussions for children with newly diagnosed cancer.
Support: Alex's Lemonade Stand Foundation (PI: Landier)

Poster # 155

TRUST IN PHYSICIANS AMONG HISPANIC CAREGIVERS OF CHILDREN WITH NEWLY-DIAGNOSED CANCER

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Background: Trust in the physician is considered a vital element of the therapeutic alliance and has been closely related to adherence to treatment and effective and satisfactory patient-provider relationships. Lack of trust in physicians or the healthcare system has been associated with poorer health outcomes and has contributed to health disparities. Historically, lower trust in the healthcare system has been reported by African-Americans. There is lack of research assessing levels of trust in physicians among other minority group caregivers, such as Hispanics.

Objectives: To explore the contextual and socio-demographic factors associated with trust among Hispanic caregivers of children with cancer, compared to non-Hispanic Whites (NHW).

Design/Method: The Pediatric Trust in Physician Scale (Pedi-TIPS) was completed by 140 caregivers of children with newly-diagnosed cancer at Rady Children's Hospital San Diego. Contextual and socio-demographic factors associated with trust in physicians were assessed including health literacy with the Newest Vital Sign, acculturation with the Short Acculturation Scale for Hispanics, and socio-demographic characteristics including parental age, income, English proficiency, number of children in the household, insurance type, education level, marital status, ethnicity, religion, employment status, and preferred spoken/written language for

medical information (English or Spanish). Associations were assessed with linear regression models.

Results: Participants were 49% Hispanic (n=69) and 67% (n=94) female. The mean difference of the Pedi-TIPS scores between Hispanics and NHW was 0.081 (p = 0.934). Lower levels of trust in physicians were significantly associated with caregivers' number of children (two or more) [p = 0.006]. Level of trust in physicians was not associated with health literacy, acculturation, Hispanic ethnicity or any of the other socio-demographic factors assessed.

Conclusion: Despite a significant number of Hispanics in our sample, Hispanic ethnicity was not associated with decreased trust in physicians among caregivers of children with newly-diagnosed cancer. Our results suggest that trust in physicians and the healthcare system may differ among different minority groups. Our findings are limited by the small sample size, and assessment in one geographic region. Improved understanding of factors associated with trust in minority groups is needed to enhance patient's satisfaction and access to care. Further research is needed in larger, geographically diverse Hispanic communities to confirm these results.

Poster # 156

DEVELOPING A GUIDELINE FOR THROMBOEMBOLISM PROPHYLAXIS IN CHILDREN WITH INFLAMMATORY BOWEL DISORDER

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Background: Patients with inflammatory bowel disorder (IBD) are more likely to form thromboembolisms[1] due to the pro-inflammatory nature of the disorder. Enoxaparin has been effective in providing anticoagulant thromboprophylaxis for this population[2].

Objectives: Our SMART goal is to increase provider consideration of thromboprophylaxis for pediatric patients with IBD admitted to the hospital by 50% in 6 months, as measured by usage of a 'dot phrase', or electronic medical record (EMR) auto-text shortcut that prompts providers to consider thromboprophylaxis in these patients.

Design/Method: We performed a retrospective chart review of 176 pediatric patients with IBD and found 7 to have had thromboembolic events. We then created guidelines for providers to identify patients at risk for thromboembolism using the risk factors found in these 7 patients as well as literature review and previous guidelines established by UC San Francisco. These were approved by the UC Davis Thrombosis and Anticoagulation Subcommittee. We created a dot phrase in the EMR for providers to use to determine and document which patients are in need of a hematology consult for evaluation for thromboprophylaxis. Pediatric resident physicians admitting these patients were instructed to use the dot phrase in EMR notes for any patient with a history of IBD who gets admitted. A chart review was conducted between 11/26/20 - 12/31/20 to assess dot phrase usage. This period served as our first PDSA cycle.

Results: Two patients met criteria for dot phrase use. One was admitted overnight for observation and discharged the next morning, and no dot phrase was used. The second was admitted for an IBD flare. The dot phrase was used and a formal hematology consult was placed, resulting in initiation of enoxaparin.

Conclusion: It has not been common practice for our pediatric gastroenterology service to consider any thromboprophylactic interventions, so our dot phrase was successful in prompting providers to do so. For our next PDSA cycle, we plan to elicit provider feedback of dot phrase ease-of-use. We will also consider making an adjustment in the guideline to exclude patients that are expected to be admitted for less than 24 hours. Additionally, based on hematologist recommendation, we plan to change our guidline to prompt users to order inflammatory markers such as D-dimer and fibrinogen to help guide evaluation. These changes will be reflected in an updated version of the dot phrase.

References
1: Lazzerini et al, *Inflammatory Bowel Diseases*, 2011.
2: Diamond et al, *The Journal of Pediatrics*, 2018.

Poster # 157

PERCEPTION OF PEDIATRICIANS TOWARDS PHO AND FACTORS INFLUENCING FELLOWSHIP ENROLLMENT IN ETHIOPIA

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Background: Cancer is predicted to be an increasingly important cause of morbidity and mortality throughout all regions of the world. The estimated annual incidence of cancer in Ethiopia is around 60,000 cases, of which approximately 12,000 (20%) are within the pediatric age group. Despite this growing burden, cancer remains a low public health priority in the country. Coverage and quality of pediatric cancer care in particular are very low. There are only seven certified pediatric hematologist-oncologists for more than 110 million Ethiopians. The lack of interest among young pediatricians to pursue further study in pediatric hematology-oncology (PHO) deserves analysis to reverse the trend.

Objectives: To identify and assess the factors influencing perception and interest of pediatricians towards pediatric oncology services in Ethiopia.

Design/Method: The study design was a descriptive cross-sectional where both quantitative and qualitative data were collected using a self-administered questionnaire in the five Institutions in Ethiopia. SPSS version 21.0 was used for data analyses.

Results: A total of 218 respondents participated in the study of which 81.7% were pediatric residents; 12.8% were General Pediatricians and 5.5% were Pediatricians with other subspecialties. 63.76% were not interested in pursuing further study in Pediatric Hematology-

Oncology (PHO) and 51% were not satisfied with the current PHO services in Ethiopia. The top five reasons were: shortage of resources; a poorly functioning multidisciplinary team; poor quality of care; lack of treatment guidelines; and poor coordination of care. There was a statistically significant association between poor interest and gender, category of profession, and institution where they are practicing.

Inadequate undergraduate PHO training was reported by 73.4% and inadequate graduate PHO training was reported by 46.8%. 16.06% of the respondents had very low, 71.56% had adequate, and 12.39% had very good knowledge about the cardinal symptoms and signs of Pediatric cancers.

Conclusion: The burden of pediatric cancer cases is increasing at an alarming rate. Among all cancer cases in Ethiopia, the pediatric age group constitutes 20%. The majority of respondents were neither interested in nor satisfied with the field of Pediatric Hematology-Oncology. Inadequacy of the existing PHO training was reported by 73.4% and 16.06% had very low knowledge about the cardinal symptoms and signs of pediatric cancers. Policymakers, health managers, training Institutions, and partners should look into this situation and make necessary interventions to meet the expected future high workforce demand in the field.

Poster # 158

THE USE OF STANDARDIZED PATIENT ENCOUNTERS TO IMPROVE COMMUNICATION SKILLS IN PEDIATRIC RESIDENTS

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Background: Communication has been described as the most common "procedure" in medicine and the importance of effective communication is well-established. Physicians' ability to communicate effectively may influence patient treatment choices, compliance, outcomes and patient satisfaction. Despite this, prior studies have demonstrated that physicians, at various levels of training, feel they lack sufficient knowledge of communication techniques and desire more formal training.

Objectives: We developed a standardized patient (SP) based communication training program for pediatric residents. The goal was to demonstrate feasibility of implementation, as well as improved self-assessed skill and comfort level in various aspects of communication in trainees.

Design/Method: The program consists of three two-hour sessions. Prior to meeting, residents are provided with material on communication strategies, and asked to complete a pre-training questionnaire. Participants are then given the opportunity to communicate difficult information, such as a new HIV diagnosis or telling a parent her child has leukemia, with minor alterations in SP response (i.e. anger or denial). Following each interaction, trainees are given feedback by the preceptor, SP and peers. Following course completion, participants complete a complimentary post-training questionnaire. The primary endpoint is change in trainee comfort level and self-

assessed skill level pre- and post-training.

Results: To date, 33 pediatric residents have participated in the program. Pre- and post-training questionnaires demonstrated trainees had an increased comfort level across many domains of communication skills such as warning a family/patient that bad news is coming and checking the patient's understanding. ($P < 0.005$). Residents also reported increased communication ability such as defining goals of a family meeting, communicating a poor diagnosis, and organizing the information that needs to be relayed ($P<0.005$).

Conclusion: In contrast to more time-consuming programs, data suggests this concise training program is effective and realistic for pediatric residents in their first year of training. Further planned study will evaluate if the program results are sustained by sending follow-up surveys to residents during subsequent years of training. Finally, to evaluate the feasibility of implementing the course more broadly, we plan to distribute a survey to assess the current status of communications skills training at other institutions, to be completed by pediatric residency program directors. The ultimate goal is to distribute the program to other centers currently lacking formal communication training.

Poster # 159

QUALITY IMPROVEMENT KNOWLEDGE IN PEDIATRIC HEME/ONC PHYSICIANS: A NEED FOR IMPROVED EDUCATION

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Background: Pediatric hematology/oncology fellows face unique patient safety challenges given the potential danger of chemotherapy and caring for immunocompromised patients. However, published curricula to teach pediatric hematology/oncology fellows about quality improvement (QI) strategies to improve patient safety are lacking.

Objectives: To perform a national needs assessment of pediatric hematology/oncology attending physicians regarding QI education for pediatric hematology/oncology fellows. Our results will guide the creation of a national QI curriculum for pediatric hematology/oncology fellows.

Design/Method: We sent an online survey to a national sample of pediatric hematology/oncology attending physicians who were not fellowship program directors, and to a national sample of pediatric hematology/oncology fellowship program directors. Our survey evaluated QI knowledge and experience, attitudes regarding the importance of QI, institutional resources available to teach QI, barriers to teaching QI, preferred educational strategies to teach QI, preferred QI topics to be taught, and descriptions of any current QI curricula for pediatric hematology/oncology fellows.

Results: We received 45 responses out of 331 surveys sent (14% response rate) from attending physicians who were not program directors, and 17 responses out of 67 surveys sent (25% response rate) from program directors. Attending physicians who were not program directors scored significantly lower than a historical group of medical trainees on one multiple choice question assessing QI knowledge (42% vs. 58% correct, p = 0.035). However, attending physicians who were not program directors performed similarly to the medical trainee group on two other multiple choice questions assessing QI knowledge. Only 13 (29%) of attending physicians who were not program directors reported competency to design and lead QI projects. Program directors described limited time for teaching QI to fellows. Program directors and attending physicians who were not program directors identified five topics for inclusion in a QI curriculum for fellows: root cause analysis, run charts, process mapping, chemotherapy/medication safety, and implementation/adherence to national guidelines.

Conclusion: Our needs assessment identified barriers to QI education for fellows: attending physicians might not have sufficient expertise to teach QI to fellows, and there is limited time for QI education. We identified the high priority QI topics for fellow education: root cause analysis, run charts, process mapping, chemotherapy/medication safety, and implementation/adherence to national guidelines. We also observed that pediatric hematology/oncology attendings themselves might need additional QI education which has important implications for continuing medical education.

Supported by 2019 American Society of Pediatric Hematology/Oncology Clinician Educator Award.

Poster # 160

RESIDENT EDUCATIONAL NEEDS ASSESSMENT & CURRICULUM IMPLEMENTATION FOR A HEMATOLOGY/ONCOLOGY ROTATION

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Background: A learning need is the difference between a person's current ability and a higher level of ability defined by either the learner, an organization, or society. A needs assessment is the process of collecting information to identify deficiencies in teaching practice and discrepancies between present and desired competence.[1] Performing a needs assessment is a critical step in curriculum development, especially in medical education. Evidence shows that a curriculum influenced by a needs assessment is more likely to cause a change in practice.[1]

Objectives: The goal of this project was to identify the learning needs of residents working on the pediatric hematology/oncology service to implement and evaluate a curriculum targeting these needs.

Design/Method: An electronic needs assessment survey was administered to all residents who work on the pediatric hematology/oncology service as part of their training. Residents rated their

comfort level at identifying and managing diseases included on the American Board of Pediatrics content specifications for hematology and oncology on a Likert scale from "not comfortable" (1) to "very comfortable" (4). They also rated their preferred learning format and listed topics that should be preferentially taught early in the rotation. Results informed the development of a novel curriculum for residents, focusing on their identified high-yield topics. To meet these learning needs, our curriculum intervention involved a two-hour "Boot Camp" at the beginning of the block, including lectures focusing on topics that residents requested early in the rotation: sickle cell disease pain management, oncologic emergencies, hematologic malignancies, chemotherapy side effects, and non-sickle cell disease pain management.
Following the implementation of the curriculum, residents are completing a pre- and post-rotation survey. The survey mimics the needs assessment and asks for feedback on their learning experiences.

Results: The needs assessment survey was sent to 112 residents and had a 34.8% (n = 39) response rate. Results demonstrated that 74.4% (n = 29) of respondents preferred protected time for in-person learning.
We are collecting data after curriculum implementation. Surveys will be analyzed to evaluate the efficacy of the curriculum at improving resident comfort level with covered topics.

Conclusion: By performing an educational needs assessment, we have developed a "Boot Camp" curriculum that provides education on specific topics requested by residents. We are currently assessing changes in resident comfort level at identifying and managing topics after curriculum implementation.

References:
1. Hauer & Quill, J Palliat Med, 2011.

Poster # 161

OUTCOMES OF CRITICAL COMMUNICATION EDUCATION IN PEDIATRIC HEMATOLOGY/ONCOLOGY FELLOWSHIPS

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Background: Despite the importance of critical communication (CC) (communication surrounding serious diagnoses, dying, end of life care, etc) for Pediatric Hematologists/Oncologists, previous literature has established that fellowship programs lack a standard approach to CC education. Experiential learning is often viewed as an alternative to formal curricula. However, limited data exist on learning outcomes (LO) of an experiential learning strategy in CC.

Objectives: This study aimed to describe the state of CC education in Pediatric Hematology/Oncology (PHO) fellowships and to evaluate the learning outcomes of CC

education.

Design/Method: Surveys were developed and distributed through Qualtrics to current PHO trainees and newly-graduated faculty (<5 years post-fellowship) to gather CC educational strategies in a "choose-all-that-apply" format. Learning outcomes were queried as end-of-fellowship and present day perceived comfort, skill, and difficulty with common communication scenarios in PHO. Recruitment occurred through email communication with fellowship programs as well as the ASPHO discussion forum. Participants accrued from February 2020 through October 2020.

Results: A total of 42 complete survey responses were collected (22 trainees, 20 faculty). Faculty were more likely to identify receiving CC education during fellowship compared to current trainees (65% vs 45%). For both trainees and faculty, the most common instructional methods were observation of senior physicians (trainees 100%, faculty 100%), direct observation of the trainee performance with feedback (trainees 100%, faculty 100%), debriefing (trainees 80%, faculty 92%), and didactic lectures (trainees 80%, faculty 69%). Mean ratings for comfort and skill were higher for faculty in all scenarios. The most challenging communication scenarios, for faculty at the present time, were determining goals of care, discussing relapse/disease progression, and discussing a new diagnosis with poor prognosis (85%, 69%, 46%); for trainees, the most challenging scenarios were determining goals of care, discussing relapse/disease progression, and discussing a new diagnosis with poor prognosis (70%, 60%, 60%). Lower mean comfort and skill ratings were identified for emotion-laden communication tasks (e.g. relapse/progression) compared to procedural communication tasks (e.g. consenting for chemotherapy) in both trainees and faculty at all time points.

Conclusion: Critical communication education in PHO fellowship training continues to be highly variable and relies heavily on experiential learning as an instructional strategy. Emotion-laden communication tasks remained difficult for faculty despite time in independent practice. Future study is needed to understand the impact of educational strategies on the perceived difficulty of this subset of CC, as well as other outcomes, such as physician wellness.

Poster # 162

IMPROVING THE RESIDENTS EXPERIENCE IN THE PEDIATRIC HEMATOLOGY ONCOLOGY ROTATION

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Background: The Pediatric Hematology/Oncology rotation is intended to familiarize pediatric residents with common problems in hematology/oncology they may encounter during their medical careers. Efficiency and communication are essential to provide adequate care to the patients and to optimize the learning experience of the residents in the pediatric hematology oncology rotation. Post-evaluations of pediatric hematology oncology rotation in our hospital which were filled out by residents showed decreased satisfaction of our rotation due to lack of

efficiency and communication during an intense and demanding rotation. Therefore, we implemented a pre-round meeting called “Sprint Rounds” where charge nurse, child life, social work, pediatric residents, pediatric hematology oncology fellow and pediatric hematology oncology attending participated in a quick discussion of each patient plans and concerns prior to formal rounds.

Objectives: The main objective was to improve efficiency and communication in the pediatric hematology rotation and optimize the residents experience by implementing a pre-round meeting called “Sprint rounds”. We also wanted to evaluate residents’ perception of improvement with a survey comparing efficiency and communication pre/post implementation of “Sprint Rounds” with the main goal of achieving a score greater 3 (Likert scale) in every statement regarding communication and efficiency.

Design/Method: A survey was developed to evaluate the implemented “Sprint rounds”. This survey was composed of three statements targeting how the “Sprint rounds” affected the rotation efficiency and communication in the form of Likert scale (Strongly disagree (1)- Strongly agree (5)). Also, the survey included two open ended questions to give further explanation if they had a disagreement with statements. We measure the improvement in efficiency and communication comparing evaluations prior and post implementation of “Sprint rounds”. Survey was given to every participant of the “Sprint Rounds” with a total of 50 surveys collected in a time period of 6 months after implementation of “Sprint Rounds”.

Results: Three main statements were evaluated with a Likert scale targeting if “Sprint rounds” improved efficiency and communication in the pediatric hematology oncology rotation. We compare scale results with previous post-rotation evaluation (Strongly disagree (1)- Strongly agree (5)). The average score of pediatric hematology oncology rotation prior to "Sprint Rounds" was 2-3 in communication and efficiency. The average score after implementation was 4.5 showing an improvement in the communication and efficiency of the rotation.

Conclusion: A schematic approach with “Sprint rounds” helped to improve the overall resident experience in our pediatric hematology oncology rotation by optimizing the efficiency and communication between our team members.

Poster # 163

PRBC: PEDIATRIC RESIDENT BOOT CAMP INCREASES RESIDENT COMFORT AND PREPAREDNESS ON HEM/ONC ROTATION

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Background: Resident training in pediatric subspecialties involves management of complex patient populations often with little orientation, requiring trainees to rely on their previous knowledge from medical school and on-the-job training. This high-stakes learning environment creates discord in resident comfort providing patient care and creates potential for patient error

due to inadequate preparation for the high-risk patients encountered in pediatric hematology/oncology.

Our Resident Experience hematology/oncology quality improvement initiative at Children's Hospital Colorado began in 2015 and has implemented many PDSA driven changes to improve the experience on the rotation. However, consistent feedback from residents regarding feeling unsafe and inadequately prepared to care for our unique patient population revealed the pressing need for an improved orientation. Our educational resource, the pediatric Resident Boot Camp (pRBC), occurs on the first day of each monthly rotation and addresses common emergencies that a resident will encounter their first day on-call.

Objectives: To determine the feasibility of implementing a boot camp orientation, and to understand the impact in resident comfort in management of hematologic and oncologic emergencies starting their rotation.

Design/Method: Graduate Medical Education evaluations provided initial problem identification. Two focus groups with five residents per group who previously completed the rotation provided the needs assessment and defined the objectives and educational strategies used in designing the curriculum. SMART aims were then used in design of curriculum and program evaluation. End-of-rotation REDCap surveys were sent to all residents completing the hematology/oncology rotation before (prior to July 1, 2020) and after the implementation of the pRBC orientation at Children's Hospital Colorado. Resident satisfaction and comfort were measured using a 5-point Likert scale (with 1-unsatisfactory to 5-superior).

Results: REDCap surveys were completed at an equal rate both before (20/24, 83.3%) and after (15/18, 83.3%) the implementation of the pRBC. Overall satisfaction on the hematology/oncology rotation was unchanged before and after the pRBC (4.1 vs 4.0, respectively). Residents felt more prepared starting the rotation following the implementation of the pRBC orientation (2.4 vs 3.5) and felt more prepared on their first night on-call (3.6 vs 3.9). Specifically, residents felt more confident in the management of common hematologic and oncologic emergencies after the implementation of the pRBC including tumor lysis syndrome (2.2 vs 3.6), fever and neutropenia (2.3 vs 4.0), acute chest syndrome (1.6 vs 3.1), and transfusion reactions (2.0 vs 2.7).

Conclusion: The pRBC orientation was logistically feasible and enhanced resident confidence in the management of critical emergencies encountered in this high-risk patient population.

Poster # 164

IMPROVING BLOOD PRODUCT TRANSFUSION PRE-MEDICATION PLAN DOCUMENTATION - A QUALITY IMPROVEMENT EFFORT

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Background: Pre-medication with acetaminophen and/or diphenhydramine to prevent febrile non-hemolytic transfusion reactions (FNHTRs) and/or minor allergic transfusion reactions (MATRs) is a common practice based on historical recommendation. However, recent studies show no benefit of pre-medication with widespread use of leukocyte-depleted products. The lack of evidence supporting pre-medication leads to practice variability and results in workflow inefficiency.

Objectives: The goal of this project was to improve the number of transfusion encounters with any documented pre-medication plan from baseline (19%) to greater than 80% in 1 year and to understand the current blood product pre-medication practice at our institution.

Design/Method: We performed a single-institution chart review on all outpatient blood product transfusion encounters in pediatric hematology/oncology patients treated from September 2018 – September 2020. Indications for pre-medication were reviewed to understand the local practice. A multidisciplinary quality improvement (QI) team designed interventions to improve the documentation of pre-medication preferences using QI methodology following the Institute of Healthcare Improvement model. Process measures included rate of documented pre-medication plans and rate of pre-medication; frequency of transfusion reaction was the balancing measure. Monthly data were analyzed using statistical process control analysis. Centerlines were shifted based on established rules for special cause variation.

Results: There were 4,646 outpatient leuko-reduced blood product transfusion encounters in 796 patients (2,427 packed red blood cells and 2,218 single donor apheresis platelets). Pre-medication was given in 1,430 (30.7%) encounters. At baseline, pre-medication regimen was documented in 19% of transfusion episodes. Rationale, listed for 12.4% (n =99) patients, included previous reaction (n=71, 72%), prevention of fever while neutropenic (n= 19, 19%), or family preference (n=9, 9%).QI interventions included development of an institutional transfusion pre-medication guideline, identifying clinicians responsible for making pre-medication recommendation, adding a passive electronic health record alert, and provider education. After the interventions, the average documentation in encounters given medication increased from 19% to 85%, while the average pre-medication rate decreased from 34% to 22%. There was no change in the average number of transfusion reactions (1.9 per 100 transfusions).

Conclusion: Using QI methods, documentation of pre-medication plans improved from 19% to 85%. Many providers use pre-medication for patients with history of transfusion reactions or to reduce potential for FNHTR during neutropenia. More research is needed to determine the role of pre-medication for blood product transfusion in these groups of patients.

Poster # 165

POSITIVE AND NEGATIVE SOCIAL MEDIA EXPERIENCES OF ADOLESCENTS AND YOUNG ADULTS WITH CANCER

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Background: Adolescents and young adults (AYA) are prolific social media (SM) users. Little is known about how AYAs with cancer use SM.

Objectives: To characterize SM use (frequency, platforms, content) and self-reported positive and negative experiences on SM among AYA with cancer.

Design/Method: AYAs with cancer aged 12-26 years and receiving care at a single pediatric cancer center completed a 28-item survey about SM use, including two open-ended questions regarding positive and negative SM experiences, in October and November of 2020. Diagnostic, prognostic, and treatment data were obtained from the electronic medical record. Survey data and open-ended items were analyzed with descriptive statistics and qualitative content analysis, respectively. Two qualitative researchers oversaw the coding process and adjudicated discrepancies.

Results: Data was obtained from 39 participants, with average age 16.4 (SD = 3.2) years. Most participants were male (21/39, 54%) and Caucasian (34/39, 87%). Diagnoses included leukemia/lymphoma (22/39, 56%), solid tumors (13/39, 33%) and brain tumors (4/39, 10%). About 44% (17/39) had <50% estimated overall survival per their oncologist. Nearly all (38/39, 97%) used SM, with Smartphone data indicating an average SM use of 3.5 (SD = 1.4) hours/day. YouTube, Snapchat, and Instagram were the most popular platforms. Participants reported they used SM to obtain information about their cancer (17/38, 45%), post about their cancer experience (18/38, 47%), and read about others' cancer experience (19/38, 50%). Nearly a third of respondents reported making a friend with cancer through SM (12/38, 32%). Qualitative content analysis revealed mostly positive SM experiences, such as feelings of support related to their cancer (20/37, 54%) and community (10/37, 27%). Others reported SM as a desired distraction from their cancer or as a source of inspiration (3/37, 8%). Most participants (28/36, 78%) reported no negative experiences with SM; however, 6/36 (17%) reported online bullying related to their cancer.

Conclusion: AYAs with cancer are avid SM users who mostly report it creates a sense of support and community. Some report online bullying. These data underscore an opportunity for AYA oncology providers to enhance positive and avoid negative aspects of SM by asking about and providing guidance for SM use.

Poster # 166

END-OF-LIFE COMMUNICATION AND MORAL DISTRESS IN PEDIATRIC ONCOLOGY CLINICIANS

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Background: Discussing goals of care and end-of-life (EOL) decisions for children with incurable cancer is challenging for families and clinicians. Data is lacking for how ambiguity or conflict about goals of care contributes to moral distress and burnout for pediatric oncology clinicians.

Objectives: To elicit clinician perspectives on communication and EOL decision-making and explore factors contributing to moral distress when caring for pediatric oncology patients at EOL

Design/Method: Pediatric oncology clinicians at our institution completed validated measures for compassion satisfaction, burnout, and secondary trauma (Professional Quality of Life Scale (ProQOL)) and moral distress (Measure of Moral Distress-Healthcare Professionals (MMD-HP)). Respondents answered questions about a hypothetical patient with osteosarcoma at four timepoints: diagnosis, relapse, progression, and terminal decline, eliciting opinions about prognostic disclosure and advanced care planning. Kruskal-Wallis tests compared MMD-HP and ProQOL scores across disciplines and years of experience. Relationships between MMD-HP and ProQOL scores were assessed using Pearson's correlation. Directed content analysis was used to analyze free text responses to the patient case.

Results: 93 respondents (46.5% response rate) included 17 attendings, 8 fellows, 11 advanced practice nurses (APNs), 48 nurses, 4 social workers and 5 other staff. 52% of nurses, 20% of physicians, and 9% of APNs had $\leq$5 years experience. Moral distress differed significantly by discipline: nurses scored higher (mean MMD-HP 123.1, SD 58) than physicians (89.4, 60.4), APNs (93.3, 51.8) or other staff (71.0, 33.7), p=0.012. MMD-HP scores varied by years experience with higher scores for clinicians with $\leq$5 and >20 years experience compared to those with 6-10, 11-15, or 16-20 years experience, p=0.003. Especially for nurses, MMD-HP scores correlated with ProQOL subscales for burnout (r=0.43) and secondary trauma (r=0.54). Case responses emphasized communicating realistic prognosis, providing anticipatory guidance, involving palliative care at time of relapse, and including the patient in decision-making. Respondents were most troubled by intrafamilial conflict, not honoring patient wishes, and parents not accepting a poor prognosis. Ethics consultation was identified as the primary resource to address conflict.

Conclusion: Among oncology clinicians at our institution, moral distress was higher for nurses and for clinicians with 0-5 years or >20 years of experience, correlating with burnout and secondary trauma. Providing aggressive care at EOL and intrafamilial conflict are significant sources of distress.

Poster # 167

IMPROVING ACCURACY OF SCHEDULING "SHUNT REPROGRAM" VISITS: A QUALITY IMRPOVEMENT PROJECT.

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Background: Children with brain tumors and programmable ventriculo-peritoneal shunts (prVPS) must have verification of correct shunt settings following magnetic resonance imaging (MRI). Failure to do so may result in significant morbidity from either over- or under-drainage of the cerebrospinal fluid. To reduce risk, we instituted a "Shunt Reprogram" visit at a high-volume tertiary care pediatric oncology hospital to verify prVPS settings. However, low rates of follow-up failed to mitigate this increased risk for patient harm. A multidisciplinary team consisting of neuro-oncology physicians, advanced practice providers, nursing, representatives from clinical operations, diagnostic imaging, radiation oncology and informational services was assembled to improve existing processes.

Objectives: To reduce the percentage of incorrectly scheduled shunt reprogram visits from 13.8% to zero within 12 months.

Design/Method: The visit was considered incorrectly scheduled if it was not scheduled at the same time as the MRI order request, scheduled on wrong date/time, or scheduled in the wrong location. Baseline data was collected by chart review. A shared database was created to log all incorrectly scheduled "Shunt Reprogram" visits. The process flow was studied and summarized in Failure Mode and Effect Analysis map. A Key Driver Diagram was constructed, and iterative Plan-Do-Study-Act cycles tested interventions. Monthly data was analyzed using statistical process control analysis. Centerlines were shifted based on established rules for special cause variation in the context of interventions.

Results: At baseline, the 13.8% (median; range 0-43%) of shunt reprogram visits were incorrectly scheduled. Interventions: (1) improved identification of patients with prVPS by streamlining communication process between new patient nurse coordinators and care teams; (2) improved accuracy of recording of prVPS in patients electronic medical record (EMR); (3) created automated alerts in EMR to remind ordering providers to schedule a shunt reprogram visit at the same time as scheduling the MRI; (4) improved scheduler and provider education. The median percent of incorrectly scheduled visits reduced from 13.8% to 0% in 12 months.

Conclusion: A multidisciplinary team effort resulted in a significant reduction of the percent of incorrectly scheduled shunt reprogram visits. We are currently in the process of creating a standard operating procedure to formalize the optimized workflow to sustain the accomplished results. The applied interventions should be disseminated broadly to reduce risk for patients.

Poster # 168

EVALUATION OF INFORMED ASSENT FOR CLINICAL TRIAL ENROLLMENT IN ADOLESCENT ONCOLOGY PATIENTS

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Background: Adolescent oncology patients present a unique challenge in obtaining informed assent due to high emotions surrounding diagnosis and complexity of care. Oncology patients as young as 12 years can provide assent for clinical trial enrollment, however there are few studies that have investigated patient assenting experiences. There is limited data available regarding the use of adult informed consent questionnaires in the adolescent oncology population to assess understanding of clinical trials and their roles as participants.

Objectives: The objectives of this study are to evaluate patient understanding of information during the assenting process for clinical trials, to examine parental influence on enrollment, and to elicit suggestions for making information more understandable to patients.

Design/Method: We conducted a descriptive mixed-methods study involving all Loyola University pediatric oncology patients aged 12-24 years who have provided documented assent for clinical trials within the past 10 years. We distributed a de-identified survey containing 16 questions from the Quality of Informed Consent Questionnaire (QuIC), which is a validated tool used in adult oncology clinical trial participants. Questions selected were those pertinent to pediatric clinical trials. Readability at 6th grade level was verified with the Flesch-Kincaid grade level test. QuIC questions measured objective understanding, with maximum score of 100 and higher scores indicating greater level of understanding. Additionally, the survey contained 6 open-ended questions regarding patient experience and suggestions to help improve patient understanding. These responses were inductively coded and analyzed using grounded theory to identify recurrent themes.

Results: A total of 19 participants were enrolled, with mean age of 17.5 years. Mean score for all adolescents was 73.76 (SD 9.02). Patients scored lower in areas of experimental procedures (54.63%), risks with participation (8.10%), and benefits to themselves that may be reasonably expected (50%). Emerging themes from open-ended responses included (i) altruism and desire to share knowledge as a motivating factor for enrolling in clinical trials (ii) desire for short video for conveying information (iii) trust in their medical providers and (iv) preference for parental presence during discussion due to shared decision making, clarification, and emotional support. Most respondents did not experience parental pressure to enroll.

Conclusion: Preliminary results suggest that certain aspects of clinical trial information require clarification for patients, and that parental presence can positively influence assenting experiences. Data collection is ongoing, but early results show that there is potential for a multimodal approach to simplify information and enhance understanding of clinical trials.

Poster # 169

UNEXPECTED OUTCOME: FREQUENT COVID19 SWABBING ENCOURAGES TRANSITION TO NON- SEDATED LUMBAR PUNCTURES

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Background: In children with leukemias or specific types of lymphomas, frequent lumbar punctures (LPs) are required for diagnostic and therapeutic purposes. For the past two decades, standard of care with these procedures has included general anesthesia or conscious sedation. In 2016, the FDA issued a warning regarding the effects of prolonged and frequent exposure to general anesthesia and other conscious sedation agents on the developing brain. A variety of neurocognitive changes have been demonstrated with prolonged or multiple exposures to general anesthesia, especially in children <5 years old (Kamat, P.P., 2016). The UC Davis Pediatric Oncology Division considered solutions for mitigating these risks, but uptake of non-sedative options was minimal due to lack of parental and patient enthusiasm. In March 2020, the onset of the COVID pandemic forced practice changes surrounding anesthesia. COVID testing was required for all patients prior to potentially aerosol generating procedures, including anesthesia for LPs. This change in requiring frequent COVID swabs created great parental anxiety and patient distress, especially in younger patients. The option for non-sedated LPs was offered to families as an alternative to frequent swabbing prior to general anesthesia and surprisingly accepted.

Objectives: The primary goal of this project was to create a non-sedated LP option for school-aged and younger patients with leukemia/lymphoma. The secondary goal was to reduce general anesthesia exposure and/or conscious sedation.

Design/Method: A multidisciplinary approach was used to create an outpatient non-sedated workflow for school-aged and younger patients. Practice changes included the use of oral midazolam as an anxiolytic agent and emphasis on the application of topical anesthetics at the LP site along with child life support before and during the procedure. Patients are carefully evaluated for suitability and extensive education is provided for the family and patient.

Results: Since July, when this practice change was implemented, 26% (54 of 201) of all procedures were non-sedated. Thus far, 14 patients (ages 3 to 19 years) have opted for non-sedated LPs. Approximately 28% are <5 years old.

Conclusion: Providing non-sedated lumbar punctures for children offers many benefits, including decreased exposure to general anesthesia, decreased time in clinical areas, better financial stewardship, and increased overall patient satisfaction. This project demonstrates the importance and feasibility of partnering with patients and families to individualize care and minimize the variety of stressors patients encounter related to oncology therapy during the COVID pandemic.

Poster # 170

CORE NEEDLE AND SURGICAL BIOPSIES HAVE EQUIVALENT DIAGNOSTIC YIELD AND SAFETY: A SINGLE CENTER STUDY

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Background: Approach to pediatric solid tumor biopsy varies by tumor type, institution, and provider specialty. Percutaneous core needle biopsy (CNB) is increasingly recognized as a less invasive, potentially safer alternative to surgical biopsy (SB), but is not widely adopted or studied.

Objectives: We aimed to retrospectively track diagnostic yield, ancillary testing, tissue banked, and complications following CNB compared to SB. We hypothesized that CNB safety and diagnostic yield would be comparable to SB, but that the ability to perform ancillary testing and enroll in tissue banking would be decreased in the CNB group.

Design/Method: Single center retrospective analysis was performed of all consecutive pediatric solid tumors biopsied at our institution between 01/2010-01/2020. Eighty biopsies were included (51 CNB, 29 SB). SB was further classified as open surgical (OSB, n=17), endoluminal (EL, n=4), or minimally invasive (MIS, n=8). Excisional biopsies were excluded.

Results: Approach to biopsy varied considerably depending upon tumor type; 44% of neuroblastomas versus 89% of hepatoblastomas were diagnosed by CNB. On average, seven cores were collected (range 2-16). Patient weight and tumor volume were comparable and diagnostic yield in both cohorts was excellent: Only one child in the CNB group required a repeat CNB to make the diagnosis. Tissue banking was tracked from 2015-2020 and revealed gross under-utilization of surplus tissue samples (2/8 consented SB and 1/9 consented CNB patients). Complication rates were comparable between CNB and all SB combined, but higher in OSB (4/17) compared to CNB (1/51) ($p<0.05$). There was no correlation between tumor size or number of cores with complications. The only CNB patient with a complication (requiring PRBC transfusion and Lasix post-procedure) was a 6-month-old with congenital heart disease and hepatoblastoma who had 4 cores taken.

Conclusion: In this single center retrospective study of 80 solid tumor pediatric patients, CNB was found to be safer than SB and yielded sufficient specimen for primary diagnosis in all but one case. We found wide variability in the number of cores taken, and therefore the number of surplus cores available for ancillary testing and tissue banking. From this limited study, we were unable to determine if biopsy type impacted enrollment in clinical trials. We plan to implement a prospective QI project that standardizes CNB and tissue banking protocols with the intent of increasing specimen yield for clinical trial enrollment and tissue banking, without increasing the risk to patients or compromising the ability to make the diagnosis.

Poster # 171

CHARACTERISTICS AND OUTCOMES OF PEDIATRIC ONCOLOGY PATIENTS AT RISK FOR TRANSFUSION REFUSAL

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Background: Myelosuppressive regimens have led to improved disease outcomes in pediatric cancer but require transfusion support. There is a paucity of literature characterizing outcomes or management of pediatric cancer patients in cases of transfusion refusal.

Objectives: To describe the clinical characteristics, care, and outcomes of oncology patients at risk for transfusion refusal.

Design/Method: A retrospective cohort of patients age 0-21 years with oncologic diagnoses and ICD-9 codes indicating transfusion refusal or Jehovah's Witness (JW) religion was identified. Patients diagnosed and treated between 2005 and 2020 at the Aflac Cancer and Blood Disorders Center, Children's Healthcare of Atlanta were included. Demographics, hematologic laboratory values, disease factors, medications, and transfusions (packed red blood cells (PRBC), platelets, fresh frozen plasma (FFP), cryoprecipitate, and intravenous immunoglobulin (IVIG)) were manually extracted from the medical record. Erythropoietin use and incident legal intervention were captured. Descriptive statistics were performed.

Results: Thirty-five oncology patients met the inclusion criteria. The median age at diagnosis was 8 years (range 0-20). The cohort is 62.9% male, 45.7% black, and 25% Hispanic. Diagnoses included leukemia/lymphoma (L/L) (51.4%), solid (28.6%), or central nervous system (CNS) tumor (17%). In 88.6% the primary guardian identified as JW; in the remaining other family members identified as such. Overall, 37% of guardians refused transfusion. Among 20 patients who received $\geq$ 1 transfusion, the guardian of 50% initially refused transfusion and legal intervention was required in 40% of those who received transfusion. An ethics consult was completed in 1 case. Transfusions included PRBC (20/20), platelets (17/20), FFP (1/20), cryoprecipitate (2/20), and IVIG (4/20). The median hemoglobin prior to first transfusion was 6.5 g/dL (range 3.4-7.9) in patients with L/L and 7.4 g/dL (range 4.7-10.2) in patients with solid/CNS tumors. Additional management included erythropoietin in 10 patients, 5 of whom never received transfusion. Additionally, 40% had an ICU admission during therapy and 37.1% enrolled on a clinical trial. Five patients were deceased; the median time from diagnosis to death was 333.5 days (range 61-1281).

Conclusion: Most patients at risk for refusal of transfusions had a primary guardian identified as JW, however transfusion was not refused by all. Association of sequelae of transfusion delays and needs for modification of cancer therapy need evaluation. Guidelines for systematic management and transfusion sparing approaches are needed to avoid disparate cancer outcomes

in this population.

Poster # 172

ASSESSMENT & PROCESS IMPROVEMENT FOR SAFETY EVENT INVESTIGATIONS IN A LARGE PEDIATRICS HEMONC GROUP

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Background: An initial assessment of routine safety event investigations indicated an unstructured orientation to the safety review process. Skill levels in methods for safety event investigation was unknown and the documentation process was not standardized.

Objectives: To capitalize on the value of routine safety event reporting and expertise of clinicians, group leadership created an orientation and new safety committee structure to facilitate safety event assessment. Formal review of safety events aimed to identify contributing factors, initiate corrective and preventive measures, and support quality improvement initiatives. PDSA cycles were designed to study the impact of education and establishment of a review process.

Design/Method: A baseline assessment using a survey administered to Safety Committee members was followed by two PDSA cycles. Survey questions were designed to evaluate understanding and comfort level about Safety Scoop System, safety event investigation process, and general safety culture in health care.

Survey was administered at baseline, after PDSA 1 and PDSA 2 to 23, 22 persons and 13 persons, respectively.

- PDSA cycle 1: Patient Safety Specialist provided training to Safety Committee members regarding event rating, investigational approach, event documentation, and human error versus system error.
- PDSA cycle 2: A weekly safety huddle with Safety Committee members was implemented. Safety events were reviewed followed by implementation of corrective and preventative measures. Survey was administered 3 and 6 months after initiation of weekly safety huddles.

Results: Baseline survey data: all trainees were able to locate Safety Scoop System, while a majority were not comfortable with documentation in the reporting system or the notion of "Second Victim". Survey showed a wide range of level of understanding about safety event investigation processes and concept of "Just Culture".

After PDSA cycle 1, a shift towards increase understanding of follow-up and documentation features and of safety event investigation processes was noted. Familiarity with general safety culture in HealthCare was increased. However in some areas, scoring remained flat or decreased following individual integration in the safety review process.

Further increase in understanding of safety event investigation processes and patient safety culture in HealthCare was observed after PDSA cycle 2.

Conclusion: Safety Event Project has allowed identification of educational needs related to safety event investigations and concept of safety culture. Future PDSA cycles will use the structure developed during this project to target areas for education and quality improvement opportunities.

Poster # 173

IMPROVING MALE ONCOFERTILITY COUNSELING IN ADOLESCENTS WITH CANCER: A MULTI-DISIPLINARY QI PROJECT

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Background: Chemotherapy has many short- and long-term side effects, including effects on fertility. Guidelines recommend that fertility risks and preservation options be discussed early during cancer treatment, especially in the pediatric population. Pediatric oncologists usually discuss specific fertility risks based on the chemotherapeutic regimen and sex and age of patient, however they do not receive targeted training in discussion of fertility preservation options.

Objectives: We conducted a Quality Improvement (QI) initiative with aim to increase the percentage of adolescent males (>12 y/o) with newly-diagnosed cancer who are counseled by the urology team on fertility risks and fertility preservation options prior to the initiation of chemotherapy from 0% to 50% over 6 months.

Design/Method: A QI multi-disciplinary team of pediatric oncologists, urologists, nurses and information technology specialists reviewed baseline data, then developed and implemented interventions using Plan-Do-Study-Act (PDSA) cycles. Barriers were identified using QI tools, including lack of knowledge on the subject and inadequate time to properly counsel the patient. Interventions included development of an onco-fertility protocol focused on fertility counseling and preservation, electronic medical record (EMR) order sets, smart phrases, and best practice alert triggers to facilitate workflow and documentation. We tracked the consultations that occurred and the number of patients who then pursued preservation options.

Results: During the study period 90.9% of eligible male patients (n=11) were seen and counseled by urology prior to systemic chemotherapy being administered. Of the ten patients counseled, six of them pursued fertility preservation (60%). The oncology providers entered ‘consult to urology’ orders the EMR in 9/11 (81.8%) of patients and documented their fertility discussion in the EMR using a dedicated smart phrase in 9/11 (81.8%). All patients counseled

by urology had documentation in the EMR, and the average time between the consult being placed and the patient being seen was approximately 2 hours and 25 minutes.

Conclusion: We achieved our aim through multidisciplinary collaboration and teamwork. Adequate provision of onco-fertility services requires continued improvement of age-appropriate care and collaboration between oncology, urology, nursing and information technology, as well as fertility clinics. Future PDSA cycles will include improving onco-fertility knowledge of patients and families, the quality of care provided and clinician's confidence in providing onco-fertility consultations.

Poster # 174

SEDATION FOR CHILDREN IN PEDIATRIC ONCOLOGY DEPARTMENT: EXPERIENCE IN A RESOURCE LIMITED SETTING

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Background: Most common procedures in pediatric oncology unit are lumbar puncture, bone marrow aspiration and biopsy. These procedures are painful and may cause emotional distress in children with cancer, hence, sedation and/or anesthesia are required. Considering the fact that above mentioned these procedures are usually short in duration, general anesthesia is often unnecessary. Procedural sedation, which previously called '' conscious sedation'', defines as a technique of administrating sedatives with or without analgesics in order to relieve pain and anxiety.

Objectives: This study aimed to describe procedural sedation and analgesia performed in children with cancer at one pediatric oncology center and to report safety and incidence of complications.

Design/Method: We conducted a retrospective review of the medical records of children (≤18 years old) diagnosed and treated at Pediatric Cancer and Blood Disorders Center of Armenia (PCBDCA), Hematology Center after R.Yeolyan, which is a resource-limited hospital, between February 2019 and July 2020 (18 months) undergoing procedural sedation. The cost of procedural sedation in PCBDCA is not high (40$). Children who underwent general anesthesia were excluded from the analysis. Clinical data were extracted, including patient age, sex, performance status, procedure type, sedation method, medications used during sedation, side effects, and complications during or after sedation.

Results: During the study period, 290 diagnostic and treatment procedures requiring procedural sedation were performed among 135 individual patients. Before each procedure, pre-anesthetic evaluation was performed among all patients. The most common oncologic diagnosis were leukemias (50, 37%), lymphomas (40, 29.6%), and solid tumors (45, 33.3%). Diagnostic and therapeutic procedures performed included: lumbar puncture (178, 61%), trephine biopsy (46, 16%), 33 central venous line placement, bone marrow aspiration (28, 10%), computerized

tomography scan (12, 4%) and 1 endoscopy. In all cases, propofol was used as the primary sedation medication[AA1] [RP2] . In 107 procedures (37%) it was used in combination with ketamine. Karnofsky performance scale score was <60% in 12 children. Reported complications were rare: 3 patients had hallucinations, 1 patient was agitated after sedation and 2 patients had apnea during sedation, which resolved quickly with bag-mask ventilation.

Conclusion: Procedural sedation and analgesia using propofol and ketamine is a safe, efficient, and not expensive strategy to facilitate diagnostic and treatment procedures in children with cancer in a resource-limited setting.

Poster # 175

A QUALITY IMPROVEMENT PROJECT TO EXPEDITE ANC RESULTS DECREASES WAIT TIMES FOR PATIENTS

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Background: Administration of chemotherapy depends on accurate and timely results of a complete blood count (CBC). Automated analyzers have markedly improved the efficiency and accuracy of CBCs, however, neutropenic patients still require manual review at our institution, due to the chance of error at the limits of the machine's parameters. In turn, patients experience increased wait times in clinic and delays in treatment initiation. Streamlining this process offers an opportunity to improve patient care and clinic efficiency.

Objectives: This project sought to reduce delays in administration of chemotherapy by shortening in-processing times for STAT CBC's requiring manual review. Working with the pathology department, we implemented a policy change in February of 2019 in which a manual differential may be certified by laboratory personnel, prior to pathologist review, for an absolute neutrophil count (ANC) < 1000/uL. We evaluated the time difference to CBC results before and after this policy change as well as the correlation between automated and manually calculated ANC's.

Design/Method: Deidentified CBC time to result and result data were acquired from the Sysmex XN 10 analyzer and the medical record system. A t-test was used to compare the mean time result of STAT CBCs before and after the policy change. Sub analysis was performed on STAT CBCs within the pediatric oncology department. Automated and manual differentials were compared through a pairwise correlation test.

Results: A total of 6,684 STAT CBCs (hospital wide) requiring manual differential between December of 2018 and August of 2019 were analyzed. 1,884 resulted prior to the policy change and 4,800 after. The time to result for STAT CBCs requiring manual differential decreased from 227 minutes to 126 minutes ($p < 0.001$). The time to result for STAT CBCs ordered in our department ($n = 568$) decreased from 103 minutes to 84 minutes ($p = 0.04$). Of the available 869

linked pairs of automated and manual differentials, there was a correlation coefficient of 0.99. Stratifying by WBC counts < 1,500 (n=54) the correlation (R) coefficient was 0.958, and for those with WBC counts >1500 (n=815) the R coefficient was 0.99.

Conclusion: Our policy change resulted in a statistically significant decrease in time to CBC results, however, there is still room for improvement given the excellent correlation between manual and automated differentials. The in-processing time for STAT CBCs could be further reduced by releasing the automated differential, specifically for WBC counts > 1,500, while maintaining a high degree of accuracy.

Poster # 176

ROLE OF HEALTH LITERACY IN CANCER KNOWLEDGE AMONG PARENTS OF CHILDREN WITH NEWLY-DIAGNOSED CANCER

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Background: Over 15,000 children are diagnosed with cancer annually. It is critical for parents of children with newly-diagnosed cancer to be knowledgeable regarding their child's cancer diagnosis to effectively navigate the complexities of their child's cancer care. Research assessing baseline levels of cancer knowledge in parents of children with newly-diagnosed cancer and associations with health literacy (HL) and socio-demographics is scarce.

Objectives: To assess baseline level of disease knowledge among parents of children with newly-diagnosed cancer and the associated role of HL and socio-demographics.

Design/Method: We prospectively enrolled parents of children with newly-diagnosed cancer (past 3 months) at Rady Children's Hospital San Diego. One hundred eighty-two English or Spanish-speaking parents completed surveys to self-assess their baseline knowledge of their child's cancer. Our main outcome measure was level of parental cancer knowledge on cancer type, stage/risk stratification, if enrolled in a treatment clinical trial or receiving standard of care treatment, and name of protocol if applicable (score 0-100% correct answers). HL was measured using the Newest Vital Sign (NVS). Socio-demographic factors included parental age, sex, ethnicity, English proficiency, marital status, education attainment, insurance type, and employment status. Outcomes were analyzed using univariate and multivariate regression models.

Results: Sixty-seven percent of participants were female (n = 112) and 47.3% were Hispanic (n = 96). The average score for parental baseline cancer knowledge was 40% (SD +/- 19). In univariate analysis, lower cancer knowledge was significantly associated with limited HL (p = 0.003), unmarried status (p = 0.015), lower education attainment [high-school or less] (p = 0.048), and public insurance (p = 0.006). In multivariate analysis, limited HL remained significantly associated with lower knowledge (p = 0.036). Moreover, parents with limited HL

were 77% less likely to know if their child was receiving treatment enrolled in a clinical trial or standard of care treatment (OR= 0.13, $p < 0.001$, 95% Confidence Intervals [CI] 0.065-0.403).

Conclusion: Parents of children with newly-diagnosed cancer overall scored low on the baseline knowledge test. Limited HL was significantly associated with lower cancer baseline knowledge after adjusting for socio-demographic factors. Our findings underscore the importance of identifying parents with limited HL to effectively increase their baseline cancer knowledge by providing targeted education and support. Future research should assess how parental baseline cancer knowledge affects clinical outcomes and include interventions to enhance educational efforts, particularly among underserved individuals with limited HL.

Poster # 177

OPTIMIZATION OF LABORATORY MONITORING FOR SIROLIMUS IN THE MANAGEMENT OF VASCULAR ANOMALIES

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Background: Sirolimus has demonstrated both safety and efficacy in pediatric patients with complicated vascular anomalies. Our institutional practice standards currently recommend monthly sirolimus trough levels, complete blood count (CBC) with differential, comprehensive metabolic panel (CMP), and fasting lipid profile. Usually the mild abnormalities in monthly tests do not require dose modification or discontinuation. Potentially spacing out monitoring parameters could:

1. Decrease costs
2. Decrease resources and nursing personnel time
3. Greater patient satisfaction (less venipunctures)

Objectives: Using the Quality Improvement method, we will develop an updated Practice Standard for management of laboratory monitoring for patients receiving sirolimus.

Design/Method: The Plan, Do, Study, Act method was used for this project. Our SMART **goal** is to decrease the monitoring frequency from monthly to every three months and eliminate unnecessary tests **without** increasing the percentage of side effects or dose modifications due to toxicities. In order to support our plan we started with a **baseline assessment** including a retrospective chart review of patients with vascular anomalies older than two years of age who have been receiving sirolimus for a minimum of one year and have at least one reported sirolimus level. A total of 50 out of the 180 patients who are currently receiving sirolimus at our center were included in the analysis.

Results: There were no significant changes in platelets, urea nitrogen, bilirubin, or alkaline phosphatase. Two patients had anemia (one grade 1 and one grade 2 caused by iron deficiency unrelated to sirolimus). One patient had grade 2 and 4 patients had grade 3 neutropenia. Sirolimus was held for grade 3 neutropenia. Thirty-four percent had grade 1

hypercholesterolemia, none grade 2. Fifty-six percent of patients had high triglycerides (grade 1) and twelve percent grade 2. Fifty-two percent had either transaminase affected. None of the patients with abnormal liver function tests required therapeutic interventions or interruption of therapy.

Conclusion: As the first step of project, we completed our **baseline assessment** and will **do** the following modifications to our monitoring plan: if the baseline panel including CBC with differential, CMP and lipid profile is normal, we will **not** re-test chemistries, renal function or bilirubin. Every three months will obtain: CBC with differential, transaminases, cholesterol and triglycerides. We will obtain an official nutritional consult for high cholesterol and/or triglycerides and will consult gastroenterology for two consecutive grade 2 transaminitis. We will proceed with this monitoring plan for 1 year and **study** the data at the end of twelve months.

Poster # 178

INFLUENZA VACCINATION IN ONCOLOGY AND SICKLE CELL DISEASE AFTER AN INPATIENT ADMISSION ORDER SET

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Background: Influenza causes greater morbidity in pediatric oncology and sickle cell disease (SCD) patients versus the general pediatric population and can lead to delays in cancer-directed therapy. Prior studies have improved vaccine uptake through outpatient interventions, but no studies have looked at inpatient interventions.

Objectives: Determine influenza vaccination rates of pediatric oncology and SCD patients in a low- vaccination state (Georgia, USA) and determine the efficacy of an inpatient opt-out admission order set for improving influenza vaccination.

Design/Method: A retrospective chart review was conducted of all pediatric oncology and SCD patients treated at Children's Healthcare of Atlanta (CHOA) during the last three influenza seasons (September 1–April 30; 2017-2018, 2018-2019, 2019-2020). For each season, eligible oncology patients were receiving or within 6 months of completion of cancer therapy at the start of each season, while eligible SCD patients were admitted at least once annually. A system-wide opt-out inpatient admission order set was implemented prior to the 2019-2020 influenza season. Vaccination status of patients that were admitted during an influenza season was collected and compared pre- and post-intervention.

Results: Approximately 2100 oncology and 750 SCD patients were eligible per influenza season. US general population influenza rates for 2017-2018, 2018-2019, 2019-2020 were 57.9%, 62.6%, 63.8% respectively; Georgia rates were 51.3%, 55.5%, 55.6% respectively. Oncology patients had lower vaccination uptake than the US population for all three seasons (49.3%, 56.5%, 58.4%, all $p<0.001$) but similar vaccination uptake to Georgia,

except for 2019-2020 (p=0.01). SCD patients had similar to higher uptake compared to the nation for all seasons (63.7%, p<0.001; 65.5%, p=0.08; 66.8%, p=0.08) but higher uptake compared to Georgia (all p<0.001). Leukemia/lymphoma patients had higher influenza vaccination uptake compared to solid tumor and brain tumor patients for all three seasons. Among the inpatient oncology and SCD cohorts, there was no significant change in vaccination uptake before and after the inpatient intervention (leukemia/lymphoma p=0.19; solid tumor p=0.42; brain tumor p=0.77; SCD p=0.33). Concurrent chemotherapy and prior influenza vaccination correlated strongly with vaccine uptake for all three oncology groups (all p<0.01). Prior influenza vaccination was strongly correlated with vaccine uptake in inpatient SCD patients (p<0.001), though history of acute chest syndrome, splenectomy, chronic transfusion, and prior pneumococcal vaccination were not.

Conclusion: Pediatric oncology and SCD populations have similar to greater vaccination uptake compared to Georgia. There was no improvement in influenza vaccine uptake from the inpatient order set, suggesting that future interventions should focus on outpatient.

Poster # 179

OPTIMIZATION OF SCHOOL REINTEGRATION FOR PEDIATRIC ONCOLOGY PATIENTS AND THEIR PEERS

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Background: Favorable survival rates in pediatric oncology allow the opportunity for patients to return to school, during or after treatment. This can be a significant challenge, exposing vulnerability to peer rejection. Successful school reintegration for childhood cancer patients and survivors is integral to their academic advancement as well as achievement of normal psychosocial milestones. School reentry assistance is provided at institutions around the United States, but that assistance is significantly varied without any guidelines for standardization.

Objectives: This double-arm descriptive study, aimed to establish a framework from which to optimize a school reintegration intervention for both patients and their classroom peers.

Design/Method: This study utilized age appropriate surveys to evaluate the knowledge and concerns of 3rd-8th grade students in Michigan regarding friends with cancer. The study also utilized age appropriate surveys to evaluate input from patients at a Michigan academic pediatric oncology practice regarding return to school during or after cancer treatment.

Results: The majority of 3rd-8th grade students correctly answered questions related to etiology, prognosis, side effects, and treatment of cancer. Respondents in 3rd-5th grade were significantly more likely than 6th-8th graders to endorse that cancer is contagious (P = 0.0036). Fewer students who had a friend with cancer were worried that their friend might die, compared to those who did not have a friend with cancer [3rd-5th graders (P = 0.0002) and 6th-8th graders (P

= < 0.0001)]. A common theme from patients was a desire to be given extra time for some assignments, though discreetly such that they do not feel singled out from their peers.

Conclusion: This study suggests that peer intervention should focus less on facts about cancer and more on positive childhood cancer outcomes, as well as how to be supportive of a peer with cancer who is returning to school. Additionally, personalized interventions and assistance for patients should strive to reduce stigma and differentiation from other students. Programs that do not already offer academic assistance, support groups, and peer education should consider adding these elements for successful return to school .

Poster # 180

PEER PATIENT ADVOCATES DEVELOPMENT OF EDUCATIONAL MATERIAL FOR ADOLOSCENT SICKLE CELL PATIENTS

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Background: Sickle cell disease, caused by a genetic mutation in the hemoglobin, leads to chronic anemia, vaso-occlusive pain episodes, multisystem organ damage, and a shortened lifespan. Adolescent and emerging adult (AEA) sickle cell patients consistently report feeling alone without support and also lack disease-specific knowledge (Sobota et al., 2014). Peer patient advocates (PPAs) have the same chronic illness as the patients and have become a developing resource in the healthcare system. Traditionally, PPAs assist patients to navigate through various medical and life events (MacLellan, 2017).

Objectives: The development of educational material by a peer patient advocate.

Design/Method: The PPA developed a booklet with 10 educational modules based on health information gathered from Got Transition, National Institutes of Health, and American Society of Hematology. The educational material was used by twelve patients ranging in age from 14-21in a group healthcare program. To assess the value of the educational material, each participant was called 1-7 days prior to the next group meeting to inquire about what they retained from the previous meeting and their experience with and use of the educational material. Each interview was then audio-recorded and transcribed into a text file that could be used for feedback analysis.

Results: The participants described the booklet as useful, easy to understand, and beneficial to their learning. Having a peer patient advocate as part of the team that creates the education material can increase pertinent, useable, and relatable information for sickle cell adolescent patients. The team learned that while the participants enjoyed the booklet, the size of the booklet needed to be adjusted to accommodate ease of transport between sessions. The team also implemented a procedure to ask participants about knowledge retention in between session and

incorporated a literacy tool to ensure that the material was age appropriate and user friendly for the participants.

Conclusion: A peer advocate, through their own personal patient experience and basic medical knowledge, can streamline information to patients. The PPA is more familiar with living with a chronic disease than health care providers that are living without the disease. In conclusion, a peer patient advocate can guide patient education material development and can ensure that the content is more pertinent and useable for adolescents and young adults with sickle cell disease. Including a peer patient advocate to develop patient education development for other chronic diseases may be valuable for AEAs with other chronic health conditions.

MacLellan, Harm Reduction, 2017
Sobota, Pediatr Hem/Oncol, 2014

Poster # 181

ZUMA-4 PHASE 1 LONG-TERM RESULTS: KTE-X19 CAR T-CELL THERAPY IN CHILDREN/ADOLESCENTS WITH R/R B-ALL

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Background: We present long-term Phase 1 results of ZUMA-4, a study of KTE-X19 autologous anti-CD19 CAR T-cell therapy in pediatric/adolescent patients with relapsed/refractory B-cell acute lymphoblastic leukemia (R/R B-ALL).

Objectives: Evaluate long-term safety and efficacy of KTE-X19 in pediatric/adolescent R/R B-ALL.

Design/Method: Patients (aged 2-21 years) with R/R B-ALL (Philadelphia chromosome-positive allowed) and >5% bone marrow blasts received 2×10^6 or 1×10^6 CAR T cells/kg following conditioning chemotherapy. The primary endpoint was incidence of dose-limiting toxicities (DLTs). KTE-X19–formulation was optimized in a second 1×10^6-dose group using a lower infusion volume (40-mL vs 68-mL).

Results: As of 9/9/2020, median follow-up was 36.1 months (range, 24.0-53.9), with 24 patients (median age, 14 years [range, 3-20]) of 31 enrolled receiving KTE-X19. Median time from leukapheresis to KTE-X19 product release was 14 days. Four patients received 2×10^6 cells/kg, with no DLTs in evaluable patients (n=3). Additionally, the 1×10^6 cells/kg dose level was explored (68-mL, n=11; 40-mL, n=9). Overall, Grade ≥3 adverse events occurred in 100% of patients, most commonly hypotension (50%) and anemia (42%). Rates of Grade ≥3 neurologic

events/cytokine release syndrome were 25%/75% (2×10^6), 27%/27% (1×10^6 [68-mL]), and 11%/22% (1×10^6 [40-mL]). All 4 Grade 5 events (B-ALL, n=2; disseminated mucormycosis, n=1; Escherichia sepsis, n=1) were considered unrelated to KTE-X19. Overall complete remission (CR) rates (CR + CR with incomplete hematologic recovery) were 75%, 64%, and 67% in the 2×10^6, 1×10^6 (68-mL), and 1×10^6 (40-mL) groups, respectively. Of responding patients, 100% had undetectable minimal residual disease (MRD). Sixteen patients (2×10^6, n=2; 1×10^6 [68-mL], n=8; 1×10^6 [40-mL], n=6) underwent subsequent allogeneic stem-cell transplantation (median, 2.3 months post–KTE-X19). In the 2×10^6, 1×10^6 (68-mL), and 1×10^6 (40-mL) groups, median durations of response (months) were 4.14, 10.68, and not reached (NR), respectively. Median overall survival (OS) was NR for the 1×10^6 groups (24-month rate: 68-mL, 73%; 40-mL, 88%) and 8 months for the 2×10^6 group. In the 1×10^6 40-mL group (selected as Phase 2 dose), median peak (range) CAR gene copies/µg DNA in blood was 2.5×10^4 ($0\text{-}2.5\times10^5$); among responders in this group, CAR T cells were undetectable by 3 months post-infusion.

Conclusion: Treatment with KTE-X19 at the recommended Phase 2 dose led to high CR rates with median OS not yet reached and a manageable safety profile. Phase 2 of ZUMA-4 is enrolling pediatric patients with R/R B-ALL or non-Hodgkin lymphoma, including patients with MRD-positive disease and early relapse (<18 months) after first-line therapy.

Study funded by Kite, a Gilead Company.

Poster # 182

EX VIVO ACTIVATION OF SARS-COV-2 SPECIFIC T CELLS USING RNA-LOADED HUMAN ANTIGEN PRESENTING CELLS

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Background: COVID-19 has caused a catastrophic pandemic. Phase III vaccine trials show promise inducing anti-SARS-CoV-2 neutralizing antibodies. However, immunosuppressed patients are still vulnerable populations. The role of T-cell responses to vaccines and adoptive T-cell approaches are underexplored. Our group has extensive experience generating CMVpp65-specific T-cells using dendritic cells (DCs) for the treatment of high-risk brain tumor patients.

Objectives: To circumvent the cumbersome nature of generating DCs, we developed a novel adoptive T-cell therapy platform to prime and expand T-cells from unexposed healthy donors (UHDs) and recovered COVID-19 patients (RCPs).

Design/Method: We used human antigen presenting cells (hAPCs), derived from peripheral blood mononuclear cells (PBMCs), transfected with full-length Spike-gp-mRNA (SmRNA) to present the encoded antigens to T-cells. We primed and expanded Spike-gp-specific T-cells (ST-

cells) from UHDs, exploiting cross-reactivity with other coronaviruses. We then expanded ST-cells from recovered COVID-19 patients. hAPCs were electroporated with SmRNA to activate ST-cells. T-cells were further stimulated with irradiated hAPCs (40Gy) and kept in culture for 16-23 days in IL-2 (50IU/ml)-containing medium. Antiviral responses were measured by ELISA IFNγ in tissue culture supernatant after challenge with Spike-gp (S1 & S2) peptides. T-cell receptor (TCRVβ) sequencing was performed by multiplex PCR.

Results: Our platform induced ST-cells responses in ~83% (n=5 out of 6) UHDs. The median IFNγ 500pg/ml (range 400-1200pg/ml). RCPs (n=2) showed ST-cells IFNγ 1655-5000pg/ml. The UHD immunophenotyping was almost predominantly $CD3^+CD4^+$T-cells against S1 and S2 Spike-gp subunits (mean±SEM; 62±8% and 63±7%, respectively) and $CD3^+CD8^+$T-cells (38 ± 6% and 36 ± 5%, respectively). RCPs showed increased expansion of $CD3^+CD4^+$T-cells (67%-95%) in contrast with $CD3^+CD8^+$T-cells (5%-33%). In UHDs, checkpoint phenotyping showed significant upregulation of PD1 and Tim3 in $CD3^+CD4^+$ and $CD3^+CD8^+$T-cells compared with baseline (PD1, 39±3% and 61±2% & Tim3, 13±5% and 15±10%, respectively; $p<0.001$) for S1 and S2 subunits. In RCPs, Tim3 was substantially increased compared with UHD levels ($CD8^+$ 47%-70%). Lag3 from UHD/RCP trended to be higher compared with baseline ($CD4^+$5±2% and $CD8^+$ 5±2.5%, p=0.07). TCRVβ sequencing confirmed significant expansion of Spike-gp specific TCR clonotypes from minimal levels to none at baseline (fold-expansion range: 21-436, $p<0.001$). ST-cells also showed polyfunctional cytokine profile.

Conclusion: We demonstrated the ability to prime and expand ST-cells from UHDs and RCPs using mRNA transfected hAPCs. Results from our RCPs are comparable to what has been described with potentially protective T cells. Our ultimate goal is to translate this technology to immunosuppressed patients who cannot mount immune responses against vaccines.

Poster # 183

MARKERS OF GRAFT REJECTION IN HEMATOPOIETIC CELL TRANSPLANT (HCT) FOR BONE MARROW FAILURE (BMF)

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Background: Graft rejection is a deleterious complication of HCT. Prolonged cytopenias and re-conditioning greatly increase the risk of infection, organ injury and death. Graft rejection can occur briskly and diligent monitoring is often insufficient to rescue the graft. We studied clinical and laboratory markers in patients transplanted for BMF and hypothesized that patients with graft rejection would have a heightened inflammatory profile compared to febrile HCT patients who did not lose their graft.

Objectives: We sought to identify markers of graft rejection in HCT for BMF.

Design/Method: We studied patients with graft rejection who underwent HCT for severe aplastic anemia (SAA), Fanconi anemia (FA), or FA-like disease. We selected patients who lost their graft within 2 months of HCT. All graft rejection patients were febrile just prior to graft loss. We then identified HCT patients with similar diagnoses and fevers in the first 2 months after HCT who kept their graft (febrile controls). Blood samples were obtained from our HCT tissue repository at baseline (pre-conditioning), day 7 and at time of fever.

Results: Twenty-two patients were studied. Graft rejection occurred at a median of 21 days from HCT (range 13-47 days). Patients with graft rejection (n=7) had higher maximum temperatures (Tmax) than febrile controls (median 105.6°F [103.3-108.5] vs 103.3°F [101.8-104.9], p=0.002). Tmax occurred later in graft rejection patients compared to febrile controls (median day 13 [7-48] vs day 6 [4-14], p=0.003). Graft rejection patients had higher CXCL9 (p=0.0012), BAFF (p=0.002) and sC5b-9 (p=0.0266) at the time of fever and graft loss compared to febrile controls. Median CXCL9 (94 vs 44 pg/mL, p=0.122) and BAFF (5240 vs 4708 pg/mL, p=0.071) levels were proportionally higher at day 7 in those with graft rejection compared to febrile controls, but did not meet statistical significance. Two graft rejection patients underwent a second HCT during our study and again experienced high fevers after HCT. Both patients received eculizumab and emapalumab at the time of fever spike and both preserved their grafts.

Conclusion: We identified high fevers, CXCL9, BAFF and sC5b9 as indicators of impending graft rejection in HCT for BMF. High fevers after day 7 should prompt attentive monitoring for graft rejection. The mechanism of the observed inflammatory surge remains unclear. We hypothesize that insufficient serotherapy allows for host T-cell production of interferons, serving as a catalyst for graft rejection. Interferon and complement blocking therapies may serve a role in treating or preventing graft rejection in high risk patients.

Poster # 184

ACUTE KIDNEY INJURY AND ELECTROLYTE DERANGEMENTS AFTER CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY

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Background: CD19-CAR T-cells are effective in treating refractory B-cell acute lymphoblastic leukemia. While commonly encountered complications such as cytokine release syndrome (CRS) and neurotoxicity are well-described, renal complications remain poorly characterized. As the use of CAR-T cells extends to other pediatric malignancies, there is a need to describe associated renal complications in an effort to prevent and treat these sequelae.

Objectives: We report the incidence, severity, and outcomes of acute kidney injury (AKI) in pediatric patients treated with CAR T-cells targeting various tumor antigens.

Design/Method: We performed a retrospective review of patients treated with investigational and commercial CAR T-cells between April 2015 and September 2020 at Texas Children's Hospital. The primary endpoint was onset of AKI using KDIGO (Kidney Disease: Improving Global Outcomes) criteria within 28 days of CAR T-cells. Resolution of AKI was defined by improvement in serum creatinine to within 1.5 times baseline by day +28. Secondary endpoints included hyponatremia, hypokalemia, and hypophosphatemia. CRS grading was according to Lee criteria prior to 2019 and ASTCT (American Society for Transplantation and Cellular Therapy) criteria after 2019.

Results: Sixty-three patients ages 1.8-21 years old (median: 12 years) received CAR T-cells directed toward CD19 (n=25), GD2 (n=19), HER2 (n=13), GPC3 (n=5), CD5 (n=2) or CD30 (n=1) for a total of 65 infusions. Two patients received 2 infusions of different CAR products. Twenty-one patients received commercial CD19 CAR T-cells while the remainder were treated on investigational protocols. Twelve patients (18.5%) developed AKI post-infusion (CD19 (n=8), GD2 (n=2), HER2 (n=1), GPC3 (n=1)); with 5 cases classified as severe. Two patients required renal-replacement therapy (RRT) following CAR T-cell infusion, one within the context of CRS (which resolved) and the other secondary to progressive leukemia. Median time to onset of CRS and AKI in all patients was 4 (0-19) and 9 days (1-28) post-infusion, respectively. CRS grades 3-4 were significantly associated with AKI (CI=95%, $p<0.001$) utilizing a linear regression model. 10/12 (83.3%) patients had resolution of AKI by day +28 post-infusion. Interestingly, the only patient with an abnormal GFR pre-infusion did not go on to develop AKI. Of 65 infusions, mild transient electrolyte abnormalities were observed, including hyponatremia n=26 (40%), hypokalemia n=10 (15.4%), and hypophosphatemia n=15 (23%), which resolved by day +28.

Conclusion: Transient AKI and electrolyte abnormalities are common in patients receiving CAR T-cell therapies and are often associated with higher grade CRS. These results may help inform baseline and longer-term renal function analyses in these patients.

Poster # 185

CHIMERISM TRENDS IN PEDIATRIC PATIENTS TRANSPLANTED FOR HEMATOLOGIC MALIGNANCIES

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Background: Analysis of donor chimerism after allogeneic hematopoietic cell transplantation (HCT) is used in assessment of engraftment and detection of graft failure. Patients transplanted for hematologic malignancies with incomplete donor chimerism may be at increased risk for relapse. However, expected chimerism values may vary by transplant and conditioning approach.

Objectives: We aim to describe trends and predictors of incomplete donor chimerism by transplant approach for leukemias, particularly by *ex vivo* T-cell depletion and *in vivo* T-cell depletion with thymoglobulin (ATG) during conditioning.

Design/Method: This was a retrospective cohort study of patients who underwent transplant for leukemias at the Children's Hospital of Philadelphia between January 2014 and June 2020. We included patients transplanted using T-replete bone marrow (BMT) from matched related (MRD) and matched unrelated donors (MUD), or using peripheral stem cell transplant (PSCT) from MUDs, mismatched unrelated donors (MMUD), and mismatched related donors (MMRD). All PSCTs underwent *ex vivo* TCR α/ß or CD3/CD19-depletion (partial for MUD and complete for MMUD/MMRD). ATG was included in conditioning for MUD BMT and all PSCTs except recent patients receiving TCR α/ß-depleted MUD PSCTs. Incomplete chimerism {short tandem repeats} was defined as measurements <99%.

Results: Analysis was done of the first 100 reviewed charts, selected at random. Two patients who received cord blood transplants were excluded. The median age was 10.1 years (0-23 years), and 54.1% were female (n=53). 59.2% (n=58) received an *ex vivo* T-cell-depleted graft (55 TCR α/ß depletion and 3 CD3/CD19 depletion). ATG was given to 55.1% (n=54). Patients who underwent T-cell depletion generally had lower chimerism values through one year post-transplant. This was most pronounced in peripheral blood (PB) and T-cell selected chimerism tests. A higher proportion of patients who underwent T-cell depletion and/or received ATG had incomplete PB T-cell chimerism at 30 days (40.7% vs 12.5% for no T-cell depletion) and 60 days (27.0% vs 22.2%), although neither of these differences reached statistical significance. Receipt of both *ex vivo* and *in vivo* T-cell depletion yielded higher rates of incomplete chimerism compared to no T-cell depletion at 30 days (50.0% vs 12.5%, p=.013) and 60 days (47.1% vs 22.2%, p=.026).

Conclusion: This analysis indicates early total and T-cell chimerism values vary by transplant and conditioning approach, particularly by T-cell depletion and ATG exposure. Future studies will assess the impact of T-cell depletion and other interventions on longitudinal chimerism values and on associations between degree and timing of incomplete chimerism and overall relapse-free survival.

Poster # 186

RIFAXIMIN TO PREVENT BLOODSTREAM INFECTIONS IN PEDIATRIC HEMATOPOIETIC CELL TRANSPLANTATION (HCT)

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Background: Intestinal dysbiosis in HCT is associated with bloodstream infections (BSI), graft-versus-host disease (GvHD), and increased mortality. Rifaximin is a nonabsorbable oral

antibiotic that can inhibit bacterial translocation. In adult HCT, rifaximin preserves short chain fatty acid producing organisms and is associated with higher survival. We hypothesized that by inhibiting bacterial translocation without disrupting microbiome diversity, rifaximin will prevent BSI in children undergoing HCT.

Objectives: To describe the impact of rifaximin on microbiome diversity and BSI in children undergoing HCT.

Design/Method: This was a prospective single arm treatment trial of rifaximin prophylaxis in children undergoing HCT. The control group was a historical cohort enrolled in an institutional biorepository protocol who were not on prophylactic antibiotics. All patients underwent HCT for a hematologic malignancy, using myeloablative conditioning. Patients received rifaximin 15 mg/kg/day divided twice daily, from Day -7 to Day 28. Stool and plasma samples were collected at baseline, then weekly until D28. Plasma sCD14, a surrogate for bacterial translocation, was measured by ELISA. Microbiome characterization was performed using 16s ribosomal RNA sequencing.

Results: Twenty-five patients were enrolled in the rifaximin study with 72 controls. No adverse events related to rifaximin occurred, but was discontinued early in 6 patients due to inability to tolerate oral medications. There were no significant differences in age, race, donor source, or graft. Cumulative incidence of enteric BSI by D30 was 0.12 in the rifaximin cohort and 0.25 in the controls (HR 0.42, CI 0.12-1.43, p=0.17). Mean sCD14 was significantly higher in the controls at D0, 7, and 14 post-HCT (p=0.03, p=0.02, p=0.002, respectively). There were no significant differences between rifaximin versus control cohorts in development of gastrointestinal GvHD, relapse, or overall survival (OS) (p=0.39, p=0.67, p=0.64, respectively). There was no significant difference in shannon-index of diversity (H) at D28 between rifaximin (H=3.3) versus controls (H=2.8, p=0.24). Overall, OS at 1-year was 89% for patients with high (≥ median) D28 diversity compared to 66% with low diversity (p=0.023).

Conclusion: Rifaximin prophylaxis may prevent enteric BSIs in the first 30 days post-HCT, possibly related to decreased bacterial translocation across the intestine as indicated by sCD14 levels. We did not observe an improvement in microbiome diversity in patients who received rifaximin. These observations should be validated using other markers of gut integrity to further examine the impact of rifaximin and BSI. Engraftment microbiome diversity was associated with OS at 1-year. Approaches to preserve microbiome diversity are likely to improve HCT outcomes.

Poster # 187

A MULTIMODAL STUDY OF CENTRAL NERVOUS SYSTEM INVOLVEMENT IN THROMBOTIC MICROANGIOPATHY

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Background: Central nervous systemic involvement in thrombotic microangiopathy (CNS-TMA) is common among many subtypes of TMA. CNS-TMA symptoms can be severe and include seizures, weakness and altered mental status. Brain biopsies are rarely performed and little is known about the histologic findings of CNS-TMA. Furthermore, no histologic criteria for CNS-TMA currently exist. Patients with CNS symptoms frequently undergo CNS imaging with computed tomography (CT) or magnetic resonance imaging (MRI). Similarly, no established radiographic criteria exist for CNS-TMA.

Objectives: Our study seeks to describe clinical, radiographic and histologic findings of CNS TMA after hematopoietic cell transplant (HCT).

Design/Method: We reviewed autopsies and biopsy specimens from 19 patients who underwent HCT complicated by TMA. Eighteen of 19 patients in the study had autopsies and 1 patient had only a brain biopsy. Specimens were reviewed with a senior pathologist. Neurologic symptoms between TMA diagnosis and death were recorded and scored. CNS imaging from before and after TMA diagnosis was reviewed with a senior radiologist.

Results: Eleven out of 19 patients had at least one neurologic symptom after TMA diagnosis. The most common symptoms were altered mental status (n=10, 52.6%) and seizure (n=6, 31.6%). Five out of 19 patients had >2 neurologic symptoms and were reviewed in more detail. Four of these 5 patients had autopsies performed, while the fifth had only a brain biopsy. Patient 1 was transplanted for an X-linked lymphoproliferative disorder-like condition and had the most severe clinical, histologic and radiographic findings. Pathology review of his brain at autopsy identified severe TMA-related changes, consistent with recognized TMA diagnostic criteria in other organ systems. The severity of histologic changes correlated with CNS imaging, which was markedly abnormal and progressive over a three-month period. The remaining four patients with >2 neurologic symptoms had variable histologic and radiographic findings without definitive evidence of acute or chronic vasculopathy at autopsy.

Conclusion: Our analysis shows that half of patients with transplant-associated TMA experience neurologic symptoms and one fourth experience multiple neurologic symptoms. Importantly, these symptoms are not specific to TMA and may be related to other complications (e.g. infection or PRES). Histologic and radiographic studies strongly correlated in severe CNS disease as well as in mild or absent CNS involvement. Abnormal histologic findings in the CNS were consistent with TMA seen in other organ systems and predominantly involved the cerebellum and brainstem white matter. Future work will establish formal criteria for radiographic and histologic findings in CNS-TMA.

Poster # 188

USE OF AMBULATORY BLOOD PRESSURE MONITORING IN PEDIATRIC HEMATOPOIETIC CELL TRANSPLANT SURVIVORS

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Background: Survivors of pediatric hematopoietic cell transplant (HCT) are at risk for long-term complications including chronic kidney disease (CKD) and cardiovascular disease, with hypertension representing one of the few modifiable risk factors. Ambulatory blood pressure monitoring (ABPM) has been shown to be superior to office-based blood pressure (BP) screening in some high-risk pediatric groups. Additionally, abnormal ABPM findings such as hypertension, elevated BP load, and loss of nocturnal dip have been associated with poor cardiovascular outcomes.

Objectives: To compare ABPM versus office-based hypertension diagnosis in pediatric HCT survivors and to describe the association between abnormal ABPM parameters and proteinuria/kidney dysfunction.

Design/Method: This was a cross-sectional study of eligible patients at our institution with a history of HCT who underwent ABPM with concomitant office BP measurement. Participants wore oscillometric Spacelabs 90217 monitors (SpaceLabs Healthcare, Issaquah, WA) for a continuous 24-hour period. Ambulatory hypertension was defined as mean BP $\geq 90^{th}$ percentile based on sex and height. Other abnormal ABPM parameters included elevated BP load ($\geq$25% systolic/diastolic readings above threshold) and abnormal dipping status (<10% decline in mean BP with sleep). Office BP was considered elevated if $\geq 90^{th}$ percentile using established norms based on age/sex/height. Proteinuria was defined as >0.3mg/mg (protein-to-creatinine ratio) or >30mg/g (albumin-to-creatinine ratio) and kidney dysfunction as eGFR <60mL/min/1.73m^2 based on the CKD-EPI or Bedside Schwartz equations.

Results: A total of 58 patients (56.9% female, 94.8% allogeneic transplants with 65.5% transplanted for malignancy) were included. Median age at time of ABPM was 15.8yrs, with 50% within 1 year of transplant. Most patients had abnormal ABPM parameters (58.6% with ambulatory hypertension, 69.0% with elevated BP loads, and 44.8% with abnormal dipping status). Elevated BP was diagnosed in the office in only 39.7% of patients. Using ABPM as the gold standard, office-based BP had a sensitivity of 52.9% and specificity of 79.2%, with 16 patients (27.6%) missed on office-based measurement, representing masked hypertension. The prevalence of proteinuria and CKD was 36.2% and 10.3%, respectively. Abnormal ABPM parameters were significantly associated with proteinuria (all $p<0.05$), but not kidney dysfunction. In contrast, office-based elevated BP was not significantly associated with proteinuria nor kidney dysfunction.

Conclusion: Our study found that a quarter of patients had masked hypertension on ABPM that was missed on office-based screening. Additionally, abnormal ABPM parameters were significantly associated with proteinuria. ABPM is a modality of BP screening that can improve hypertension management compared with current methods in this high-risk patient population.

Poster # 189

PALLIATIVE CARE INTEGRATION IN PEDIATRIC BONE MARROW TRANSPLANTATION: A QUALITATIVE STUDY

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Background: Consultation of specialty palliative care remains low in pediatric bone marrow transplant (BMT) despite evidence that early integration of palliative care improves outcomes in patients with advanced cancer or undergoing BMT. Little is known about how the multidisciplinary structure of BMT teams impacts palliative care integration.

Objectives: To understand how specialty palliative care interacts and integrates with a multidisciplinary pediatric BMT team and to identify barriers and facilitators to increased integration.

Design/Method: Between July and September 2020, 17 members of an established BMT team at medium sized children's hospital participated in semi-structured, in-depth interviews. Participants included attending physicians, nurse practitioners, registered nurses, social workers, and a child life specialist. Interviews were transcribed and analyzed using thematic analysis to identify emerging themes.

Results: Major themes emerged from the analysis including: a favorable perception of the palliative care team by the BMT team, a desire for increased palliative care integration in BMT, a perception of inadequate availability of the palliative care team, and the lack of a standardized palliative care consultation process in BMT. Regardless of discipline, BMT team members recognize that involvement of the palliative care team adds value and improves patient care. Despite this, the palliative care team is consulted predominantly for acute symptom management; and the full range of services that the palliative care team can provide is not well recognized. Regardless of discipline, BMT team members desire more comprehensive palliative care involvement for a greater number of patients early in the transplant course. Study subjects perceive the palliative care team as under-staffed and insufficiently resourced to provide care to BMT patients. Physicians observed that the lack of a standardized process for palliative care consultation in the highly protocolized BMT process prevents earlier consideration of palliative care. Responding to the lack of standardization, nurses and social workers leverage their relationships with patients and caregivers and roles in the BMT team to advocate for increased specialty palliative care support.

Conclusion: Across disciplines, BMT team members desire broader and earlier palliative care team involvement for BMT patients. Major barriers to increasing palliative care integration in BMT are the BMT team's perception of insufficient bandwidth of the palliative care team and the lack of a standardized consultation process in the protocolized BMT workflow. Future research is needed to explore how implementation of existing models of palliative care integration could improve standardization and increase integration of specialty palliative care in BMT.

Poster # 190

GUIDELINE FOR MANAGEMENT OF HEALTHY CHILDREN WITH FIRST EPISODE OF FEBRILE NEUTROPENIA

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Background: While the management of febrile neutropenia in patients with cancer has clear, evidence-based guidelines, the management of previously healthy, immunocompetent children with a febrile illness and first episode of neutropenia is less understood and often similarly treated with empiric antibiotics and hospitalization. Many studies have shown that this population is at low risk of serious bacterial infections if they are well appearing with a short history of neutropenia. Therefore, less aggressive management should be considered in patients meeting low risk criteria.

Objectives: The aim of our quality improvement study was to decrease the number of unnecessary hospitalizations and empiric antibiotics prescribed by 50% for healthy, well appearing patients presenting to the emergency department (ED) with a first episode of febrile neutropenia (absolute neutrophil count (ANC) < 0.5 x 10^9/L) over a 12-month period.

Design/Method: A team of stakeholders from Hematology, Infectious Disease, Pediatrics and Emergency Medicine was formed. A review of the literature, peer institutions and local practices on febrile neutropenia in healthy children was performed. A guideline for the management of healthy children with first episode of febrile neutropenia was developed and refined using plan-do-study-act cycles. Using the Model for Improvement, a family of measures was developed to assess project impact over time, as well as potential unintended consequences.

Results: Baseline data was collected between June 2018 and January 2020. Nineteen low risk patients were identified. Data analysis revealed that 84% of these patients were hospitalized and/or received antibiotics. A knowledge gap surrounding the correct definition of severe neutropenia was also identified. Many patients were misdiagnosed with neutropenia by forgetting to count the bands in the ANC. This was addressed through education and pathway modifications. In January 2020, the guideline was launched for clinical use in the ED. Seventeen patients met low risk criteria. Hospitalization and/or antibiotics use for this population decreased to 29%. All blood cultures were negative.

Conclusion: We contributed to improving the quality of care of this population by reducing potential harm from unnecessary hospitalizations and antibiotics in low risk patients. The development of this guideline led to improve resource stewardship and value-based care. Next steps include further iterations to the guideline to increase impact along with sustainability planning.

Poster # 191

CLOFARABINE THERAPY IN A PEDIATRIC PATIENT WITH MULTIFOCAL INTRACRANIAL JUVENILE XANTHOGRANULOMA

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Background: Juvenile xanthogranuloma (JXG) is an uncommon, non-Langerhans histiocytosis (non-LCH) that typically presents in early childhood as a solitary dermal lesion associated with a clinically benign course. Systemic involvement is uncommon. Isolated central nervous system (CNS) JXG is extremely rare but can be associated significant neurological deterioration. Radiologic imaging is non-specific; biopsy is needed to establish the diagnosis. However, distinguishing JXG from other histiocytic disorders, like Erdheim Chedster Disease (ECD), can be challenging, and genomic investigation may assist in confirming the diagnosis.

Objectives: To describe a child with isolated CNS multifocal JXG successfully treated with clofarabine

Design/Method: Review of patient medical records, radiographic imaging, tissue pathology and literature

Results: A previously healthy 3-year-old boy presented with 3 months of progressively worsening polyuria, polydipsia, and appetite. Physical examination showed height and weight in 9th percentile and no organomegaly, dermatologic or neurologic abnormalities. Brain magnetic resonance imaging (MRI) showed avid gadolinium-enhancing masses of the pituitary gland, infundibulum, pineal gland, and bilateral cerebellar folia, suggesting germinoma. Spinal MRI, cerebral spinal fluid (CSF) analysis, serum and CSF alfa-fetoprotein and beta-HCG were normal. Stereotactic biopsy of a cerebellar lesion was performed. Histopathology showed medium to large size histiocytes with elongate nuclei showing occasional indentations and folds, and associated Rosenthal fiber-rich piloid gliosis. Immunohistochemistry (IHC) stains were strongly and diffusely positive for CD66, Factor XIIIa and p16; weakly and focally positive for *CD163, CD14, CD68*; and negative for S-100, CD1a, langerin, CD34, and BRAF v600E. Panel-based genomic evaluation (UCSF500) showed no pathogenic alterations. Taken together, the diagnosis of JXG was established. He was treated with intravenous clofarabine 25mg/m2/dose administered every 4 weeks for 6 doses. MRI showed partial response after 2 courses and complete response (CR) after courses 5 and 6. MRI continues to demonstrate CR 4 months later.

Conclusion: Though rare, isolated CNS JXG should be considered in children presenting with diabetes insipidus or other abnormal neurologic symptoms, even in absence of cutaneous or other systemic abnormalities. As no pathognomonic radiologic features exist, biopsy is crucial for establishing diagnosis and directing treatment. While no somatic gene alterations were evident in this patient, previously reported diverse kinase-activating gene mutations vary in frequency among LCH and the non-LCH histiocytosis. While BRAF V600E alterations are common in LCH and ECD, they have been inconsistently demonstrated in JXG. Molecular profiling is

indicated to further characterize histiocytosis subgroups, and to provide targeted treatment options, particularly in patients not responding to conventional therapies.

Poster # 192

NOVEL MUTATION IN RPL35A CONFERRING PHENOTYPIC NON-CLASSICAL DIAMOND-BLACKFAN ANEMIA

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Background: Diamond-Blackfan anemia (DBA) is a rare bone marrow failure syndrome predominantly involving erythroid lineage caused by defective ribose synthesis leading to increased apoptosis of erythroid progenitors. It is a clinically and genetically heterogeneous condition. It presents during infancy or early childhood with macrocytic, normocytic anemia, reticulocytopenia, and elevated fetal hemoglobin. DBA is associated with other congenital abnormalities including poor growth, microcephaly, upper limb and hand deformities, genitourinary malformations, and cardiac lesions in 40% of patients. Long-term hematological and solid malignancies are major complications of DBA. Majority of the cases are inherited dominantly with haplodeficiencies noted in small and large subunits of ribosomal protein. One third of patients have genetic mutations in small ribosomal units RPS19, RPS24, and RPS17. Recently mutations in other ribosomal subunits including RPL5, RPL11, RPS10 and RPS26 have also been reported. RPL35A encodes a subunit of the large ribosomal protein 60S and has been reported in 3% of DBA cases with whole gene deletions.

Objectives: We report a case of a patient with novel mutation in RPL35A gene leading to phenotypic DBA.

Design/Method: Case Report

Results: We report a 4-month-old male born premature at 36 weeks who presented with severe anemia (Hemoglobin 4-5 g/dL), moderate to severe neutropenia (absolute neutrophil count 200 – 800 thous/CUMM), and thrombocytosis (platelet count 600 000 – 1 059 000/CUMM), reticulocytopenia, and macrocytosis. Erythroid adenosine deaminase was not elevated. Other congenital abnormalities have been ruled out. Due to multiple lineage involvement, he underwent bone marrow biopsy which showed 40% hypocellularity with erythroid hyperplasia and normal cytogenetics. Genetic studies including bone marrow failure panel confirmed heterozygous frameshift mutation leading to premature stop codon in RPL35A gene (c.278del, p.(Pro93Leufs*11). This is a novel mutation that is a single base pair mutation leading to RPL35A protein haploinsufficiency. JAK2 mutations were also performed due to overt thrombocytosis which were negative. He remains on chronic transfusions every 6-8 weeks awaiting bone marrow transplantation without any further complications at this time.

Conclusion: DBA is clinically and genetically heterogeneous condition that is classically thought of as a disorder of red blood cell aplasia. RPL35A gene mutations have been reported to

be associated with not only severe anemia but also neutropenia. They tend to have variable steroid responsiveness upon treatment. Strong index of suspicion is needed to look for this rare bone marrow failure syndrome when patients present with multiple hematopoietic cell lineage involvement.

Poster # 193

TWO CASES OF REFRACTORY PEDIATRIC ANTIPHOSPHOLIPID SYNDROME

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Background: The epidemiology of pediatric antiphospholipid syndrome (APS) is not well defined. About half are secondary to rheumatologic diseases, infections or medications, the remaining are idiopathic. One percent of APS present as catastrophic APS (CAPS), which has a 50% mortality rate due to multisystemic involvement. Evidence-based data for treatment of pediatric APS is scant.

Objectives: To describe two children with difficult to manage refractory APS requiring multimodal CAPS like treatments.

Design/Method: Case series.

Results: Patient 1 is a 17-year-old boy with uncontrolled ulcerative colitis who presented with superior sagittal sinus (SSS) thrombosis. He was treated with unfractionated intravenous heparin, then transitioned to warfarin. Two weeks later, he experienced worsening headaches and right arm paresthesia. Imaging showed extension of the SSS thrombosis. He underwent mechanical thrombectomy. Over the next weeks, new venous thromboses developed in multiple organs while on therapeutic heparin perfusion, as well as massive pulmonary embolism. APS was suspected. Lupus anticoagulant antibody was positive. Treatment was intensified with high-dose methylprednisolone, cyclophosphamide, rituximab, gammaglobulin, and 7 days of plasmapheresis. APS secondary to ulcerative colitis was diagnosed.

Patient 2 is a 16-year-old boy who initially presented with epigastric pain, dyspnea, and a 3 months history of hematuria and lower extremity purpuric ulcerative lesions. Blood work revealed thrombocytopenia, prolonged INR and aPTT. Imaging studies showed proximal bilateral venous thrombosis of the legs and bilateral pulmonary embolisms. APS was suspected. A retractable inferior vena cava filter was installed. Unfractionated intravenous heparin was started initially at half-dose because of the thrombocytopenia, then increased to full dose on day 2. High-dose methylprednisolone, rituximab and gammaglobulins were introduced. Lupus anticoagulant was positive. Anticoagulation was therapeutic by day 5. On day 9 of admission, follow up imagery showed proximal extension of pulmonary artery thrombus. Treatment was intensified with a 5-day course of plasmapheresis. Patient 2 had idiopathic APS.

Both patients had a negative immunologic and hematologic workup looking for other secondary

causes of APS. Both patients' thromboses resolved.

Conclusion: We present two patients with severe APS who required CAPS-like treatment to stop the progression of thromboses. These cases stress the importance of both having a high index of suspicion of APS in cases of thrombosis progression despite effective anticoagulation and the necessity for frequent follow-up imaging to ensure regression of thromboses. These cases also illustrate the potential need for multimodal aggressive treatment including anticoagulation, pheresis and immunosuppressive therapies in the management of severe pediatric APS.

Poster # 194

PERINATAL PARVOVIRUS B19 AND SUBSEQUENT TRANSFUSION DEPENDENCY DESPITE VIRAL CLEARANCE

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Background: Hypoplastic anemia, also referred to as pure red cell aplasia, is characterized by reticulocytopenia and paucity of erythroid precursors in the bone marrow. Hypoplastic anemia may present as a primary disease such as Diamond-Blackfan Anemia (DBA) or secondary to infectious or autoimmune etiologies.

Objectives: We describe a 5-year-old girl with a history of perinatal parvovirus B19 (B19) infection referred for hypoplastic anemia requiring chronic transfusions despite evidence of viral clearance and negative molecular diagnostics for DBA.

Design/Method: Case report

Results: Patient was born at 36 weeks gestation with congenital hydrops secondary to maternally transmitted B19, confirmed by PCR and IgM. No syndromic features were present. She received RBC transfusions and IVIG at birth for a hemoglobin of 6.3g/dl and again at 5 months of age for a hemoglobin of 3.4g/dl, resulting in remission. At 5 years of age, she was referred to our institution due to recurrence of hypoplastic anemia requiring chronic RBC transfusions. Bone marrow evaluations showed loss of erythroid precursors, but no dysplasia and a negative B19 PCR. B19 serology revealed IgG positivity only. Additional viral testing (CMV, EBV, HIV), DAT, ANA, and complement testing were negative. Erythropoietin was elevated while RBC enzymes, eADA, T/B cell subsets, and immunoglobulins were within normal limits. Genomic workup utilizing a DBA gene panel, whole exome and genome sequencing, and RNA-Seq failed to identify a genetic cause. In attempt to avoid hematopoietic stem cell transplantation (HSCT), a trial of corticosteroids was initiated with prednisolone 2mg/kg PO daily, however, there was no response after 5 weeks. Hypothesizing that the disease may be caused by antibodies against erythroid precursors, a course of IVIG 0.5g/kg/day over 4 days was initiated. Immediately following completion of IVIG, a 10-fold increase in reticulocyte count was noted, followed by hemoglobin normalization. Maintenance IVIG 0.2g/kg/dose continued every 2-3 weeks and she

remained transfusion independent for 1 year, when repeat bone marrow analysis revealed trilineage maturation with normal erythroid precursors. Notably, discontinuation of IVIG resulted in a hemoglobin decrease to 9.6g/dl and reticulocytopenia, which normalized after re-challenge with IVIG 1g/kg. At last follow-up, she is 7 years old, maintaining normal counts with IVIG 0.2g/kg/dose administered every 4 weeks.

Conclusion: This case presents an example of hypoplastic anemia responding to IVIG despite evidence of B19 clearance. This suggests an immune-mediated destruction of erythroid precursors, thereby potentially leaving room for other targeted immunomodulation before moving to HSCT as definitive therapy.

Poster # 195

SEVERE CONGENITAL NEUTROPENIA AND MYELOFIBROSIS SECONDARY TO A NOVEL HETEROZYGOUS MUTATION IN VPS45

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Background: Severe congenital Neutropenia is a rare group of hematologic disorders characterized by severe neutropenia and early stage maturation arrest of myelopoiesis. This group of disorders was originally described with autosomal recessive inheritance, however new evidence indicates that there are both autosomal dominant and sporadic cases with different point mutations. Patients defined as SCN type 5 and their clinical phenotype are a result of *VPS45* mutations. VPS45 is a protein in the SNARE complex formation which is critical to neutrophil function. Severe congenital neutropenia Type 5 is a very rare cause of severe neutropenia and myelofibrosis, with characteristic resistance to stimulation with G-CSF

Objectives: We report a three-year-old female with a novel mutation in *VPS45* leading to severe neutropenia and subsequent marrow myelofibrosis.

Design/Method: Review of the literature.

Results: 3-year-old previously healthy female who presented to the ER for prolonged fevers and found to be neutropenic. Admitted to the hematology service for fever/neutropenia and further evaluation. Bone marrow evaluation negative for malignancy and therefore G-CSF initiated with minimal response. Congenital neutropenia panel resulted +*VPS45*, compound heterozygosity. *VPS45* is a gene located at Chromosome 1q21-q22 and is a Sec1p/Munc18 like family of proteins that are vital for endosomal/lysosomal protein trafficking. The first relevant mutations were described in 2013. Deficiency in these proteins leads to a primary myelofibrosis. There are 16 patients reported in the literature to this point, all previous cases have been reported in consanguineous parents and have been noted to show homozygous recessive inheritance.

Conclusion: Our patient had no consanguinity noted in her family and was found to have novel compound heterozygous mutations: c.15dup (p.Ala6fs) and c.1118T>C (Leu 373Pro)

[NM_007259.4] which with confirmatory testing in her parents were shown to be in *trans* and therefore called pathogenic. Interestingly, not only did our patient exhibit a lack of response to G-CSF, but she had a significant bone pain at low doses which may be suggestive of the progression to myelofibrosis which was confirmed on her follow-up pre-transplant bone marrow. Given lack of sibling donor and rapid progression to myelofibrosis with progression toward pancytopenia and transfusion dependence, emergent referral to HSCT was pursued. She completed HSCT successfully and had engraftment on day 28 99.4% cellularity with her most recent bone marrow evaluation revealing good cellularity and no fibrosis

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Poster # 196

HEREDITARY PYROPOIKILOCYTOSIS REVEALED BY NEXT GENE SEQUENCING- A RARE CASE AND LITERATURE REVIEW

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Background: Hereditary elliptocytosis (HE) is a common type of cell membrane disorder. Its prevalence is closed to 1 in 2000 to 1 in 4000 worldwide. Hereditary Pyropoikilocytosis (HPP) is the most severe type of HE. It is often seen in African, European, and Arab descent population. HPP has an autosomal recessive inheritance pattern. Diagnosis required two defective genes encoding α-spectrin (*SPTA1*), β-spectrin (*SPTB*), or protein 4.1R (*EPB41*) or one severe alpha spectrin defect and a defect in alpha-LELY.

Objectives: This case report aims to describe a unique case of a child diagnosed with HPP by Next gene sequencing

Design/Method: Single subject case report

Results: A 16-month-old male, born full-term with history of hyperbilirubinemia at birth requiring phototherapy for 1 day presented with moderate microcytic anemia and fecal occult blood positive, in the setting of increased cow's milk consumption. His exam was remarkable for sclerae icterus and mild splenomegaly. Both of his parents are from Haiti with non-significant medical history. On initial encounter milk intake was decreased and patient was prescribed ferrous sulfate; however, his anemia was refractory despite prolonged treatment. Supplementation was discontinued and extensive workup for anemia was performed. His peripheral blood smear suggested schistocytes, elliptocytes, spherocytes, and marked polychromatophilia. Alpha thalassemia gene sequencing reports single gene deletion. Osmotic fragility was increased. Red blood cell Band 3 fluorescence staining was decreased. EMA binding assay showed one RBC with an equivocal pattern and another population with decreased mean fluorescence intensity. Hemolytic anemia comprehensive Next gene sequencing revealed, that, he has two heterozygous missense alterations in the alpha spectrin gene (SPTA1) as well as a common phenotype modifying polymorphism alpha-LELY. He was also noted to be heterozygote for UGT1A1 TA7(28) polymorphism. He was diagnosed with Hereditary Pyropoikilocytosis, silent carrier of Alpha Thalassemia, and Gilbert syndrome. Folic acid 1mg

daily was initiated.

Conclusion: HPP commonly presents in the neonatal period with jaundice secondary to hemolytic anemia. Those neonates with laboratories remarkable for hemolytic anemia should be evaluated for complete metabolic hematology profile. Hemolysis in this disorder is predominantly extravascular. Complications noted later in life are splenomegaly or pigmented gallstones.

Poster # 197

RECURRENT NON-IMMUNE HEMOLYTIC CRISES AND SPLENOMEGALY: HAVE YOU THOUGHT ABOUT ALPS?

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Background: Autoimmune lymphoproliferative syndrome (ALPS) is a rare non-malignant disorder characterized by chronic lymphoproliferation, autoimmune manifestations, and increased risk of malignancy caused by defective FAS-mediated apoptosis. Defective apoptosis leads to accumulation of self-reactive T and B cells, as well as double-negative T cells (DNT), which are thought to be responsible for the clinical manifestations. Patients often present within the first 2 years of life with chronic lymphadenopathy, splenomegaly, and autoimmune hemolytic anemia. Phenotypic expression is variable and symptoms mimic other hematologic disorders, making diagnosis often elusive.

Objectives: Describe the case of an 11-year-old female with recurrent hemolytic crises, massive splenomegaly, lymphadenopathy and pancytopenia found to have FAS and CASP10 mutations.

Design/Method: Chart review.

Results: An 11-year-old female presented with recurrent severe hemolytic crises with associated fever, malaise and abdominal pain, without weight loss, easy bruising or bleeding. Family history was positive for spherocytosis in a second-degree relative. Initial exam was significant for tachycardia, jaundice, bilateral cervical lymphadenopathy and massive splenomegaly. Laboratory evaluation revealed pancytopenia, reticulocytosis, negative direct antiglobulin test, elevated ESR and indirect hyperbilirubinemia. Infectious workup revealed only positive mycoplasma IgM. Hemoglobin electrophoresis, osmotic fragility test, hemolytic anemia evaluation, acute leukemia screen and lupus panel were normal. PET scan showed mesenteric and retroperitoneal lymphadenopathy, massive splenomegaly, and abnormal uptake in the liver, spleen, axial, and appendicular skeletons. Cervical lymph node biopsy yielded DNT percentage of 13% by flow cytometry, but no malignancy. Bone marrow aspiration showed myeloid hyperplasia and lymphoid proliferation (increase in CD3+ T cells, and decrease in CD4/CD8+) suggestive of autoimmune phenomena. Chromosome analysis and FISH Leukemia and MDS panels were negative. ALPS panel scored 3/4 (TCR a/b DNT 2.2%, CD3+CD25+/HLA DR ratio

0.8%, and CD27+B cells 2%). ALPS gene sequencing revealed a heterozygous mutation in FAS gene associated with ALPS type Ia, and a heterozygous variant of unknown significance in the CASP10 gene (associated with ALPS type II), confirming the diagnosis. She was treated with prednisone and IVIG with resolution of her pancytopenia and decrease in spleen size, then started Mycophenolate and discontinued steroids.

Conclusion: Although rare, ALPS should be considered in patients with lymphoproliferation and autoimmunity (including hemolytic anemia), especially with negative workup for infection and malignancy. Few cases with mutations in more than one gene have been reported. The combined effect may contribute to the development of a more severe phenotype. Further studies are required to prove this association.

Poster # 198

COMPLEMENT IN THROMBOTIC MICROANGIOPATHIES

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Background: Thrombotic Microangiopathy (TMA) is a group of disorders characterized by microangiopathic hemolytic anemia (MAHA), thrombocytopenia, and any organ injury. Atypical hemolytic uremic syndrome (aHUS), paroxysmal nocturnal hemoglobinuria, and transplant associated-TMA are some of the recognized causes of TMA. Complement-mediated (CM)-TMA is now increasingly recognized in other diseases where complement activation has been implicated in the pathophysiology, leading to acute multi-organ dysfunction (MOD) and associated morbidity and mortality.

Objectives: We highlight 4 cases with variable presentations of TMA and laboratory analyses demonstrating complement pathway (CP) activation. Two of these patients demonstrated prompt clinical response to eculizumab, monoclonal antibody to C5.

Design/Method: Retrospective chart review. The described patients underwent some/all of the following workup: complement component 3, complement component 4, free complement component 5, CH50, complement component fragments Ba, Bb, C3a, C3c, C5a, and membrane attack complex (C5b-9).

Results: Case 1: A twenty-month-old male presented with fever, respiratory distress, MAHA, thrombocytopenia, and acute renal failure. Workup revealed *Streptococcus pneumoniae* sepsis and peanut lectin panel confirmed pneumococcal HUS. Testing revealed significant CP activation. Patient improved on supportive therapy. Case 2: Eleven-year-old male presented with relapsed immune-mediated thrombotic thrombocytopenic purpura and complement testing revealed activation. He improved with immunosuppression. Case 3: Fifteen-year-old female with sickle cell anemia and history of delayed hemolytic transfusion reactions presented with fever, vaso-occlusive crisis, and acute chest syndrome. She rapidly developed MAHA, thrombocytopenia, and MOD. Complement testing revealed significant activation of the

alternative, proximal and terminal CP. She received eculizumab to minimize endothelial injury and prevent hyperhemolysis of transfused red cells. Prompt clinical improvement with normalization of complement markers was observed. Case 4: Seventeen-year-old male with SARS-COV-2 related acute respiratory distress syndrome, renal failure, and neurological dysfunction responded minimally to convalescent plasma and steroids. Due to extensive alternative, proximal and terminal CP activation, eculizumab was initiated with prompt respiratory and renal recovery and subsequent normalization of CP markers.

Conclusion: While further biochemical and genetic studies are needed to elucidate the role of complement in multiple systemic inflammatory states, appropriate and early CP workup may offer mechanistic insights into organ injury and life-threatening complications. Patients with mild to moderate CM-TMA (with C5a, C5b-9 up to 1.2 times upper limit of normal (ULN) in cases 1-2) may improve with effective treatment of underlying disease. However, in more severe presentations (C5a, C5b-9 two to five x ULN in cases 3-4), early use of eculizumab may contribute to improved renal and other organ recovery, and patient outcomes.

Poster # 199

SIBLINGS WITH HOMOZYGOUS QUALITATIVE PROTEIN S DEFICIENCY

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Background: Protein S (PS) is a vitamin K-dependent cofactor of activated protein C, encoded by the PROS1 gene on chromosome 3q11.1. PS inactivates factor Va and VIIIa. Over 400 mutations in PROS1 have been reported. PS deficiency is a rare, autosomal dominant condition. Homozygous PS deficiency causes purpura fulminans in the neonatal period. Type IIb, or qualitative, PS deficiency has rarely been reported and long-term outcomes are unknown.

Objectives: Describe diagnosis, management, and complications in siblings with homozygous type IIb PS deficiency

Design/Method: Case report

Results: A now-23-year-old female initially presented as a neonate with rapidly enlarging, purpuric thigh lesions with central black, gangrenous features, first managed as sepsis. At that time, labs revealed thrombocytopenia and hypofibrinogenemia. MRI showed intraocular and cerebral hemorrhages. Skin biopsy of the thighs demonstrated purpura fulminans. Workup for homocystinuria, protein C and antithrombin III deficiency, and factor V leiden was negative. She had normal free and total PS antigen levels but low PS activity of 11%, confirming type IIb PS deficiency. She received treatment with weekly fresh frozen plasma (FFP) infusions and anticoagulation with low molecular weight heparin (LMWH), which has been maintained for over two decades.

This patient’s younger brother was born at 34 weeks gestation at another institution, with his

neonatal course complicated by necrotizing enterocolitis. His PS testing also revealed type IIb PS deficiency (PS activity < 8%). He was started on chronic FFP infusions and anticoagulation. He presented to our institution at 22 months of age with superior vena cava syndrome due to an infected central line-associated thrombosis and widespread thromboses in all extremities. He is now 21 years old and is similarly maintained on weekly FFP and LMWH.

Both siblings have cortical blindness, global developmental delay, and history of multiple line-associated thromboses. Despite being obligate heterozygotes, neither parent had thrombotic complications.

In both patients, genetic testing revealed a novel homozygous, intron 5, c.470-2A>T splice site PROS1 mutation and no mutations in PROC or SERPINC1. This pathogenic mutation has not been previously described and results in loss of function.

Conclusion: This case illustrates the presentation and subsequent management of siblings with homozygous type IIb PS deficiency. Both patients have a novel PROS1 mutation. Their courses have been complicated by numerous thrombotic complications, yet they have survived to adulthood. PS deficiency requires lifelong protein S replacement and anticoagulation and can be associated with long-term sequelae due to thrombosis.

Poster # 200

AFFIRMING HORMONE TREATMENT FOR A TRANSGENDER ADOLESCENT AFTER A VENOUS THROMBOEMBOLIC EVENT

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Background: Medical affirmation, including gender-affirming hormones, is an essential component in the treatment of transgender and gender-diverse (TGD) youth. While affirming hormone therapy is generally well-tolerated, some may experience adverse events, including venous thromboembolism (VTE). Estrogen is a known risk factor for VTE development in TGD and cisgender populations. Furthermore, studies performed on adult cisgender males found a possible association between testosterone therapy (TT) and elevated VTE risk. However, the risk of VTE development during TT for gender-affirming care is not fully elucidated. Those with a history of VTE and ongoing gender dysphoria may require continuous hormonal therapy to attenuate mental health risks. In these cases, medical decision-making requires informed consent and care in a risk-reduction model, weighing the risks of VTE recurrence with continued hormone therapy against possible intolerable mental health outcomes with long-term discontinuation of hormone therapy.

Objectives: Highlight the possible risk of VTE during TT for TGD youth and the application of anticoagulation for secondary thromboprophylaxis as part of a risk-mitigating strategy during ongoing TT for the treatment of gender dysphoria.

Design/Method: This is a case report.

Results: A 17-year-old transgender male with gender dysphoria treated with TT for twenty-one months presented with an upper extremity deep vein thrombosis. There were no known additional risk factors, personal or family history of VTE events, or inherited clotting disorders. The patient began apixaban for anticoagulation, and to give time for decision-making, TT was temporarily discontinued. Due to the patient's concerns about feminizing, a three-month injectable gonadotropin-releasing hormone agonist was administered for menstrual and sex-steroid suppression. Laboratory evaluation for inherited or acquired thrombophilia was negative. After three months of anticoagulation therapy, the patient was restarted on TT and transitioned to rivaroxaban due to once-daily dosing for long-term secondary thromboprophylaxis.

Conclusion: This case presents a previously healthy adolescent transgender male undergoing masculinizing therapy with testosterone who presented with a VTE. Prophylactic anticoagulation for secondary prevention was initiated to mitigate the patient's continued risk of VTE and foster the patient's need to continue masculinizing therapy for quality of life. The patient restarted TT and has not experienced a recurrent VTE for at least six months. The possibility of TT as a risk factor for VTE may suggest the need to include this information during informed consent discussions; however, additional research to establish this association, particularly among TGD youth, is warranted. This case demonstrates a possible affirming treatment course upon VTE diagnosis in the care of TGD youth.

Poster # 201

A CASE OF PEDIATRIC ACQUIRED FACTOR 12 DEFICIENCY SECONDARY TO COVID-19

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Background: As the world grapples with the Covid-19 pandemic, new information continues to come to light about the effects of the virus. While at the beginning of the pandemic children were relatively unaffected by Covid-19 compared to adults, the development of multisystem inflammatory syndrome in children (MIS-C) and the constellation of symptoms associated with it has made clinicians requestion this. Of particular interest is the propensity for clotting disorders displayed by Covid-19 patients. The following case highlights a discovery of acquired factor 12 deficiency in a child being treated for MIS-C.

Objectives: To highlight a case of acquired factor 12 deficiency secondary to Covid-19 infection in a pediatric patient.

Design/Method: A 13-year-old male diagnosed with Covid-19 six weeks earlier presented to the emergency room with a 4 day history of fevers, malaise, abdominal pain, and diarrhea concerning for MIS-C. The patient was negative for active Covid-19 on PCR testing but was positive for Covid-19 IgG antibodies. Upon admission, the patient's initial labs

revealed an elevated CRP of 11, ESR of 27, D-dimer of 3.06, and fibrinogen of 586. Troponin and pro-BNP were normal. Coagulation testing showed a slightly elevated PT of 15.9 but a severely prolonged PTT greater than 200. An elevated fibrinogen level made disseminated intravascular coagulation (DIC) less likely while a normal liver profile helped rule out underlying liver dysfunction. An antiphospholipid antibody panel was also negative.

The child continued to have fevers and elevated inflammatory markers so treatment for MIS-C was started with IVIG, aspirin, and pulse dose steroids. As treatment progressed his symptoms and lab markers began to gradually improve but an echocardiogram was concerning for possible coronary artery abnormalities. The patient also experienced intermittent sinus tachycardia and occasional PVCs during hospitalization. The patient was started on a short course of high dose aspirin and was later discharged with a holter monitor and instructions to continue low dose aspirin.

Results: Given the child's severely prolonged PTT, a mixing study was performed which showed evidence of a factor deficiency. Factor levels were obtained and confirmed that the child had a Factor XII deficiency. The PTT normalized by the time of discharge making this a likely acquired condition secondary to MIS-C.

Conclusion: Acquired factor 12 deficiency is a possible new complication of Covid-19 and should be monitored for in hospitalized patients with significantly prolonged coagulation studies. This information can help providers more confidently use anticoagulation in COVID 19 patients when clinically indicated.

Poster # 202

SUPERIOR OPHTHALMIC VEIN THROMBOSIS IN A TEEN WITH PLASMINOGEN ACTIVATOR INHIBITOR-1 4G/4G GENOTYPE

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Background: Limited data exist to guide anticoagulation therapy for superior ophthalmic vein thrombosis (SOVT). The decision to anticoagulate for SOVT weighs the risk of hemorrhage (7-35%) against the risk of progression to a cavernous sinus thrombosis (CST), which has an associated 20-30% mortality risk. Plasminogen activator inhibitor-1 (PAI-1) is the primary inhibitor of fibrinolysis, and homozygosity for the 4G PAI-1 allele is associated with deep vein and portal vein thromboses, myocardial infarction, and placental insufficiency.

We present a case of a 14-year-old male with preseptal cellulitis who developed SOVT and whose hypercoagulability workup showed 4G/4G PAI-1 genotype.

Objectives: To describe a case of two previously unassociated conditions, SOVT and PAI-1 4G/4G homozygosity, and to review the literature surrounding SOVT management.

Design/Method: We reviewed the patient's chart and conducted a literature review on SOVT and PAI-1.

Results: A 14-year-old male presented with 2 days of fever, congestion, swelling and erythema of the left upper and lower eyelids, and pain with left upward and downward gaze. CT of the orbit and MRV revealed sinusitis, left preseptal and developing orbital cellulitis, and left SOVT without CST. Ophthalmologic exam demonstrated left inferior optic disc margin blurring without disc hemorrhage. Empiric ceftriaxone and clindamycin were initiated, and maxillary sinus culture grew mixed aerobic gram-positive organisms. Anticoagulation was advised although the patient and parents were initially hesitant. Hypercoagulability workup revealed 4G/4G PAI-1 polymorphism and elevated lupus anticoagulant. The patient was treated with enoxaparin for 3 months without bleeding complications. Post-therapy MRI showed complete resolution of SOVT and a normalized lupus anticoagulant.

Conclusion: There are 69 reported cases of SOVT in English since 1975; of those 22 had infectious etiologies. Only 5 pediatric cases were identified, of which 2 had traumatic etiologies, 2 were idiopathic, and 1 was secondary to infection. Overall, previous reports favored anticoagulation for SOVT, unless contraindicated, to minimize risk of propagation to CST. Numerous types of thromboses have been associated with the 4G/4G PAI-1 polymorphism, but we report the first case of SOVT associated with this genotype. The thrombosis risk associated with homozygosity for the 4G polymorphism remains unclear, but continues to be studied. Presence of the 4G/4G polymorphism does not change management, but the literature highlights numerous cases in which the 4G/4G genotype led to lifelong anticoagulation. This case highlights the importance of hypercoagulability workups when thromboembolic events occur in rare locations, as well as the need for further research into the thrombotic risk of PAI-1 polymorphisms.

Poster # 203

CORONARY AND CEREBRAL ARTERY ANEURYSMS IN A PEDIATRIC PATIENT WITH CHRONIC ACTIVE EPSTEIN-BARR VIRUS

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Background: Patients with hydroa vacciniforme-like lymphoproliferative disorder (HV-LPD) and chronic active EBV (CAEBV) have skin lesions induced by sun-exposure, and high levels of EBV DNA in T- and/or NK-cells in blood and skin lesions. Cutaneous disease may progress to systemic disease—typically with fever, weight loss, LAD/HSM, cytopenias, and lymphoproliferation; and may further progress to lymphoma or hemophagocytic lymphohistiocytosis. Arterial aneurysm is a rare but reported complication of CAEBV.

Objectives: To describe a pediatric patient with CAEBV and HV-LPD whose medical course was complicated by severe arterial aneurysms.

Design/Method: Case Report.

Results: An 11-year-old Hispanic female presented with waxing/waning malar rash exacerbated by sunlight, submandibular lymphadenopathy, scleritis/keratitis, and oral ulcers/abscesses. She was diagnosed with HV-LPD and T-cell CAEBV by biopsy of oral ulcerations. At 16 years, she developed systemic symptoms with 5-kg weight loss, intermittent fever, headache, and transient delirium. Blood and CSF were positive for clonal TCR-beta and TCR-gamma gene rearrangements, and blood and CSF EBV DNA levels were elevated (>2 million and 313,868 DNA copies/mL, respectively). Treatment included oral dexamethasone, intrathecal/intra-Ommaya methotrexate/hydrocortisone, and ganciclovir/bortezomib. Pre-HSCT echocardiogram revealed pulmonary artery hypertension (PAH) and bilateral coronary artery aneurysms (CAA), confirmed by cardiac catheterization and chest CT/Angiogram (CTA). Pre-HSCT head CTA was negative for arterial aneurysms. Management included anticoagulation for CAA and macitentan for PAH. She underwent 9/10 MMUD PBSCT with RIC regimen (irradiation-free; serotherapy-free prep per NIH Primary Immunodeficiency protocol) and intra-Ommaya MTX/hydrocortisone. Her donor was EBV seropositive. She had neutrophil engraftment on day +16. Day +30 marrow showed 60% cellularity and 94% donor chimerism. She had grade 2 steroid-responsive GI cGVHD, but no aGVHD or VOD. Six months post-HSCT, blood and CSF EBV DNA were <200 copies/mL and 1109 copies/mL, respectively. On day +212, she had a syncopal episode with closed head trauma. Head CT revealed a subarachnoid hemorrhage (SAH) and intraventricular hemorrhage. Head CTA demonstrated a 9 mm fusiform aneurysm of the right middle cerebral artery (MCA). She underwent flow-diverting stenting with aneurysm coiling, and returned to her neurologic baseline. Eight months post-HSCT, she had a massive spontaneous SAH due to MCA aneurysm rupture. She expired one day later.

Conclusion: This case highlights the risk of arterial aneurysms in patients with CAEBV and HV-LPD. We suggest screening these patients for arterial aneurysms. HSCT may be curative, but relapse or sequela of CAEBV may result in death post-HSCT. Early referral of these patients for HSCT may improve outcomes.

Poster # 204

SUCCESS OF SYSTEMIC THROMBOLYSIS FOR SADDLE PULMONARY EMBOLUS IN NEONATE WITH INTRACRANIAL BLEED

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Background: Venous thromboembolism (VTE) is a recognized complication in preterm infants which is increasing in incidence and has significant morbidity. Preterm infants are

especially vulnerable due to immature coagulant systems and higher incidence of known precipitating factors (infection, catheterization, cardiorespiratory disease, exposure to maternal prothrombotic processes). Treatment approaches are case dependent but may be limited in this age group by younger gestational age, birth weight, and concurrent disease, including hemorrhage. In the literature, there is little use of systemic thrombolytic therapy in the setting of concurrent thrombosis and hemorrhage given increased risk of bleeding and death; however, this treatment approach is recognized for potential success in life-threatening conditions.

Objectives: Describe the use of systemic tissue plasminogen activator (tPA) in the setting of a life-threatening pulmonary saddle embolus in a neonate with concurrent intracranial hemorrhage, with a successful outcome.

Design/Method: Case report of a 32-week-old male infant, born preterm at 29-weeks gestational age, who presented with a sub-occlusive central venous sinus thrombosis (CVST) with subdural hemorrhage and right-sided pulmonary saddle embolus after acute hypoxemic event, successfully treated with tPA without bleeding complications or long-term sequalae.

Results: A preterm 32-week-old male infant, born at 29-weeks for maternal pre-eclampsia, developed a sub-occlusive CVST with subdural hemorrhage following an acute hypoxemic event. He required immediate intubation and oscillatory ventilation. Echocardiogram showed depressed right ventricular function and a right pulmonary saddle embolus extending into the left pulmonary artery with severe pulmonary hypertension. His blood cultures later grew staphylococcus Hominis at 28 hours. He was not a candidate for catheter-based thrombolysis given his critical condition and size. He was given 15 ml/kg fresh frozen plasma prior to starting systemic tPA at 0.06 mg/kg/hr and low dose heparin at 10 units/kg/hr. Serial head ultrasounds showed no evidence of bleeding, and the patient's ventilatory support was weaned. tPA was discontinued at 60 hours of infusion after imaging revealed resolution of pulmonary embolus and no secondary complication. He was subsequently discharged home from the NICU without long term complications.

Conclusion: The evidence for safe use of systemic thrombolytic therapy for treatment of VTE and pulmonary embolism in preterm infants is limited given increased risk for morbidity and mortality. In cases of life-threatening VTE with hemodynamic instability, systemic thrombolysis with concurrent anticoagulation may be the only viable option for patients. Further research is warranted on the use of systemic thrombolysis in preterm infants.

Poster # 205

MRSA BACTEREMIA SECONDARY TO PELVIC SEPTIC THROMBOPHLEBITIS ASSOCIATED WITH SEXUAL TRAUMA

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Background: Septic pelvic thrombophlebitis (SPT) has historically been associated with obstetrical patients. The pathogenesis often involves a uterine infection that spreads to the pelvic vein and results in phlebitis. We present the case of a 14 year old, previously healthy female who presented with a 5 day history of fever, diffuse myalgias, emesis, dizziness, fatigue and irregular vaginal bleeding. She had been sexually assaulted, vaginally, 2 weeks prior to presentation. Her labs were significant for leukocytosis, bandemia and elevated CRP. She also had evidence of acute kidney injury and mild transaminitis. Laboratory tests for ingestion and pregnancy were negative. She was started on broad spectrum antibiotics, Vancomycin and Ceftriaxone. On hospital day (HD) 2 she was diagnosed with sepsis secondary to MRSA bacteremia. Her antibiotics were changed to Daptomycin (MIC 0.5 ug/ml) and Ceftaroline (MIC 0.5 ug/ml) due to MIC of 1 ug/mL to Vancomycin. Her blood cultures remained positive for 4 days. A CT of the chest with IV contrast, ordered on HD 2 due to hypoxia, revealed septic emboli. An MRI/MRV of the pelvis demonstrated multiple diffuse abscesses within the muscles of the back, pelvis, bilateral lower extremities and a right internal iliac vein thrombus extending from the right common iliac vein at the bifurcation with extension into multiple pelvic branching veins. Given her findings, she was started on therapeutic Enoxaparin for anticoagulation.

Objectives: To discuss a rare etiology of SPT so that it may heighten provider awareness.

Design/Method: This case report describes the rare presentation and management of MRSA SPT following sexual assault in an adolescent female. An extensive literature search was performed to review the etiologies of SPT.

Results: The patient was discharged home with a PICC line to complete an antibiotic course and an 8 week course of Enoxaparin. A repeat MRV prior to her discharge demonstrated mild improvement of the right internal iliac venous thrombus and significant improvement of the multiple diffuse intramuscular abscesses. Upon our literature review, there were no cases of SPT associated with sexual trauma.

Conclusion: We suspect that our patient was either colonized with or exposed to MRSA at the time of her assualt. Following local trauma, the organism caused pelvic thrombophlebitis and prolonged bacteremia with multiple septic emboli. We believe SPT should be included in the differential of patients presenting with similar symptoms after sexual assault and not be limited to the obstetic population.

Poster # 206

NOVEL PRESENTATION OF FACTOR V LEIDEN MUTATION IN A NEONATE WITH UMBILICAL VEIN VARIX

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Background: Thromboses are rare occurrences in the neonatal population, but when they occur, they are most often associated with indwelling vascular catheters.

Objectives: In this report, we present a case of a neonate diagnosed with Factor V Leiden mutation after initial presentation with an umbilical vein varix noted on fetal ultrasound.

Design/Method: Abdominal ultrasound performed shortly after birth showed extension of the umbilical vein thrombus into the left portal vein. After consultation with a pediatric hematologist, basic thrombophilia labs were obtained from both parents despite negative family history.

Results: Maternal labs revealed no abnormalities, but the father was found to be heterozygous for both Factor II (prothrombin) gene mutation and Factor V Leiden mutation. The baby tested negative for Factor II mutation but was heterozygous for the same Factor V Leiden mutation. Based on the asymptomatic nature of the thrombus and benign echocardiogram, the decision was made to monitor clinically and with periodic abdominal ultrasounds while holding anticoagulation medications.

Conclusion: Factor V Leiden mutation presenting as an umbilical vein varix in utero has not been described in the literature. Furthermore, involvement of the portal vein is rare, and the majority are caused by a mispositioned umbilical venous catheter, which this neonate did not have. Based on this case, we suggest diagnosis of a fetal umbilical vein varix in utero be followed up with a postnatal ultrasound study as well as investigation of both parents and newborn for evidence of a prothrombotic disorder. Timely diagnosis allows for parental discussion delineating the increased risk of an inherited thrombophilia with future pregnancies and could result in potentially life-altering findings of parental thrombophilia disorders with appropriate outpatient hematology follow up.

Poster # 207

CHROMOGENIC FACTOR X FOR MONITORING WARFARIN-ANTICOAGULATION IN A CHILD WITH PROSTHETIC MITRAL VALVE

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Background: Mechanical mitral valve replacements in infants and young children are associated with significant morbidity and mortality. These valves are durable but require frequent upsizing of the valve due to somatic growth of the patients. A mechanical valve in the mitral position is also at a higher risk of thrombosis than the aortic position due to physiologically low pressure gradients and increased stasis of blood around the mitral valve. Therefore, mechanical mitral valves in children require higher level of anticoagulation with Warfarin, which requires meticulous monitoring due to the risk of bleeding and/or thrombosis. Warfarin-anticoagulation is classically measured using the international normalized ratio (INR), which can be falsely elevated and lead to false reassurance in some cases.

Objectives: We report a case of mechanical mitral valve thrombosis in a four year old female despite a therapeutic INR.

Design/Method: We measured Chromogenic Factor X values alongside INRs in a patient with thrombosis of her mechanical mitral valve on warfarin anticoagulation.

Results: INRs of 2.2, 2.3, 2.8, and 3.5 corresponded to Chromogenic Factor X of 47%, 49%, 42%, and 35%.

Conclusion: Chromogenic factor X levels were discordant with INR measurements, which suggested a falsely elevated INR in this patient. Chromogenic factor X levels were used to interpret INR measurements and guide adequate anticoagulation following her thrombosis. We propose a new role of chromogenic factor X: to verify INR from the onset of warfarin anticoagulation in high risk pediatric patients such as those undergoing mechanical mitral valve replacement.

Poster # 208

HYPERHOMOCYSTEINEMIA RESPONSIVE TO VITAMIN THERAPY IN A PATIENT WITH HOMOZYGOUS MTHFR MUTATION

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Background: Methylenetetrahydrofolate reductase (MTHFR) is an enzyme involved in the conversion of homocysteine to methionine. Mutations in this gene are well described and can lead to subsequent hyperhomocysteinemia. Circulating homocysteine can spontaneously undergo oxidation and cause oxidative damage to the endothelial lining and alterations in the balance of the clotting cascade, resulting in a prothrombotic state. Hyperhomocysteinemia has been linked to end stage renal disease, cardiovascular events including coronary artery disease and myocardial infarction, deep vein thrombosis, pulmonary embolism, and long term neurocognitive outcomes such as Alzheimer's disease and vascular dementias. Data published currently have demonstrated varied results in showing significant changes in clinical outcomes by using vitamin therapy (vitamin B6, vitamin B12, and folate) to decrease homocysteine levels. A common limitation in these studies is the threshold used for hyperhomocysteinemia, typically 15 umol/L. Patients with elevations beyond this threshold are an understudied group.

Objectives: This case seeks to demonstrate interventions and clinical management of a patient with hyperhomocysteinemia that surpasses typically elevated ranges. The long term goals of these interventions are to decrease risk of future adverse cardiovascular and neurocognitive outcomes.

Design/Method: This is a case report of an 18 year old male with homozygous MTHFR mutation (C677T) and hyperhomocysteinemia who was initiated on vitamin B6, B12, and folate.

Results: With initiation of supplementation of vitamin cofactors involved in MTHFR/folate pathway, homocysteine levels decreased from 66.3 umol/L to 12.3 umol/L over a 3 month period.

Conclusion: Patients with MTHFR and hyperhomocysteinemia have interventions available to decrease circulating homocysteine levels. Particularly in patients with hyperhomocysteinemia that falls outside the range of most studied populations, this decrease could provide benefit in decreasing adverse cardiovascular and neurologic outcomes into adulthood.

Poster # 209

PLATELET MICROPARTICLES AS A POTENTIAL CAUSE OF CEREBRAL INFARCTS IN A PEDIATRIC PATIENT WITH ITP

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Background: Immune thrombocytopenia (ITP) is the most common autoimmune cytopenia in children. It often causes a severely low platelet count, but bleeding manifestations are variable. Platelet microparticles (PMP), a procoagulant platelet factor in platelet activation, may play a role in phenotypic variability by contributing to a thrombotic paradox and increasing the risk of ischemia in some patients. There is limited data on the clinical significance of PMP in children with ITP.

Objectives: To describe a case of cerebral infarcts in a pediatric patient with acute ITP and headaches, possibly caused by increased PMP.

Design/Method: A PubMed search was conducted for keywords and phrases including “Immune Thrombocytopenia”, “Cerebral Infarctions”, “stroke”, “Platelet Microparticles”, and “Pediatrics.” Relevant papers were selected for literature review.

Results: An 8-year-old previously healthy female with a history of headaches presented to the Pediatric Emergency Department with a 2 day history of diffuse bruising and a petechial rash, ankle arthralgias, fatigue, and worsening headaches. The platelet count was found to be 4,000 thou/comm with an otherwise unremarkable complete blood count, leading to a diagnosis of acute ITP. Due to her complaints of headaches in the setting of thrombocytopenia, a Head Computed Tomography (CT) was performed, which showed bifrontal hypodense areas without evidence of acute intracranial bleeding. She was treated with prednisone 2 mg/kg/day for a total of 7 days as an outpatient. Magnetic Resonance Imaging (MRI) of the brain was performed 2 weeks later, which revealed scattered foci of abnormal T2/FLAIR signal in the supratentorial white matter, which corresponded with the areas of hypodensity seen on the prior CT that were concerning for watershed infarcts. Comprehensive hypercoagulable and rheumatologic

evaluations did not reveal evidence of a systemic disorder. Her platelet count normalized with steroid treatment and no subsequent ITP directed therapies were required. We hypothesize her cerebral infarcts may have been caused by elevated PMPs.

Conclusion: We present an unusual presentation of cerebral infarcts in a previously healthy pediatric patient with ITP, one of the most common hemorrhagic disorders in childhood. Her MRI findings may be associated with PMP from ITP causing small vessel ischemic changes. Elevated PMP levels have been associated with acute ischemic strokes in adult patients with concurrent ITP, promoting that PMP levels as a novel evaluation parameter for patients with ischemic changes in the setting of ITP. However, the clinical significance of PMPs in the setting of pediatric ITP is unknown and warrants further investigation.

Poster # 210

COMPLETE REMISSION OF CHRONIC RESISTANT ITP FOLLOWING COVID-19 INFECTION IN A PEDIATRIC PATIENT

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Background: There are many studies regarding the effect of coronavirus disease 2019 (COVID-19) on platelets but a few have studied this relationship in pediatric patients due to their highly variable presentations. Several theories have been proposed regarding the link between COVID-19 and thrombocytosis, but there is limited evidence that elucidate these effects in pediatric age group, particularly in those with underlying hematological abnormalities.

Objectives: To discuss the unique case of chronic resistant immune thrombocytopenic purpura (ITP) in a pediatric patient who developed complete remission following COVID-19 infection.

Design/Method: Case report and review of literature; data was collected retrospectively by analyzing hospital records.

Results: A 14-year-old male with history of chronic resistant ITP, treated with sirolimus and romiplostim infusions, presented with a 3-day history of fever, cough, and congestion. Patient was hypoxemic on presentation, requiring oxygen support and had elevated platelets ($498x10^3$/mcL). RT PCR of nasopharyngeal secretion was positive for SARS CoV- 2 infection. A chest CT scan showed ground glass appearance with " paving pattern" of his left lung consistent with COVID pneumonia. During his hospital stay, his platelet counts increased up to $1.88x10^4$/mcL. He had multiple episodes of blood pressure lability with a depressed cardiac function, which normalized after initiation of amlodipine. He was subsequently weaned off oxygen support. His platelet counts declined ($824x10^3$/mcL) at the time of discharge. Follow-up at 2 weeks showed normalization of his platelet levels ($244x10^3$/mcL), so further doses of sirolimus and romiplostim infusions were withheld. His platelet counts continue to be in

remission for 10 months post infection.

Conclusion: Thrombocytosis in pediatric COVID-19 patients has been rarely reported in literature, especially in patients with chronic resistant ITP. It has been proposed to be due to involvement of proinflammatory cytokines that trigger the proliferation of megakaryocytes, thereby increasing the platelet counts in these patients. The management of this condition in COVID-19 disease is complicated by the lack of available data - especially in pediatric populations. The unique presentation of this case with normalization of platelet counts in a patient with chronic resistant ITP following COVID -19 infection, is noteworthy as this has not been reported in literature so far. Further discussion of this case may assist in the recognition and treatment of other cases when combating this novel virus and its hematological manifestations.

Poster # 211

NOVEL MECOM PATHOGENIC VARIANTS IN PATIENTS WITH NEONATAL THROMBOCYTOPENIA AND BONE MARROW FAILURE

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Background: Radio-ulnar synostosis with amegakaryocytic thrombocytopenia (RUSAT) has been associated with heterozygous pathogenic variants (PVs) in *MECOM* and *HOXA11*. More recently *MECOM* PVs have been shown to cause a wider clinical spectrum including skeletal anomalies, bone marrow failure, cardiac, renal malformations, hearing loss, B-cell lymphopenia and hematologic malignancies. Due to the expansion of the clinical spectrum, *MECOM*-associated syndrome (MAS) is the proposed syndrome name to include patients with a PV in *MECOM.*

Objectives: We describe two patients with different phenotypes. Both patients have novel *MECOM* PVs.

Design/Method: Case series and literature review

Results: Case 1
A full-term male, born to a mother with a history of two miscarriages, was found to have petechiae at birth. His CBC was normal except for severe thrombocytopenia (4K/µL). Forearm X-rays revealed bilateral radio-ulnar synostosis and RUSAT was diagnosed. Chromosomal microarray was normal. At one year of age, his platelets were consistent >100K/µL and other cell lines were normal. However, he had global developmental delay and bilateral conductive hearing loss. When he was six years old, he again developed petechiae. CBC showed pancytopenia. Bone marrow (BM) evaluation revealed hypocellularity of 50% with no dysplasia nor malignancy. A repeat BM evaluation after five months showed worsening BM hypocellularity (30%). Genetic testing of *HOXA11* was normal but *MECOM* analysis revealed a heterozygous splice donor variant c.2285+1G>T. Immunoglobulins and CD19 cells were within

the normal range. He is currently being evaluated for bone marrow transplantation.

Case 2
A late-preterm newborn female with truncus arteriosus and interrupted aortic arch was found to have thrombocytopenia (22K/μL) at birth. Physical examination revealed a single umbilical artery, micrognathia, and bilateral clinodactyly. Mother had two miscarriages and was diagnosed with antiphospholipid syndrome (APS), for which she was on prophylactic enoxaparin. Repeat testing for APS during pregnancy was negative. Chromosomal microarray revealed an interstitial deletion involving 3q26.2 expected to include *MECOM* exons 5-17. Forearm radiographs were negative for radio-ulnar synostosis She developed pancytopenia, chylothorax, and staphylococcal bacteremia after pulmonary artery banding. She died of cardiac arrest with septic shock.

Conclusion: A high suspicion for MAS should be maintained when evaluating neonates with unexplained thrombocytopenia accompanied by dysmorphic features, which may or not include radio-ulnar synostosis as the phenotype can be widely variable. The mechanisms whereby *MECOM* variants or exonic deletions result in thrombocytopenia and also generate other phenotypic abnormalities requires further definition. Bone marrow transplantation can be curative and should be considered when this diagnosis is confirmed.

Poster # 212

CVT ASSOCIATED WITH LEPTOMENINGEAL ENHANCEMENT MIMICKING MENINGITIS IN AN ADOLESCENT FEMALE WITH ITP

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Background: The association of leptomeningeal enhancement with cerebral venous thrombosis (CVT) has rarely been reported. Patients with immune thrombocytopenia (ITP) treated with thrombopoietin-receptor agonists (TPO-RAs) may present with thrombotic complications including CVT. In this report, we describe the associated findings of leptomeningeal enhancement in the setting of CVT, which mimicked bacterial meningitis.

Objectives: We describe a female adolescent with chronic ITP receiving treatment with eltrombopag (ELT) and combined oral contraceptives (COCP) who developed CVT. Brain magnetic resonance imaging (MRI) showed bifrontal leptomeningeal enhancement.

Design/Method: Case report and literature review

Results: A 12-year-old female with chronic ITP and persistent platelet count <10K/μL was started on ELT, with adequate platelet response (>50K/μL) at a dose of 75 mg/d. She was also on COCP due to menorrhagia associated with thrombocytopenia and was taking intermittently higher doses of COCP for breakthrough menorrhagia. Three months after initiation of ELT and three weeks after a course of high dose COCP the patient presented with severe intermittent headaches and fevers. Brain MRI showed extensive CVT and bifrontal leptomeningeal

enhancement. A lumbar puncture was done due to concern for bacterial meningitis and was negative. Platelets on admission were 201K/µL. Thrombophilia work-up was unremarkable. The patient was treated with low molecular weight heparin with complete resolution of CVT on repeat imaging three months later. Platelet count remained stable above >50K/µL while on eltrombopag and enoxaparin. COCP was discontinued.

Conclusion: Although very uncommon in pediatric patients, a small number of thrombotic complications including CVT have been reported with the use TPO-RAs for ITP, particularly in association with additional risk factors for thrombosis including the concurrent use of COCPs. Differential diagnosis of leptomeningeal enhancement includes infection. Work-up for meningitis may be necessary depending on symptoms and platelet count should be adequate for lumbar puncture. This case presents a unique clinical scenario of CVT and highlights the challenges in the management of both bleeding and thrombotic complications that may arise in patients with ITP treated with TPO-RAs.

Poster # 213

IMMUNE THROMOBOCYTOPENIA FOLLOWING DENGUE FEVER. A PEDIATRIC CASE PRESENTATION

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Background: Dengue fever is a mosquito-borne infectious disease caused by an Arbovirus, with a well known natural history, at clinical and laboratory levels. Dengue fever can be asymptomatic and symptomatic. The latter could present with or without warning signs, or as a severe illnes with plasma leakage, organ failure and shock.

Objectives: Immune thrombocytopenia (ITP) is an entity of autoimmune/idiopathic etiology, defined by low platelet counts <100 x 109/L, with an increased bleeding risk. There are anecdotal cases that have been published of ITP presenting after dengue fever.

Design/Method: A school-aged boy presents with dengue fever with warning signs, serologically confirmed by positive IgM antibody. During his admission, he was complicated by prolonged thrombocytopenia <20 x 109/L, despite resolution of the dengue clinical syndrome.

Results: He was managed in a third level hospital with supportive care and required transfusions of blood products, adding the use of glucocorticoids and anti-CD-20 monoclonal antibody (100 mg/m2 x 1 dose), as has been published, to treat the severe thrombocytopenia and bleeding manifestations, with subsequent recovery and discharge.Follow-up of the patient at 15 months show a healthy child with normal development and unremarkable complete blood counts.

Conclusion: Immune thrombocytopenia can present as prolonged thrombocytopenia after a diagnosis of dengue fever. ITP should be suspected and managed with the guidance of a pediatric hematologist in specialized centers.

Poster # 214

PLATELET DELTA STORAGE POOL DISORDER: A MULTIGENERATIONAL CASE REPORT

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Background: Delta storage pool disorder represents a group of platelet pathologies that result in a qualitative or quantitative deficiency in dense granules. Typical symptoms observed in an affected individual are mild to moderate mucocutaneous bleeding, easy bruising, petechiae, and epistaxis. However, in the event of surgery or trauma, the risk of bleeding significantly increases in persons with the disorder. The condition can be either syndromic form, which manifests as a part of hereditary syndrome such as Hermansky-Pudlak or Chediak-Higashi syndrome, or non-syndromic form that presents as an isolated disease of the platelet lineage. The diagnosis of non-syndromic delta storage pool disorder remains complex and poorly standardized, but early diagnostic evaluation is crucial to prevention of bleeding complication in the future.

Objectives: Describe a family pedigree of a pediatric patient with delta storage pool disorder and discuss the importance of early diagnostic testing, genetic evaluation and patient education.

Design/Method: Case report

Results: An 18-year-old female initially presented at age of 15 with chief complaint of easy bruising and gum bleeding and was evaluated for possible genetic etiology prior to undergoing wisdom teeth extraction. Patient denied history of bleeding symptoms until 2018 but reported a significant family history of delta storage pool deficiency on her maternal side of the family. Patient's mother confirmed the diagnosis of delta storage pool deficiency in her mother, three aunts, sister, male cousin and nephew. Patient's mother and younger sister reported history of menorrhagia and anemia, and patient's father experienced petechiae with minimal trauma. Initial labs were unremarkable, including coagulation and platelet studies. Our patient underwent further workup that showed sparsity of dense bodies on platelet electron microscopy and abnormal clotting time on thromboelastography. Given the diagnosis of the disorder, patient was cleared for wisdom teeth extraction, after receiving a platelet transfusion. For chronic management of bleeding, initiation of oral contraceptives to regulate her menorrhagia and use of antifibrinolytic medications for emergent control of bleeding were discussed. The patient was counseled about use of a medical alert ID. We plan to test her younger siblings and refer her mother for evaluation and diagnosis.

Conclusion: The case implies the importance of early hematologic evaluation and testing those with a significant family history of delta storage pool disorder in multiple generations. The patient education through close follow-up with their hematologist plays a crucial role in prevention of bleeding complications. Reference: Dupuis, et al., Journal of Clinical Medicine, 2020

Poster # 215

DEVELOPMENT OF ANTIPHOSPHOLIPID ANTIBODIES AFTER IMPROVED PLATELETS IN PATIENTS WITH SYSTEMIC LUPUS

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Background: The development of thrombocytopenia is a potential sequela occurring in 15-20% of patients with systemic lupus erythematosus (SLE) secondary to the production of a variety of autoantibodies. They are at an increased risk of developing antiphospholipid antibodies (aPL). We demonstrate the possible correlation of increased thrombosis risk with the resolution of thrombocytopenia due to aPL development in patients with SLE.

Objectives: To present two adolescent females with a history of thrombocytopenia and SLE found to have positive aPL after resolution of thrombocytopenia.

Design/Method: Comparative case reports.

Results: Case 1: A 16-year-old female presented with thrombocytopenia minimally responsive to IVIG. Persistent thrombocytopenia was treated with a 3-day steroid burst and then maintained on oral steroids. Testing for aPL was negative at that time. One month after presentation labs revealed positive anti-double stranded DNA antibodies; she was diagnosed with SLE and began treatment. Due to persistently elevated inflammatory markers and joint pains, she received Rituximab twice. Her platelets remained stable above 100,000. She presented with neurological symptoms including headache and left arm twitching with MRI revealing acute right frontal lobe infarct and subacute left frontal lobe ischemic stroke. Labs then revealed the presence of positive anti-cardiolipin IgM antibodies. She was started on anticoagulation due to high risk of clotting.

Case 2: A 14-year-old female presented with thrombocytopenia unresponsive to steroids and IVIG. She was started on Eltrombopag which was discontinued due to side effects. Testing for aPL was negative at that time. Romiplostim was initiated and platelets remained stable above 100,000. One month after presentation labs revealed positive anti-nuclear antibodies; she was diagnosed with SLE and began treatment. Anti-cardiolipin IgG antibodies and B2-glycoprotein IgG antibodies were positive. She was started on Aspirin due to concern for high risk of clotting.

Conclusion: Thrombocytopenia has been shown to be associated with aPL in patients with SLE, which in turn increases their risk of thrombosis development. Both patients initially tested negative for aPL in the presence of thrombocytopenia and were found to be positive for aPL after the resoluton of thrombocytopenia. In patients with SLE and thrombocytopenia, improvement of thrombocytopenia may be associated with an increased risk of clot formation. Although further studies are needed to demonstrate the prevalence of this phenomenon, this correlation could be useful information when managing these patients in the future and suggests the indication of

closer monitoring for the development of aPL and increased risk of clotting even after improvement of platelet counts.

Poster # 216

NEONATAL POLYCYTHEMIA ASSOCIATED WITH NONIMMUNE THROMBOCYTOPENIA

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Background: Neonatal thrombocytopenia is most commonly due to infection or immune-mediated (auto or allo-immune maternal antibodies). Neonatal thrombocytopenia associated with polycythemia is not well established in the literature.

Objectives: Report of two cases of polycythemia associated with nonimmune thrombocytopenia.

Design/Method: Retrospective chart review, review of laboratory studies, literature review.

Results: *Case 1:* A 3-month-old male infant was delivered at 39 weeks gestational age via caesarean section due to fetal distress to a 19-year-old mother who had diet and exercise controlled gestational diabetes mellitus (A1GDM). Immediately after delivery, he was noted to be severely hypoglycemic (12mg/dl), polycythemic (hemoglobin 24.7g/dl/hematocrit 67.8%) and thrombocytopenic (platelet count 60 000). Hypoglycemia required continuous intravenous dextrose (highest 12.5%), weaned off by 4 days of life. He showed no signs of bleeding. Maternal platelet count was normal. Evaluation for infections and neonatal allo-immune thrombocytopenia were negative. Platelet count (304 000) and hemoglobin (18g/dl) normalized in 3 weeks.

Case 2: A 2-month-old male infant was delivered at term via spontaneous vaginal delivery to a 43 year old multiparous mother with A1GDM. On the first day of life, the neonate developed petechiae over his trunk and he was thrombocytopenic (platelet count 78 000) and polycythemic (hemoglobin 23.6 g/dl/hematocrit 66%). He had no bleeding symptoms or other complications. Platelet count (362 000) and hemoglobin (14.8 gm/dl) normalized in 2 weeks.

Conclusion: Both cases were infants of diabetic mothers (IDM) born to mothers with normal platelet counts. No interventions were required for the polycythemia or thrombocytopenia in either newborn. Platelet counts normalized after polycythemia resolved.

Several hypotheses may explain this relationship between neonatal polycythemia and thrombocytopenia. Similar to intrauterine growth restriction and gestational hypertension, IDM are potentially exposed to chronic intrauterine hypoxia. Chronic hypoxia upregulates erythropoietin production leading to polycythemia and may inhibit hematopoietic precursor megakaryocyte differentiation, leading to thrombocytopenia (1,2). Since polycythemia increases total blood volume, these infants may actually have a relative thrombocytopenia and normal total

platelet mass (3). The same hematologic sequelae of chronic hypoxia have been demonstrated in children with cyanotic congenital heart disease, whereby changes in microRNA expression leads to secondary erythrocytosis and thrombocytopenia (4).

Clinicians should be aware of this association between polycythemia and thrombocytopenia in infants potentially exposed to chronic intrauterine hypoxia.

1. Fandrey, Am J Physiol Regul Integr Comp Physiol, 2004
2. McDonald et al., Exp Hematol, 1992
3. Vlug et al., Expert Review of Hematology, 2014
4. Mukai et al., Pediatric Research, 2018

Poster # 217

A CASE OF DIZYGOTIC TWINS WITH SEVERE THROMBOCYTOPENIA AND A LITERATURE REVIEW OF FAMILIAL ITP

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Background: The etiology of chronic immune thrombocytopenic purpura (ITP) has been suggested to be autoimmune and can either be idiopathic or be preceded by a viral illness. In 2011, the PARC Registry on ITP estimated that 2 % of children and 3 % of adults with ITP had other family members with thrombocytopenia. Parent-child relationships have shown to be the most frequent association, however there are cases that have also suggested an association between siblings, as well as monozygotic twins.[1] However, we did not identify a case of dizygotic twins developing chronic ITP.

Objectives: To present rare cases of ITP in dizygotic twins with the onset 6 months apart from each other. This suggests that there may be a genetic predisposition increasing susceptibility to acquiring ITP or a familial component.

Design/Method: We present the cases of dizygotic caucasion twin sisters with no past medical history and non-contributory family history. At age 16, twin A presented with a progressive petechial rash along her clothing line, gum line bleeding, oral “blood blisters” and increasing fatigue. Her CBC showed profound thrombocytopenia of 8K/uL. Seven months later, twin B presented with heavy menstrual bleeding and profound thrombocytopenia of 4K/uL. Both patients' exams were notable for multiple purpura. Testing for toxoplasma, HBV, HCV, HIV, cytomegalovirus, Epstein-Barr virus, folate or vitamin B12 deficiency, bone marrow hypoplasia or aplasia, hepatopathy and/or hypersplenism, disseminated intravascular coagulation, thrombotic thrombocytopenic purpura, alloimmune, genetic or drug-related thrombocytopenia, or any type of immunodeficiency was unremarkable. Lyme IgG and IgM were present in both patients, although they exhibited no symptoms of the disease at the time of presentation.

Results: These patients showed a short term response to IVIG but ultimately had to be treated with Eltrombopag. These cases suggest that thrombocytopenia could occur as an occult inheritable trait in immune regulation that increases susceptibility to chronic ITP.

Conclusion: Further evaluation of familial or genetic form of ITP would improve its detection and thereby, allow us to further characterize the etiologies of ITP. There have been case reports of tick borne illnesses causing thrombocytopenia in acute infection, however, our literature review did not reveal a symptomatic chronic thrombocytopenia as seen in these patients. We believe these cases could be added to the literature of other causes in familial forms of ITP.

[1]Pujol-Moix, Núria, et al. "Familial Immune Thrombocytopenia. Report of 16 Cases and Literature Review." *Journal of Rare Diseases Research & Treatment* 3.4 (2018).

Poster # 218

SEVERE THROMBOCYTOPENIA IN A NEWBORN

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Background: Fetal and neonatal alloimmune thrombocytopenia (F/NAIT) is categorized by transplacental alloantibodies against fetal human platelet antigen (HPA), most commonly HPA-1a. Specifically, the pathogenesis involves maternal sensitization against paternal HPA and subsequent antibody production leading to severe thrombocytopenia. F/NAIT is estimated to occur in approximately 0.15% of live births, with only approximately 25% of cases diagnosed. Intracranial hemorrhage (ICH) occurs in 20% with 10% mortality.

Objectives: To describe a subtle presentation of suspected F/NAIT and increase awareness of this life-threatening condition.

Design/Method: Case report and literature review

Results: We present the case of a six-hour-old male infant who was found to have scattered petechiae on his back and subtle ecchymosis hidden under acrocyanosis on the plantar surfaces of his feet. Initial complete blood count (CBC) was notable for severe thrombocytopenia with platelet count of 13,000/μL; repeat CBC confirmed the finding. The patient was transferred to the neonatal intensive care unit for close monitoring and sepsis was ruled out. CMV was negative and transcranial ultrasound showed no evidence of ICH. His platelet count rose to 30,000/μL after 1 platelet transfusion and fell to 18,000/μL the next day. A second unit of platelets was transfused which lead to a platelet count of 90,000/μL at discharge and 54,000/μL upon follow-up at one week of life. At four weeks of life, his platelet count had risen to 363,000/μL without any further intervention. Parental examination of HPA and antibody production were pending at the time of this writing, however, F/NAIT is suspected.

Conclusion: Early recognition and management of F/NAIT is critical as it is the most common cause of ICH in neonates. One case series describes ICH as the presenting symptom in 14% of cases of F/NAIT. Maternal antibodies will generally clear over the course of several weeks, and the child's platelet count is expected to rise to normal levels. Subsequent pregnancies, however, carry implications for potentially poor outcomes. Although cost-savings have been demonstrated, implementation of a screening program has not been successful and likely not desired by mothers. Bonstein et al recently demonstrated that there continues to be a significant lack of awareness of F/NAIT. Regardless of the final parental test results, our case serves as a reminder that it is incumbent upon not only pediatric hematologists, but all providers involved in the care of newborns to have a high index of suspicion for F/NAIT given the relatively subtle presentation and potentially devastating sequelae if unrecognized.

Poster # 219

REAL-WORLD EXPERIENCE OF PEDIATRIC PATIENTS WITH SICKLE CELL DISEASE TREATED WITH OXBRYTA®

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Background: Sickle cell disease (SCD) is an inherited disorder in which sickle hemoglobin (HbS) polymerization triggers red blood cell sickling, chronic hemolysis, anemia, and episodic vaso-occlusion. Complications include cumulative organ damage and disability, as well as accelerated mortality. Oxbryta® (voxelotor) is a first-in-class therapy that increases hemoglobin (Hb) levels and reduces markers of hemolysis. It is FDA approved for treatment of SCD in patients aged ≥12 years.

Objectives: To quantify the clinical response to treatment with Oxbryta tablets in a single-center series of 17 pediatric patients with SCD.

Design/Method: We collected real-world clinical data on 17 pediatric (aged 12-21 years) patients with SCD at Prisma Health - Upstate Comprehensive SCD Program, Greenville, South Carolina, USA, under a data collection protocol for standard-of-care clinical data. Laboratory data were collected before initiation of Oxbryta and were compared to the most recent laboratory value collected during Oxbryta treatment. Included patients received Oxbryta for ≥2 consecutive weeks (1 patient not included in this analysis immediately discontinued treatment due to a serious hypersensitivity reaction).

Results: A total of 17 patients (aged 12-21 years, 71% female) were included in the current analysis. HbS genotypes were 94% SS and 6% $S\beta^0$-thalassemia. All patients were receiving hydroxyurea when they initiated Oxbryta. At the time of analysis, patients had been receiving Oxbryta for an average (range) of 2.5 months (1-6 months). Hb improved (post vs pre-Oxbryta) by an average (SD) of 1.49 g/dL (0.82 g/dL). Reticulocyte percentage decreased by 4.14% (3.78%), and total bilirubin decreased by 1.71 mg/dL (3.10 mg/dL). The patients all reported

clinical improvements that correlated with their recorded hematologic responses to Oxbryta, most commonly manifesting as increased energy, decreased pain symptoms, and reduced scleral icterus. The most common reported side effects were mild diarrhea and nausea, both of which were self-limited and did not require any supportive care.

Conclusion: This study is the first to examine the real-world impact of Oxbryta in a pediatric patient population. The effects of Oxbryta on Hb, reticulocyte percentage, and total bilirubin were of similar magnitude to those reported in the HOPE trial, which also included adults. In addition, there was consistent evidence of improved clinical status that was associated with the robust hematologic response. In summary, our study suggests that pediatric patients with SCD achieve meaningful clinical benefit with Oxbryta therapy.

Poster # 220

AML IN CHILDREN WITH SICKLE CELL DISEASE ON PROLONGED HYDROXYUREA THERAPY: REPORT OF TWO CASES

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Background: Patients with sickle cell disease (SCD) have an increased incidence of cancer, especially leukemia. The mechanism of leukemia development in this population is not clear, but may be related to chronic inflammation, increased cell turnover, or increased infection risk over time. The effect of hydroxyurea on normal hematopoiesis has also been implicated, although no association has been shown between hydroxyurea use and increased leukemia incidence. An increased leukemia risk has not been described specifically in pediatric patients with SCD.

Objectives: To report two cases of acute myelogenous leukemia (AML), diagnosed in children with Hgb SS and prolonged hydroxyurea therapy

Design/Method: Case series

Results: Patient 1, a 13-year-old female with Hgb SS, treated with hydroxyurea since age 6, was noted to have persistent neutropenia for 6 months despite reduced hydroxyurea dosing. Notably, Hgb F levels continued rising despite decreased hydroxyurea, suggesting stress hematopoiesis due to emerging leukemia. A bone marrow biopsy revealed AML with a normal karyotype (46 (XX)), and negative FISH and molecular work-up. CNS was negative. She was treated per AAML1031 with cytarabine, etoposide, and daunorubicin and achieved remission with negative minimal residual disease (MRD) testing by flow cytometry at the end of induction (EOI). Patient 2, a 9-year-old female with HbSS, treated with hydroxyurea since age 5, had myeloblasts noted on a routine CBC for SCD monitoring. Diagnosis of AML with a normal karyotype (46 (XX)) and negative FISH and molecular work-up was confirmed by bone marrow biopsy. CNS was negative. Treatment was initiated per AAML1031 as above, and she achieved remission with negative MRD at EOI. Her course, however, was complicated by fungemia, actinomyces bacteremia, and anakinra-resistant HLH requiring treatment with a prolonged course of steroids

and emapalumab. Neither patient had a matched sibling donor. Although hematopoietic stem cell transplantation (HSCT) was offered to both patients, the first patient's family chose to proceed with chemotherapy only, while the second patient's family chose to pursue bone marrow transplant after three cycles of chemotherapy.

Conclusion: These two cases of AML diagnosed in children with sickle cell disease highlight a population that may be at increased risk of malignancy and presents a management challenge. The role of HSCT is unclear in children with low risk AML and previously well controlled SCD on hydroxyurea. With hydroxyurea no longer an option for sickle cell disease treatment, both patients were offered transplant, which has potential to eradicate SCD as well as AML.

Poster # 221

A RARE CAUSE OF LYMPHADENOPATHY IN A CHILD WITH SICKLE CELL DISEASE: KIKUCHI-FUJIMOTO DISEASE

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Background: Kikuchi-Fujimoto Disease (KFD), also known as histiocytic necrotizing lymphadenitis, is an extremely rare, benign, self-limiting condition with an unknown incidence. Currently, the etiology and pathogenesis remains unknown. However, theories suggest that KFD is an autoimmune process that is triggered by unidentified agents, likely viruses, in subjects with a genetic predisposition. KFD is more common in males in the pediatric population, and is characterized by localized tender cervical lymphadenopathy, fever and constitutional symptoms. There have been only four reported cases of KFD in pediatric patients with sickle cell disease (SCD). Our case highlights the challenging diagnosis of KFD in an immunocompromised male with SCD.

Objectives: To raise awareness amongst clinicians of this rare condition, which may help prevent misdiagnosis, extensive investigations and inappropriate treatment.

Design/Method: Case report with literature review.

Results: A 7-year-old African American male with SCD presented with fever and right neck swelling, was diagnosed with right peritonsillar, parapharyngeal and retropharyngeal abscesses on CT imaging along with prominent right cervical lymphadenopathy. He underwent drainage, which grew MRSA, and an excisional right cervical lymph node biopsy demonstrated lymphoid hyperplasia with no evidence of malignancy or lymphoproliferative process on flow cytometry. He received a one-month course of appropriate antibiotics confirmed via sensitivity susceptibilities. He has since been readmitted multiple times with fever and alternating right and left cervical lymphadenopathy that was resistant to appropriate antibiotics. Throughout these admissions, an extensive infectious etiology work up was done which excluded EBV, CMV, HIV, Toxoplasmosis, Tuberculosis, and COVID-19. Due to the lack of clinical improvement with appropriate antibiotics, a left cervical lymph node biopsy was performed which again

revealed no evidence of malignancy, however, confirmed histopathological findings consistent with KFD. Patient was treated with escalating his dose of hydroxyurea with pain control as needed. He was discharged in good condition.

Conclusion: In the United States, approximately 30-40% of KFD cases were initially misdiagnosed as lymphoma or malignancy, subjecting these patients to unnecessary and invasive investigations including bone marrow biopsy. In children with SCD, it is important to consider KFD in the differential diagnosis of lymphadenopathy and fever. Patients with KFD usually recover spontaneously within 1- 4 months; however, there have been associations with autoimmune conditions, including systemic lupus erythematous. This also supports the importance of confirming the diagnosis because patients with KFD require close monitoring and periodic testing for the development of other autoimmune diseases.

Poster # 222

COVID-19 IN PEDIATRIC PATIENTS WITH SICKLE CELL DISEASE: A SINGLE INSTITUTION EXPERIENCE

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Background: Sickle cell disease is a chronic inherited condition that affects the red blood cell which results in acute chronic, and recurring complications due to abnormal blood flow through multiple organ systems, especially the lungs. Acute chest syndrome can be life-threatening and a serious sequelae of sickle cell disease and with the COVID-19 pandemic, this particular population is vulnerable to morbidity and mortality. Systematic reviews report that less than 6% of COVID-19 cases have occurred in pediatric patients. Although the incidence is low in the pediatric population, sickle cell disease poses an additional co-morbidity which is important to understand.

Objectives: Demonstrate the finding of COVID-19 and its effects on patients with sickle cell disease in the pediatric population.

Design/Method: IRB approved retrospective chart review of pediatric patients with sickle cell disease who tested positive for COVID-19 between March 2020 and January 2021. Risk factors, laboratory evaluation, and clinical course were reviewed.

Results: Ten patients were included in the analysis. Median age 9.5 years (range 5-17 years) with 7 males and 3 females. Three patients were asymptomatic and were only tested due to exposure or pre-procedure requirements. Among the symptomatic patients, symptoms included cough (6/7), chest pain (2/7), fever (3/7), back pain (1/7) and vomiting (1/7). Median BMI 19.9 kg/m2, with 1 obese patients with BMI of 32.6 kg/m2. D-dimer was only obtained from 5/10 patients during hospitalization with a median of 4.31(range 9.89-1.11). Two patients had respiratory failure requiring intubation for a total of 4 days each, requiring erythrocytapheresis, steroids and remdesivir. An additional 2 patients had an oxygen

requirement. Fifty percent of patients were diagnosed with acute chest syndrome. Only 2 patients were placed on anticoagulation for elevated D-dimer levels. All patients recovered from COVID-19 with no significant current morbidities.

Conclusion: COVID-19 can have detrimental effects especially on patients with sickle cell disease. It is important to recognize specific pediatric populations who are vulnerable to the pulmonary complications and be proactive in early and aggressive treatment, including erythrocytapheresis.

Poster # 223

COVID-19 AND SICKLE CELL DISEASE (SCD): MULTI-SYSTEM INFLAMMATORY SYNDROME IN CHILDREN WITH SCD

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Background: The CDC defines multi-system inflammatory syndrome in children (MISC) as an individual <21 years presenting with fever, inflammation, severe illness requiring hospitalization, two involved organ systems, and recent or current SARS-CoV-2 infection. Sickle cell disease is a chronic inflammatory state that predisposes patients to vaso-occlusion and multi-system involvement. There is overlap between the inflammation seen in SCD and COVID-19 complications such as MISC.

Objectives: We report a case of an adolescent with SCD-SS disease with recent SARS-CoV-2 infection and clinical illness concerning for MISC and highlight the diagnostic challenges in this patient population.

Design/Method: Chart review and case presentation.

Results: A 15 y.o male with SCD-SS disease and SARS-CoV-2 infection documented 8 days prior to admission was transferred from an outside hospital with fever, hypoxia, bilateral leg, back, and shoulder pain, and confusion. Upon presentation, he was febrile to 38.6 C, HR of 93, RR of 25 and had a BP of 146/96. Labs on admission were notable for hemoglobin 7.3 g/dL, WBC 13.1, platelets 120, d-dimer >99,000 ng/mL, PT/INR 14.9 s/1.3, CRP 34.93 mg/dL, ESR 37 mm/hr, AST 219 U/L, ALT 71 U/L and creatinine of 0.8 mg/dL (baseline 0.5 mg/dL). CXR showed no acute cardiopulmonary abnormalities. He remained persistently febrile to Tm 39F and his hemoglobin dropped from 7.3 g/dL to 4.5 g/dL with an ARC 69.1 and nRBC 22.7. DAT notable for known positive Anti-S alloimmunization. He was treated with one dose of IVIG 60 g, solumedrol 1 mg/kg/dose q6, and received 2 units pRBC with resolution of fever and improved inflammatory markers within 24 hours

Conclusion: Inflammation plays a central role in sickle cell disease pathology and in the many complications seen in COVID-19. In a cross-sectional study assessing D-dimer levels in patients with SCD with vaso-occlusive crisis (VOC), the mean D-dimer was 566 ± 739 ng/ml during

steady state and 1038 ± 1010 ng/mL during VOC. Furthermore, a case series described the clinical characteristics of children with MISC and the median D-dimer level was 3578 ng/mL. The overlap between inflammatory mediators such as D-dimer seen in SCD and COVID-19 can lead to significant diagnostic challenges. However, D-dimer elevation in COVID related complications tends to be greater than elevations seen in VOC. Clinicians must be able to differentiate between the inflammation seen in chronic conditions such as SCD and the hyper-inflammation associated with COVID-19 in order to provide the appropriate management.
(Francis RB, Haemostasis,1989)
(Whittaker E, JAMA, 2020)

Poster # 224

IRON DEFICIENCY ANEMIA AND CEREBRAL THROMBOSIS: A CASE SERIES AND LITERATURE REVIEW

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Background: Iron deficiency anemia (IDA) is a rare etiology of thrombosis, with several hypothesized underlying mechanisms. IDA is thought to promote hypercoagulability via reactive thrombocytosis, increased blood viscosity, promoting turbulent blood flow, and increased oxidant stress. There are 26 reported pediatric cases, most of which had a combination of reactive thrombocytosis and/or a hypercoagulable state, and only 2 cases without a prothrombotic condition. The factors needed for thrombosis to occur in the setting of IDA and the rates of thrombosis secondary to IDA in the pediatric population remain unknown.

Objectives: To evaluate two cases of IDA-induced cerebral thrombosis and to review the existing literature.

Design/Method: We reviewed the charts of our patients with IDA-induced cerebral thromboses, and conducted a literature review on thrombosis and IDA.

Results: Case 1: A 25-month-old previously healthy female presented with new-onset seizures and emesis. Notably she had been drinking 2.5 gallons of milk weekly. Initial lab workup was notable for hemoglobin of 4.7 g/dL, mean corpuscular volume of 49 fL, platelets of 290,000/μl, iron of 11 μg/dL, total iron binding capacity of 514 μg/dL, and ferritin of 3 ng/mL. Hypercoagulability workup was negative and no prothrombotic risk factors were identified. Magnetic resonance imaging of the brain revealed an extensive occlusive thrombus in the left transverse sinus, sigmoid sinus, straight sinus, internal cerebral veins, and inferior sagittal sinus with multiple areas of infarct and hemorrhage. She was treated with 6 months of enoxaparin, with repeat imaging showing reduction in clot burden.

Case 2: A 7-year-old previously healthy female presented with sudden-onset left hemiparesis. She was found to have a right ACA stroke and bilateral pulmonary emboli, secondary to severe IDA. Her hypercoagulable workup was positive only for homozygous MTHFR mutation, but

with normal homocysteine levels at admission and with each subsequent check. She was treated with 6 months of enoxaparin and iron supplementation, with complete resolution of her thromboemboli.

Conclusion: Case 1 highlights the rare phenomenon of how IDA in the absence of thrombocytosis or other prothrombotic conditions can cause thrombosis. The cases together also highlight the importance of early detection and treatment of IDA given the potential for reducing thrombotic risk. Future research is needed to determine the conditions required for thrombosis to occur in the setting of IDA, and whether patients with IDA have increased thrombotic risk as compared to the non-IDA pediatric population.

Poster # 225

MANAGEMENT OF SARSCoV2 INFECTION PRESENTING AS ACUTE CHEST SYNDROME IN A PATIENT WITH HEMOGLOBIN SD.

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Background: Hemoglobin SD – Los Angeles (HbSD) disease is a compound heterozygous hemoglobinopathy with a mild clinical course compared to homozygous sickle cell disease (HbSS). Infection with SARS-CoV-2 has been associated with acute chest syndrome (ACS) in children with HbSS, but this complication has not previously been reported in children with HbSD. Dexamethasone has been shown to improve outcomes in non-sickle cell patients with SARS-CoV-2 pneumonia or adult respiratory distress syndrome (ARDS); however, its use in ACS is controversial due to reports of early recurrence after discontinuation and increased risk of vaso-occlusive painful crisis (VOC) in patients treated with dexamethasone. Herein, we report the successful treatment of SARS-CoV-2 associated ACS with dexamethasone in a child with HbSD.

Objectives: Describe the clinical course of a child with HbSD and SARS-CoV-2 associated ACS.

Design/Method: Case report and literature review.

Results: A 7-year-old girl with HbSD presented to the Emergency Department with fever, cough, and breathing difficulty for 1 day. Past history was significant for splenectomy at 4 years of age due to recurrent splenic sequestration crises and severe anemia. She had no prior episodes of ACS or pain crises. Home medications were Penicillin VK and Folic acid. She was not on Hydroxyurea. At presentation, she was febrile (40°C), tachypneic with decreased air entry on the left base and Oxygen saturation 85% on room air. Laboratory values showed leukocytosis, neutrophilia, and elevated inflammatory markers. Chest X-Ray showed left middle and lower lobe infiltrates. Findings were consistent ACS. She was started on supplemental Oxygen and empiric antibiotics. Reverse Transcriptase-Polymerase Chain Reaction for SARS-CoV-2 was positive. She was started on Dexamethasone 6 mg/ day divided BID on the day of

admission. Within 24 hrs, her respiratory distress improved. Antibiotics were discontinued when blood cultures were negative after 48 hrs. Supplemental oxygen and Dexamethasone were discontinued after 3 days and she was discharged home in good condition on Penicillin VK. At follow-up in clinic, she had no evidence of ACS or VOD.

Conclusion: The use of dexamethasone in our patient was associated with a rapid improvement of ACS without recurrence of her symptoms or readmission for VOC after discontinuation of dexamethasone, a concern for many patients with ACS. This may reflect the fact that the pathophysiology of her illness did not include a significant component of vaso-occlusion, pulmonary hemorrhage, or superimposed bacterial infection. Early use of dexamethasone should be considered in the treatment of SARS-CoV-2 associated ACS. Further study is warranted.

Poster # 226

COMPLEX ANTICOAGULATION MANAGEMENT IN A PEDIATRIC PATIENT WITH SICKLE CELL HEMOGLOBIN D DISEASE

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Background: Sickle cell hemoglobin D disease (HbSD) is a rare variant of sickle cell disease (SCD). Vaso-occlusion and hemolytic processes lead to hypercoagulability in SCD with a cascade of events contributing to this state. Deep vein thrombosis (DVT) is a known complication of SCD in adults with several case reports in the pediatric population. There are no specific guidelines for thrombosis management in sickle cell disease and so patients with thrombosis have been acutely managed with a heparin drip. Data is limited on the use of bivalirudin in the sickle cell population particularly in pediatrics.

Objectives: A 17 year old male with HbSD on hydroxyurea admitted with vaso-occlusive crisis (VOC) found to have acute chest syndrome on imaging (ACS). He developed progressive respiratory distress, anemia and thrombocytopenia concerning for multiorgan failure.

Design/Method: Not applicable

Results: He underwent red blood cell exchange pheresis after urgent placement of right femoral catheter on hospital day (HD) 1 resulting in improvement. Hydroxyurea held due to thrombocytopenia. On HD#11 patient complained of new right leg pain. Lower extremity doppler ultrasound revealed extensive DVT from external iliac to popliteal vein with near complete occlusion. Patient started on enoxaparin but unable to reach therapeutic levels, despite escalating dose. He went for thrombectomy with interventional radiology on HD#16. Hydroxyurea restarted on HD#16. Team unable to reach therapeutic levels on heparin despite maximum dosage and adequate antithrombin III levels. Repeat ultrasound on HD#19 showed re-accumulation of thrombus prompting escalation to continuous bivalirudin infusion titrated to achieve therapeutic level (goal PTT 80-100). Patient underwent partially successful repeat

thrombectomy on HD#23. Post-operatively, bivalirudin resumed. Noted to have thrombocytosis (Platelet count > 1 million) and started on aspirin as well as increased hydroxyurea dose. Thrombocytosis persisted requiring treatment with one dose of intravenous immunoglobulin (IVIG) as well as a course of oral steroid therapy for presumed thrombotic storm. He underwent repeat thrombectomy and non-drug eluting stent placement with venoplasty in the right external iliac vein on HD#30. Post-operatively Bilvalirudin resumed then eventually transitioned to Apixaban. Follow-up ultrasound prior to discharge showed residual non occlusive thrombus with a patent external iliac stent. Platelet count decreased (608k). Hypercoagulable work-up negative.

Conclusion: This is the first case to describe a patient with HbSD with DVT, subsequent thrombocytosis requiring treatment with bivalirudin, IVIG, steroids and a direct oral anticoagulant (DOAC). This case highlights the physiologic complications of a common presentation in SCD and the challenge of pediatric thrombosis management.

Poster # 227

A MISSED DIAGNOSIS OF SICKLE CELL DISEASE PRESENTING AS TRANSIENT SYNOVITIS/OSTEOMYELITIS.

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Background: Sickle cell disease (SCD) remains a global health problem. The implementation of newborn screening (NBS) for SCD in 1972 in the U.S allowed identifications of newborns with SCD, thereby drastically reducing mortality rate of children with SCD. However, routine NBS and healthcare knowledge for SCD continue to be lacking in other developing countries. SCD is highly prevalent in the Democratic Republic of Congo (DRC), with approximately 2% of newborns homozygous for hemoglobin S. However, SCD remains relatively unrecognized in the DRC. Despite various technological advancements made in the past 5 decades to diagnose SCD, thorough history and physical exam remain the key to diagnose SCD.

Objectives: To describe an uncommon late diagnosis of sickle cell anemia in a child born in the DRC.

Design/Method: A case report of a child born in the DRC originally diagnosed with transient synovitis found to have red marrow hyperplasia on MRI concerning for SCD.

Results: A 23 month old female born in the DRC, immigrated to Los Angeles at 2 months of age with a recent diagnosis of presumed transient synovitis represented with difficulty walking associated with swelling and tenderness of bilateral feet. Review of systems were notable for fevers, fatigue, and joint pain. Complete blood count was notable for a normal white blood count, anistocytosis and microcytic anemia (hemoglobin 10.5 g/dL; MCV 71.6 fL). She had elevated ESR of 35 mm/hr and CRP of 5.9 mg/dL. Her iron panel was unremarkable. In consultation with infectious disease, MRI of her foot was performed, which demonstrated multiple regions of enhancing T1 hypointensity and T2 hyperintesity within the first through

third metatarsals, calcaneus, and distal tibia concerning for osteomyelitis. However, the involvement of multiple noncontiguous bones with red marrow hyperplasia was suspicious for sickle cell anemia in the context of her anemia. Hemoglobin electrophoresis confirmed homozygous sickle cell anemia, which demonstrated a pattern of SS with hemoglobin S (81.4%), hemoglobin F (15.2%) and hemoglobin A2 (3.4%). She was started on penicillin prophylaxis and folic acid, with hematology outpatient follow-up scheduled.

Conclusion: Fever and bone pain in a child with SCD are concerning for sepsis or vasoocclusive crisis, which requires prompt initiation of antibiotics, hydration and pain control. Diagnosis of SCD should not be delayed in order to quickly provide necessary education on SCD and to initiate proper healthcare screening. In a child born in a developing country where SCD is prevalent, SCD must be considered and ruled out.

Poster # 228

ANTI-M ALLOANTIBODIES: AN UNDER-RECOGNIZED CAUSE OF PROLONGED FETAL ANEMIA

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Background: Approximately 10% of pregnant women with positive antibody screens have detectable anti-M antibodies, which are often IgM subclass, clinically insignificant, and rarely associated with hemolytic disease of the fetus and newborn (HDFN). Among Asian women, IgG anti-M alloantibodies capable of transplacental transmission resulting in HDFN have increased over the past two decades.

Objectives: Describe a newborn delivered with severe fetal anemia due to suspected anti-M alloantibodies, who experienced prolonged reticulocytopenia and repeated red blood cell transfusions.

Design/Method: Case Report

Results: A 2645g Asian female infant was born at 35 weeks gestation via emergent Cesarean section to a primigravid mother for decelerations on fetal heart tracing and signs of severe anemia detected on fetal middle cerebral artery Doppler ultrasound. The pregnancy was complicated by advanced maternal age and a positive anti-M antibody screen. Maternal prenatal history and prenatal infectious disease serologies were unremarkable. After birth, APGAR scores were 7 and 8, but required brief positive pressure ventilation for poor respiratory effort and hypoxemia. Hemoglobin was 6.6 g/dL with a low reticulocyte count and an antibody screen positive for anti-M. HDFN was suspected so M-negative blood was transfused. Maternal blood type was B+. The infant's blood type was O+. Lactate dehydrogenase was elevated, but peripheral smear revealed no evidence of hemolysis. Total bilirubin was 2.6 g/dL, and she was placed on prophylactic phototherapy due to concern for ongoing hemolysis and in anticipation of severe hyperbilirubinemia. Bilirubin level peaked at about 12.3 g/dL. The patient required

another transfusion on day of life 19 for a hemoglobin of 6.7 g/dL and reticulocytopenia. Erythropoietin level was normal. Additional workup for TORCH infections and parvovirus was unremarkable. After discharge from the hospital, her reticulocyte count remained low, and she required two additional blood transfusions on days of life 46 and 61. Maternal anti-M antibodies were still detected but with decreasing titers over time. The reticulocyte count improved at approximately two months of age and the infant no longer required transfusions.

Conclusion: Consistent with prior reports, this case demonstrates that maternal anti-M alloantibodies can be associated with HDFN in an infant of Asian descent. While classical RhD-HDFN is characterized by extravascular hemolysis and brisk reticulocytosis, infants with anti-M antibody associated anemia lack significant hemolysis and lack compensatory reticulocytosis suggesting arrest of erythropoiesis. Therefore, anti-M alloantibodies may play a role in suppressing the differentiation and expansion of erythroid progenitors.

Poster # 229

PAIN MANAGEMENT WITH EPIDURAL ANALGESIA TO LIMIT OPIOID DEPENDENCY IN PEDIATRIC SICKLE CELL DISEASE

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Background: Epidural analgesia (EA) in the management of adult vaso-occlusive crises (VOC) in patients with sickle cell disease (SCD) has been widely reported on, however there are few reported cases of EA in the management of severe VOC in the setting of pediatric SCD. Epidural use has shown to greatly improve oxygenation by relieving pain-induced respiratory splinting and reducing opioid induced respiratory depression. In addition, it has been effective in controlling pain that was previously unresponsive to high dose opioids.

Objectives: The aim is to describe a case of a 14 year old male with SCD and avascular necrosis (AVN) who underwent a right total hip arthroplasty with pain managed by EA to decrease complications of SCD such as prolonged VOC and acute chest syndrome (ACS), and thus decrease overall use of opioid medications.

Design/Method: Single study case report

Results: Our patient with SCD and AVN of the right hip received 2 units of packed red blood cells preoperatively to maintain a hemoglobin of 10 mg/dL. He was admitted to the pediatric intensive care unit on postoperative day (POD) #1 after total right hip arthroplasty with an epidural catheter in situ for pain management. He was started on 0.125% bupivacaine and 2 mcg/mL fentanyl with a continuous basal rate of 6 mL and a 2 mL bolus every 15 minutes with a lockout of 14mL. He was also given IV Toradol and oral Tylenol. After having inadequate pain control over the first 24 hours, pain management was optimized with an increase of his basal rate to 9 mL/hr. His EA was discontinued after 48 hours. He was transitioned to oral Oxycodone every 4 hours and encouraged to ambulate. Over the next 24 hours, he required 2 doses of

intravenous Morphine. By POD #3, he received only oral pain medications. On POD #4, his pain remained well controlled, and he only received pain medications as needed. Additionally, he ambulated with support. He was discharged on POD #5.

Conclusion: The use of EA likely resulted in an overall decreased length of hospitalization, a decrease in long term pain management with opioids, early ambulation, and an avoidance of complications such as ACS. Our findings suggest that EA is a safe and effective means for post-operative pain management in SCD. This case postulates that the use of EA in pediatric patients with SCD in the setting of severe VOC will decrease long term opioid use and limit opioid dependency.

Poster # 230

QUITE A PUZZLE: A CASE REPORT OF A 15-YEAR-OLD FEMALE WITH SEVERE ANEMIA DUE TO SCURVY.

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Background: Scurvy is historically thought of as a disease affecting sailors in the seventeenth century. Vitamin C deficiency is rare in the developed world. It is mainly found in patients with poor nutrition and specifically those with developmental delay. The spectrum of scurvy is varied and includes dermatological, dental, bone, and systemic manifestations. We present to you a case of a 15-year-old female with a history of trisomy 21 presenting with severe anemia as a direct cause of vitamin C deficiency.

Objectives: Presenting a case report illustrating scurvy as a rare cause of anemia in pediatric patients.

Design/Method: Consent obtained from the parents to write a case report and include serial photographs documenting her case presentation. A literature review of scurvy in pediatrics was conducted.

Results: She presented with a one-month history of progressive bilateral lower extremity , bruising and inability to walk. Physical exam notable for trisomy 21 features. Bilateral swelling in lower extremities with the right calf more swollen than left. It was associated with large areas of ecchymosis associated with significant tenderness.Perifollicular hyperkeratotic papules with surrounding pinpoint hemorrhage in upper extremities with coiled hair.The remainder of the physical exam and review of the systems were unremarkable.

She underwent extensive workup which showed normocytic anemia (Hgb 8.7 g/dL). Elevated D dimer (1.18 mcg/ml). Normal Iron studies, comprehensive metabolic panel, coagulation studies, autoimmune work were unremarkable. Hemolysis labs were grossly unremarkable.

Hematological work up including ADAMTS12, Paroxysmal nocturnal hemoglobinuria, factor

deficiencies, platelet function assay, protein C, S were unremarkable. A duplex ultrasound, CT, and CTA of lower extremities were unremarkable. Vitamin C levels were low and barely detectable at <0.1mg/dl.

She was started on vitamin C supplementation of 250 mg twice a day and iron supplementation. She was found to have low B12 and vitamin D which was treated with supplementation. Significant improvement was notable in three weeks of treatment as the patient was able to walk. She also had near-complete resolution of her ecchymosis and significant improvement in her anemia.

Conclusion: Scurvy is considered rare especially in the developed world. A number of care reports discussed variable presentation such as a limp, ecchymoses, and other systemic symptoms. This case likely to suggest that scurvy is a potential cause of anemia in pediatric patients especially in patients with developmental delay.

Poster # 231

SYNCHRONOUS LEUKEMIA AND EPENDYMOMA IN A PEDIATRIC PATIENT WITH NO GENETIC PREDISPOSITION

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Background: Multiple primary malignancies are defined as synchronous if occurred within a 6-month period from the diagnosis of initial cancer or metachronous if happened later. The incidence in the pediatric population is unknown. Most cases have been related to genetic predisposing genes such as germline P53 mutated Li-Fraumeni syndrome, Ras pathway disorders including Neurofibromatosis type-1, Fanconi anemia and Beckwith-Wiedemann syndrome, or environmental factors as exposure to infection or previous treatment.

Objectives: We report a rare case of two synchronous malignancies in a healthy child with no cancer-predisposing condition.

Design/Method: A previously healthy 13-year-old boy presented with abnormal leukocytosis and blasts on a routine lab. Subsequently, a bone marrow examination revealed immature mononuclear cells with fine chromatin and scant cytoplasm consistent with blasts. Immuno-phenotyping revealed TDT, CD19, and CD20 positivity with aberrant B lymphoblast population consistent with B-cell Acute Lymphoblastic Leukemia (ALL) which was negative for BCR-ABL-1, ETV6/RUNX1, and KMT2A rearrangements. The patient was subsequently started on 4-drug induction chemotherapy with Vincristine, Daunorubicin, steroids, and Peg-aspargase. On day 15, he presented to the emergency room with weakness in both lower limbs with decreased reflexes but normal sensations bilaterally. The patient had a lumbar puncture that morning for intrathecal chemotherapy and had no complications during the procedure.

Results: MRI spine showed a fluid collection in the thecal sac representing bleed or leptomeningeal enhancement and incidentally demonstrated a mass in the 4th ventricle. The imaging characteristics were concerning for an Ependymoma. The patient was scheduled for surgical resection of the mass, and pathology revealed moderately cellular monomorphic cells with round to oval nuclei with some perivascular pseudo-rosettes consistent with grade 2 Ependymoma. ALL therapy was placed on hold, the patient underwent proton therapy at 180 cGy/fraction for a total of 4860 cGy to the mass with a boost. ALL therapy was resumed and he remains with no evidence of disease and in molecular remission.

Conclusion: The etiology of childhood cancers is multifactorial involving a combination of genetic, biological, and environmental factors. Using data from 29 countries, there was a significant positive correlation between the incidence rate of ALL and Astrocytoma but no correlation was found with Ependymoma. More studies are being obtained to identify a potential relationship between his Ependymoma and ALL. Our patient is unique with no genetic predisposing condition to develop tumors but yet had two synchronous tumors of different histologies. This case highlights the unique occurrence and management challenges.

Poster # 232

TREATMENT OF OSTEOCLAST BONE DYSPLASIAS WITH DENOSUMAB

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Background: Central giant cell granulomas (CGCG) and aneurysmal bone cysts (ABC) are rare tumors affecting adolescents and young adults. These osteolytic lesions cause bone destruction via signaling through receptor activator of nuclear factor-kB ligand (RANKL). Treatment involves surgical excision and/or curettage, which may result in functional morbidity. Denosumab is a monoclonal antibody targeting RANKL thereby inhibiting osteoclast activity and bone resorption indicated for treatment of adults and skeletally mature adolescents with unresectable giant cell tumor of bone. Denosumab has also been proposed as a treatment option for other osteoclastic bone disorders.

Objectives: We describe a case series of six patients with osteoclast bone dysplasias treated with denosumab (CGCG, n=5; ABC, n=1).

Design/Method: Case Series.

Results: Five patients, ages 10-29 years, presented with jaw pain and swelling and were found to have CGCG of the mandible. Denosumab was used as first-line therapy in four patients with CGCG as resection could cause functional morbidity. One patient with CGCG underwent multiple resections with recurrence refractory to intralesional steroids and calcitonin, before receiving Denosumab therapy. A sixth patient with recurrent ABC, initiated denosumab having recurred after curettage and bone-grafting. Five of six patients completed one year of therapy

with monthly injections. One patient has currently received six doses of denosumab, with plans to complete one year of therapy. Of the five who completed therapy, one patient had decreased lesion size and subsequently underwent surgical excision. All six patients had sclerosis of lytic bone lesions reflecting new bone formation and cessation of osteoclast bone destruction. The remaining four demonstrated stable tumor size on follow-up imaging. All six patients had rapid symptomatic improvement of pain. To date, no patients have had recurrence of disease.

All patients received prophylactic vitamin D and Calcium supplementation. One patient developed hypocalcemia during therapy requiring cholecalciferol and calcitriol supplementation, and completed one year of denosumab therapy after dose reduction. Two of six patients (ages 13 and 14 years) developed grade 4 rebound hypercalcemia (CTCAE v5) after completion of denosumab requiring hospitalization, intravenous hydration, calcitonin and bisphosphonates.

Conclusion: Denosumab may be an effective therapy for osteoclast bone dysplasias not amenable to surgical resection and/or curettage. We present six patients with osteoclast bone dysplasias successfully treated with denosumab who had 100% disease control rate, bone sclerosis and symptomatic improvement. Careful observation of younger patients for rebound hypercalcemia after completion of therapy is warranted.

Poster # 233

MULTIFOCAL MACRO-CYSTIC LESIONS: A CASE OF DIAGNOSTIC MIMICRY

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Background: Management of pediatric vascular anomalies is increasingly triaged to pediatric hematologist/oncologists. Although disease classification for vascular anomalies have improved, diagnostic imaging mimicry continues to be challenging. Malignant pathology can appear similar to a benign lesion and can delay appropriate therapy. Multifocal cystic lesions can be particularly challenging to characterize and require a multidisciplinary approach with multiple subspecialists to ensure an accurate diagnosis.

Objectives: We present a case of diagnostic mimicry where clinical intuition overcame conformational bias to identify the appropriate diagnosis.

Design/Method: Local IRB approval was obtained to complete a retrospective electronic chart review.

Results: A 17-year-old boy presented to the Vascular Anomalies Center at the Children's Hospital Colorado for a left neck macro-cystic lymphatic malformation. Initial visit identified the subcutaneous cystic neck lesion and distended abdomen with palpable abdominal mass. He reported abdominal pain and unintended weight loss. Full body MRI/MRA reported multifocal macro-cystic abdominal masses and a macro-cystic left neck mass with concern for generalized lymphatic anomaly. He underwent sclerotherapy of the left neck and intraabdominal macro-cysts

with consideration for surgical debulking if symptoms persisted or masses did not respond. Aspiration of the macro-cysts of the abdomen revealed fluid less consistent with the appearance of lymph or chyle; the patient reported worsening abdominal pain. The patient underwent surgical debulking. Intraoperative frozen sections were consistent with lymphatic malformation. A near-complete surgical resection of the abdominal lesions was performed. Formal pathology returned consistent with a mixed germ cell tumor. Care was transitioned to the solid tumor oncology team to initiate therapy with bleomycin, etoposide, cisplatin (BEP) chemotherapy.

Conclusion: During this initial evaluation there were data points overemphasized to support the existing hypothesis of lymphatic malformation including outside diagnosis of a neck lymphatic malformation, MRI read supportive of lymphatic malformation and pathology review of lymphatic malformation. Conformational bias overshadowed data to refute this diagnosis including lack of response to sclerotherapy, fluid aspirate inconsistent with lymphatic fluid, and a clinical history of acquired weight loss. The lack of response to first-line therapy resulted in a change in care plan to pursue a pathologic diagnosis that ultimately revealed the correct diagnosis of a mixed germ cell tumor. Accurate diagnosis required looking beyond the area of chief concern, pausing to re-evaluate diagnosis with a lack of response to first-line therapy and investigating further to provide a more accurate pathologic diagnosis. Improving the diagnostic process represents a moral, professional, and public health imperative.

Poster # 234

RHABDOMYOMA AND CAVERNOUS HEMANGIOMA OF THE HEART

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Background: Tumors of the heart are typically benign. Rhabdomyomas account for approximately 60% of all primary cardiac tumors in children. Most commonly, rhabdomyoma is found as an abnormality on 20-week prenatal scan, and diagnosis is confirmed by fetal echocardiogram. Cardiac hemangiomas, by contrast, are quite rare. These benign, yet potentially dangerous overgrowths can result in hemodynamic instability secondary to massive inflow or outflow tract obstruction, or arrhythmia refractory to antiarrhythmic pharmacotherapy, in most instances requiring surgical resection.

Objectives: To describe two children with primary tumors of the heart.

Design/Method: Case series.

Results: Case 1: A female newborn was known to have a cardiac tumor via pre-natal ultrasound. The infant was delivered via C-section with APGARs of 9^{1} and 9^{5}. A post-natal US showed a large intraventricular mass near the mitral valve causing outflow tract obstruction. Presuming rhabdomyoma, the patient was started on sirolimus at a dose of 0.8 mg/m^2. She was on inotropes for 2 days. Genetic testing for Tuberous Sclerosis (TS) was negative, She was

discharged home on sirolimus and was followed with ultrasounds. Her tumor decreased in size by week 6 and sirolimus was discontinued. A follow up echocardiogram showed regrowth of multiple but small masses in the heart, however at 18 months she remains asymptomatic and in follow up. **Case 2:** A 4 year old male referred to cardiology for an incidental finding of a systolic murmur. Echocardiography found a sessile mass attached to the left side of the interatrial septum at the mitral valve hinge point, measuring 12 x 11 mm. The patient had an extensive work-up with MRI of the brain and the heart; and ultrasound of the kidneys looking for clinical features of TS, which were all negative. Genetic testing for TS was negative. Due to the unclear etiology and the location the patient underwent uncomplicated gross total surgical resection. The pathology confirmed a cavernous hemangioma. He is currently undergoing follow up with echocardiograms Q3 months. Repeat echocardiograms have shown preserved function of the mitral valve without recurrent tumor.

Conclusion: Although the most common tumor of the heart in infants is a rhabdomyoma associated with TS it is important to have a full evaluation and consider other etiologies. Rhabdomyomas tend to be multiple and responsive to Sirolimus. Pedunculated lesions are unusual for rhabdomyomas. The incidence of cavernous hemangiomas is extremely rare. We calculated the incidence of cavernous hemangioma as 0.48/1 million children.

Poster # 235

POSTERIOR RESVERSIBLE ENCEPHALOPATHY SYNDROME AFTER DINUTUXIMAB

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Background: Posterior reversible encephalopathy syndrome (PRES) is a reversible disorder associated with edema of subcortical white matter and cortical gray matter that involves the occipital and parietal lobes. Endothelial injury secondary to abrupt blood pressure changes breaks down the blood brain barrier leading to brain edema.

Per the ANBL0032 Fall 2015 Study Progress Report, Dinutuximab was the probable cause of PRES in two patients. There have been published reports of PRES with other anti-GD2 antibody therapies but few reports of Dinutuximab as the causative agent.

Objectives: To report a case of PRES after Dinutuximab

Design/Method: Case Report

Results: A 4-year-old male with stage IV neuroblastoma presented to the emergency department (ED) with new onset seizure activity described as generalized stiffening with his eyes rolled back five days after completion of his second course of Dinutuximab and IL-2. His blood pressure was elevated in the ED, as high as 156/129. He was agitated on exam with a nonfocal neurologic exam. He was admitted to the intensive care unit where he had recurrent seizure activity that

progressed to status epilepticus. MRI of the brain was significant for an abnormal T2 and FLAIR signal hyperintensity involving the cortex and subcortical white matter of the occipital lobes, posterior parietal lobes, and posterior temporal lobes, most consistent with PRES. He remained inpatient until elevated blood pressures and seizure activity resolved. He tolerated further cycles of Dinutuximab without incident.

Conclusion: Pediatric patients receiving anti-neoplastic therapy are at risk for developing PRES, mostly reported in patients with leukemia. The recognition of PRES is increasing likely secondary to increased awareness of this syndrome and improved radiographic technique. Hypertension is a common side effect of some antineoplastic agents and appears to be a key risk factor in developing PRES, as was likely the case with the patient described here. Our patient developed symptoms five days after completing antibody and IL-2 therapy. The half-life of Dinutuximab is ten days, versus one hour for IL-2. Hypertension is a known adverse effect of Dinutuximab but not IL-2. These factors support Dinutuximab as a contributing factor to his presentation rather than IL-2.

There have been other cases of PRES documented in patients receiving different forms of monoclonal antibody immunotherapy. There is not enough data to establish a causative association with monoclonal antibody therapy and PRES. However, the index of suspicion for PRES should be high, especially when patients present with acute neurological symptoms after receiving this therapy.

Poster # 236

JUVENILE XANTHOGRANULOMA OF THE PANCREAS MIMICKING PANCREATIC NEOPLASM WITH HIGH CA19-9

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Background: Juvenile Xanthogranuloma (JXG) is a rare, non-Langerhans cell histiocytosis. It is usually a benign and self-limiting condition and commonly occurs in the skin and soft tissue. Pancreatic involvement is extremely rare. We present the only pediatric case with JXG of the pancreas with hyperbilirubinemia and elevated CA19-9 at presentation.

Objectives: We present an unusual case of a 13-month-old patient with JXG of the pancreas.

Design/Method: Case Report

Results: A 13-month-old female patient presented with a 3-week history of jaundice, associated with pruritus, diarrhea and pale stools. No skin rash was reported. Laboratory investigations revealed normal CBC, elevated direct bilirubin with high alkaline phosphate and GGT suggestive of obstructive biliary pathology. CA 19-9 was significantly elevated and CEA was within normal. MRI showed a hypointense mass-like enlargement of the pancreatic head/uncinate process with post-contrast enhancement and diffusion restriction relative to the

body and tail along with marked intrahepatic and extrahepatic biliary ductal dilatation proximal to the mass. Given the patient's age and the inability to obtain tissue diagnosis via and endoscopic techniques, a surgical resection was warranted to both resect the mass and relieve her biliary obstruction. She underwent a Whipple type pancreaticoduodenectomy pylorus preserving procedure. She tolerated the surgery very well with no immediate post operative complications. Histopathological examination revealed foamy and spindled histiocytes admixed with scattered inflammatory cells. Histiocytes showed strong CD68, CD163 and FXIII immunoreactivity; establishing the diagnosis of JXG of the pancreas. Given that extracutaneous presentation of JXG can be associated with multiple site involvement, a metastatic work up including a brain MRI, whole body positron emission tomography and an ophthalmological exam were performed and were negative for metastatic lesions. Molecular profile of the tumor did not show any driver mutations but the following somatic variants of unknown significance were reported (EPHB1, APC, NQO1, KMT2C, and CSF1R). Liver function and CA-19.9 normalized postoperatively and she is growing and developing well. No signs of pancreatic insufficency. Six month post-surgery MRI did not show any evidence of disease.

Conclusion: Given the rarity of JXG in general and especially in the pediatric population, very little is known about the least invasive diagnostic modalities. JXG should always be considered as a differential diagnosis for pediatric patients presenting with a pancreatic mass, solid and/or cystic in nature. In order to avoid unnecessary invasive diagnostic procedures, further studies are warranted to explore different clinical, radiological and biologic markers for the diagnosis of JXG of the pancreas.

Poster # 237

PARANEOPLASTIC PEMPHIGUS VULGARIS AND CASTLEMAN DISEASE - TWO REPORTS OF EVENT FREE SURVIVAL

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Background: Castleman disease is a non-malignant, lymphoproliferative disease that can be characterized as either multicentric or unicentric. Unicentric Castlemans involves a single lymph note that once surgically resected is typically followed by resolution of symptoms requiring no further treatment. Unicentric Castleman is most often hyaline vascular type. Multicentric Castleman involves multiple sites of disease, causes more systemic symptoms and requires systemic therapy including immunotherapy agents (siluximab, rituximab), chemotherapy, IVIG and steroids in addition to resection. It is usually plasma cell or mixed variant type. The association of pemphigus vulgaris is a rare and unfavorable complication of Castleman disease. Due to its rare occurrence standardized treatment protocols have not been developed. Castleman Disease associated paraneoplastic pemphigus vulgaris carries a poor prognosis and high mortality rates.

Objectives: This case report presents two adolescent patients diagnosed with Castleman disease associated paraneoplastic pemphigus vulgaris who experienced disease remission with event-free survival at two- and five-years post-treatment, respectively. The objective is to review the presenting symptoms, labs and imaging, treatment course, disease response and successful resolution of disease despite the poor prognosis related to this diagnosis. The goal of reporting these patients is to help develop more standardized treatment protocols for Castleman Disease associated pemphigus vulgaris and improve patient outcomes.

Design/Method: Retrospective case analysis and review was completed on both patients and included history and physical, clinical photographs, lab and imaging results and medication dosing and frequency. This case study is significant due to the high morbidity of this diagnosis and the successful disease response of these patients who remain disease free years post diagnosis.

Results: Both cases involved adolescent, African American, male patients who presented initially with oral, mucosal and skin lesions. Diagnosis of pemphigus was made by lesion biopsy and subsequent imaging showed an abdominal mass in one patient and cervical adenopathy in the second. Pathology of mass/lymph node biopsies confirmed Castleman disease in both patients - one with hyaline variant type and one with mixed variant. Both were HHV8 negative. IL6 levels and cutaneous immunofluorescence testing were used for disease monitoring. Treatment regimens included oral steroids, rituximab, siltuximab and high-dose IVIG. Complications during treatment included pulmonary embolism. Both patients had resolution of symptoms and were disease free on repeat imaging at one-year post-treatment and remain disease-free.

Conclusion: Patient's with Castleman associated pemphigus vulgaris can acheive event free survival despite high morbidity rates. More work is needed to develop standardized care protocols for these patients.

Poster # 238

TREATMENT WITH ROMIPLOSTIM FOR CHEMOTHERAPY INDUCED THROMBOCYTOPENIA

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Background: Chemotherapy-induced thrombocytopenia (CIT) is common in pediatric patients with relapsed or refractory solid tumors who have been exposed to multiple chemotherapy agents and prior radiation therapy. The standard of care is supportive treatment with platelet transfusions, dose reductions, and treatment delays until count recovery. Thrombopoietin-receptor-agonists (TRAs) have been used in adults as an off-label therapy for CIT. The literature for the treatment of CIT in pediatric patients with solid tumors is lacking, and there are no current guidelines that include the use of TRAs.

Objectives: To describe the use of romiplostim in the management of CIT in a pediatric patient with a relapsed solid tumor.

Design/Method: Case report.

Results: An 8-year-old male with pineoblastoma was diagnosed in April 2019. His initial treatment course included surgical resection, proton beam radiation therapy, and six cycles of chemotherapy with vincristine, cisplatin, and cyclophosphamide. The patient completed chemotherapy in February 2020 but relapsed in June 2020 with several enhancing and enlarging sub-ependymal lesions on imaging. Salvage chemotherapy was initiated with bevacizumab, irinotecan, and temozolomide. Chemotherapy cycle two was delayed by two weeks due to prolonged severe thrombocytopenia with a platelet count of 18 $x10^9$/L, requiring a platelet transfusion and subsequent dose reduction in chemotherapy. To prevent further dose reductions or treatment delays, we initiated treatment with weekly subcutaneous romiplostim, starting at 2 mcg/kg and titrating every week to achieve a platelet count greater than 100 $x10^9$/L. Weekly dosing with romiplostim continued through the chemotherapy cycles, eventually reaching the maximum recommended dose of 10 mcg/kg/week. After initiation of romiplostim, the patient did not require any further platelet transfusions or dose reductions, and the platelet count nadirs after chemotherapy were less severe.

Conclusion: Previous chemotherapy and radiation therapy often result in prolonged thrombocytopenia in patients receiving salvage chemotherapy regimens. This case report outlines the use of romiplostim in a pediatric patient with a relapsed non-hematologic solid tumor to improve CIT by reducing transfusions for severe thrombocytopenia, reducing treatment delays, and avoiding further dose modifications. The use of romiplostim in adult patients receiving chemotherapy has shown reduced severe grade IV thrombocytopenia, higher median nadir platelet count, avoidance of dose reductions, and increased likelihood to receive chemotherapy on schedule. Our report aligns with previously published adult data and shows the effectiveness of romiplostim in the treatment of CIT. Further research is needed to explore the application of romiplostim to mitigate CIT in select pediatric populations and potentially improve outcomes.

Poster # 239

RESOLUTION OF MONOSOMY 7 AFTER IMMUNOSUPPRESSION IN A 12-YEAR-OLD MALE WITH SLE AND LUPUS NEPHRITIS.

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Background: Complete or partial loss of chromosome 7 is a common and well-known cytogenetic abnormality associated with pre-leukemic myelodysplasia and myeloid leukemia. Detection of this molecular change represents poor prognosis. When malignant transformation occurs, the condition tends to be chemotherapy-resistant requiring stem cell transplantation to obtain a cure. Disappearance after immunosuppressive therapy has been documented in children

with hematological disorders but not in association with systemic lupus erythematous (SLE).

Objectives: To describe the resolution of monosomy 7 in a 12-year-old male diagnosed with SLE and nephritis after treatment with cyclophosphamide (CTx).

Design/Method: Case report

Results: A 12-year-old male with SLE and nephritis previous treated with mycophenolate (1000 mg/day), oral prednisone (10 mg/day) and hydroxychloroquine (200 mg/day) was admitted to PICU due to septic shock complicated by cardiac arrest. Physical exam did not show hepatosplenomegaly or lymphadenopathy. A complete blood count (CBC) had leukocyte count of 88,000/μL with 96% neutrophils, 1% lymphocytes, 4% monocytes, hemoglobin of 9.8 g/dL and platelet count of 181,000/μL. Flow cytometry revealed changes concerning for possible myelodysplastic syndrome. A bone marrow aspirate and biopsy (BMA/Bx) showed moderate erythroid hyperplasia with prominent dyserythropoiesis and less than 10% of nucleated red cells, normocellular marrow with increased reticulin fibrosis, and no blast population. Cytogenetics analysis indicated 46, XY and monosomy 7 by FISH analysis. Due to worsening renal function, patient was started on hemodialysis and monthly CTx for 6 treatments[(dose ranged from 250-500 mg, adjusted for renal function and leukopenia). A follow up BMA/Bx 2 months after initial presentation and treatment with 3 doses of CTx was significant for normocellular marrow with trilineage hematopoiesis, mild erythroid hyperplasia, dyserythropoiesis (<10% of erythroid lineage), and adequate megakaryocytes. Cytogenetics analysis showed 46, XY and no abnormalities by FISH. BMA/Bx after completion of CTx demonstrated normocellular marrow with trilineage hematopoiesis, mild granulocytic hyperplasia, adequate megakaryocytes with no significant dysplasia or blast population. Cytogenetics, FISH, and CBC were normal. Clinically his SLE is in remission with normal blood counts. He remains on peritoneal dialysis for end stage renal disease (ESRD)

Conclusion: Monosomy 7 is associated with poor prognosis. There are few reports of spontaneous remission with only 1 report in the pediatric literature showing disappearance after immunosuppressive therapy. The mechanism by which immunosuppression is effective in the eradication of monosomy 7 clone is uncertain. More research is needed to understand the mechanism of spontaneous vs. immunosuppression induced resolution of the abnormality.

Poster # 240

TREATMENT OF REFRACTORY HYPEREOSINOPHILIC SYNDROME WITH WEEKLY VINCRISTINE

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Background: Hypereosinophilic syndrome (HES) is a group of rare disorders characterized by persistent peripheral eosinophilia $\geq$ 1.5x10^9, evidence of marked tissue eosinophilia with associated symptoms, or end organ damage related to eosinophilia (1,2,3). Subtypes of HES

include: myeloproliferative HES for which a unique genetic marker (FIP1L1-PDGFA) has been identified, chronic leukemia eosinophilia not otherwise specified, lymphocytic-variant which is associated with high levels of interleukin 5 and idiopathic.

Objectives: To demonstrate the effectiveness of weekly vincristine in treatment of idiopathic HES refractory to standard therapies.

Design/Method: 12 year old male with 3 weeks of abdominal pain, nausea, vomiting, diarrhea and 13 pound weight loss. Found to have an absolute eosinophil count of 56,900. Admitted to the pediatric intensive care unit secondary to restrictive cardiomyopathy from eosinophilic infiltrate. Bone marrow aspirate and biopsy did not demonstrate underlying malignancy or known genetic abnormality (FIP1L1-PDGFA fusion gene) associated with HES, and IL-5 levels were not elevated. Infectious workup for both parasitic, viral and fungal etiologies were negative as was evaluation of gastrointestinal disease. Solumedrol was started with a good initial response. However, this was not sustained and hydroxyurea and vincristine were then added. A decrease in the AEC of 10,000/mm^3 was noted within hours of starting vincristine. At the time of discharge the AEC continued to decrease. Vincristine was continued for six weeks along with daily hydroxurea. Steroid dosing was decreased gradually to 10 mg daily for treatment of the restrictive cardiomyopathy. The AEC was consistently less than 3,000/mm^3 at 6 weeks and vincristine was stopped.

Results: Patient was noted to have an increasing AEC following admission for treatment of biventricular thrombi. Mepolizumab a monoclonal AB directed at IL-5 was administered with minimal response. Therefore, vincristine therapy was reinitiated and again the patient responded. Since restarting weekly vincristine hydroxyurea has been stopped and the AEC remains below 5,000/mm^3. In an attempt to identify a cause and definitive treatment we are currently exploring whole exome sequencing and hematopoietic stem cell transplant.

Conclusion: Vincristine has been used in the treatment of HES as it has been shown to rapidly decrease the AEC. Furthermore, it has been proposed as a treatment of pediatric hypereosinophilic syndrome for children that have refractory disease (5) as is the case in this patient. In conclusion weekly vincristine treatment has shown to be a viable treatment of treatment refractory hypereosinophilic syndrome.

Poster # 241

BRENTUXIMAB VEDOTIN RELATED PERIPHERL NEUROPATHY ASSOCIATED TO UGT1A1*28 GENE MUTATION

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Background: Brentuximab vedotin (Bv) is an antibody-drug conjugate (ADC) used for the treatment of Hodgkin and ALK positive lymphoma. One of Bv's most notorious toxicities is peripheral neuropathy. Patients with Gilbert syndrome (GS) are known to have a genetic variant

of UGT1A1 containing seven thymine-adenine repeats (UGT1A1*28), versus six in the wild type allele. It is known that patients with GS have reduced enzyme activity and decreased drug glucuronidation of SN-38, the active metabolite of irinotecan, and experience greater risk of toxicity.

Objectives: To present a patient that received Bv for treatment of Hodgkin lymphoma, developed jaundice and grade 3 peripheral neuropathy and was found to have UGT1A1 mutation.

Design/Method: Case report.

Results: A 16-year-old female had stage IIB Hodgkin lymphoma was treated with ABVE-PC and radiation therapy but experience early relapse. Retrieval therapy with 2 cycles of gemcitabine and vinorelbine followed by high dose chemotherapy and autologous stem cell transplantation. During the transplant period she experienced hyperbilirubinemia, which was considered transplant related toxicity and resolved with ursodiol. She then received post-transplant consolidative Bv at 1.8 mg/kg every three weeks. After receiving 12 of the planned 16 Bv doses the patient reported severe sensorial and motor neuropathy with the inability to grab utensils and walk unassisted. She required a wheel chair for ambulation. Bv treatment was terminated and her neuropathy recovered progressively over 16 weeks. During Bv treatment, liver enzymes, protein/albumin, and creatinine remained within normal parameters. She did not experience neutropenia or thrombocytopenia . After completion of therapy and while off all home medications she was noted to have intermittent indirect hyperbilirubinemia without hemolysis. Upon further discussion the patient reported that a few days after Bv treatments her scleras would turn yellow. This clinical finding prompted testing for Gilbert syndrome. This patient was found to have a homozygous pattern of the UGT1A1*28 allele confirming GS.

Conclusion: To the best of our knowledge, the relationship of impaired glucuronidation due to the homozygosity of UGT1A1*28 and Bv related neuropathy has not been described. We speculate that monomethyl auristatin E (MMAE) elimination may be UGT1A1 dependent leading to hyperbilirubinemia and increased Bv toxicity in the presence of the UGT1A1*28 allele, similar to what has been described in the elimination of the SN-38 metabolite. This is of significance since current recommendation is to omit Bv in the setting of hyperbilirubinemia.

Poster # 242

LYNCH SYNDROME WITH A NOVEL MUTATION IN A 10-YEAR-OLD BOY

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Background: Colorectal cancer (CRC) is rare in the pediatric population and when diagnosed is often due to a sporadic mutation. Lynch syndrome (LS) is an inherited cancer syndrome which occurs due to a germline mutation in DNA mismatch repair genes. Presently, there is a limited amount of published data on appropriate management for children diagnosed with CRC, let alone

in the setting of LS.

Objectives: This case report is meant to describe a novel LS mutation including its clinical presentation and course as well as to outline the therapeutic measures taken and the screening schedule developed for the affected patient.

Design/Method: Case Report

Results: We present a previously healthy 10-year-old male who presented with 2 weeks of abdominal pain, vomiting, constipation and anemia with a hemoglobin of 10.2 g/dL. An exploratory laparotomy with planned sigmoidectomy and primary anastomosis revealed adenocarcinoma of the colon. This was staged at T3N0M0. Immunohistochemistry testing of the specimen showed loss of nuclear expression of mismatch repair proteins MSH2 and MSH6. A germline mutation was discovered in the MSH2 gene which consisted of a gross duplication spanning coding exon 2 through 3 (MSH2 Ex2_3dup). Presence of this mutation was originally deemed a variant of unknown significance. However, additional RNA analysis reclassified the mutation to a likely pathogenic variant confirming the diagnosis of LS for the patient.

The patient underwent a total abdominal colectomy with ileorectal anastomosis. A screening schedule was developed for the patient partly based off of the National Comprehensive Cancer Network (NCCN) guidelines for management of Lynch syndrome. The patient was seen every three months for the first two years. A CBC with differential and CEA were performed at each visit. Alternating abdominal ultrasound and CT of the chest/abdomen/pelvis were done every three months. In addition, the patient will continue to be screened with rectoscope every 1-2 years, EGD with duodenoscopy every 3-5 years as well as UA, neurological exam and dermatological exam annually. He has been followed for two years since diagnosis according to screening guidelines outlined above with no findings concerning for recurrence or metastasis of disease.

Conclusion: This case reports a novel sequence alteration in exons 2-3 of the MSH2 gene classified as a likely pathogenic variant of LS. It additionally demonstrates the multidisciplinary effort necessary to manage a pediatric patient diagnosed with LS and outlines an effective screening schedule developed for the patient.

Poster # 243

INSULIN INFUSION FOR TREATMENT OF ASPARAGINASE-ASSOCIATED PANCREATITIS WITH HYPERTRIGLYCERIDEMIA

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Background: Asparaginase (ASN) is an important component of acute lymphoblastic leukemia (ALL) treatment. ASN-associated pancreatitis (AAP) is reported in approximately 10% of patients. Severe AAP can lead to long-term complications and discontinuation of ASN is linked

to inferior outcomes. AAP has a multifactorial pathophysiology and is sometimes associated with hypertriglyceridemia (HTG) from ASN-induced inhibition of lipoprotein lipase (LPL). Insulin activates LPL and has been used to treat ASN-induced HTG. We hypothesize that insulin can be used for severe AAP with HTG to mitigate complications of AAP.

Objectives: We describe the clinical course of three patients with AAP (Grade 3) with HTG (Grade 4) treated with insulin infusion.

Design/Method: We reviewed charts of three patients treated at our institution for AAP from October 2019-June 2020.

Results: Patients presented with severe abdominal pain not relieved by oral opioid.

15-year-old Hispanic male with B-ALL, consolidation phase of chemotherapy. One prior dose of ASN, 10 doses Erwinia chrysanthemi (ASN hypersensitivity). Nine days after starting Erwinia course, presented with elevated lipase (2923 U/L) and TG (2420 mg/dL). Received insulin infusion at 0.1 U/kg/hr for 17 hours with 10-fold decrease in TG, decline in lipase, and symptom resolution during seven-day hospitalization. Radiographic findings of pancreatic tail necrosis before insulin initiation resolved on imaging 10 weeks post-admission.

14-year-old white, non-Hispanic female with B-ALL, consolidation phase of chemotherapy. Two prior doses of ASN; 23 days following last dose, presented with elevated lipase (180 U/L) and TG (4631 mg/dL). Received insulin infusion at 0.05 U/kg/hr for 45 hours with 10-fold decrease in TG, decline in lipase, and symptom resolution during eight-day hospitalization. Radiographic findings of peripancreatic edema before insulin initiation resolved on imaging 3 weeks post-admission.

14-year-old white, non-Hispanic male with T-ALL, interim maintenance phase of chemotherapy. Three prior doses of ASN; 13 days following last dose, presented with elevated lipase (738 U/L) and TG (4890 mg/dL). Received insulin infusion at 0.1 U/kg/hr for 82 hours with 9.3-fold decrease in TG, decline in lipase, and symptom resolution during ten-day hospitalization. Radiographic findings of peripancreatic fluid collection resolved on imaging 10 weeks post-admission.

No patient developed recurrent pancreatitis or HTG. Future ASN was discontinued. Patients are receiving maintenance chemotherapy without leukemia relapse.

Conclusion: Insulin infusion was used to successfully treat three patients with severe AAP and associated HTG. We are currently reviewing a larger patient cohort to compare insulin infusion to supportive management alone and determine whether prospective studies of this intervention are warranted.

Poster # 244

HUGHES-STOVIN SYNDROME AND FANCA GENE DELETION: A RARE AND UNCONVENTIONAL CASE

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Background: Hughes-Stovin syndrome, a variant of Behcets Disease, is a rare autoimmune condition with a high mortality rate. Diagnosis includes a combination of thrombophlebitis and pulmonary or bronchial aneurysms in a patient who does not meet full diagnostic criteria for Behcets Disease. We report the initial evaluation, symptoms, and treatment course of an 18-year-old female with a new diagnosis of Hughes-Stovin Syndrome.

Objectives: To present a rare disorder and the decision to treat in an unconventional way

Design/Method: A case report

Results: At 18 years old, our patient presented with worsening chest pain, shortness of breath, intermittent fevers, and flank pain two weeks after initiating warfarin therapy for bilateral pulmonary emboli. Computed Tomography Angiography (CTA) showed extensive pulmonary emboli, massive venous thrombi involving the inferior vena cava (IVC) and bilateral renal veins, and substantial inflammatory changes surrounding the IVC. Warfarin therapy was switched to a continuous heparin infusion to prevent worsening thrombi. Evaluation for malignancy (including bone marrow biopsy and aspirate), autoimmune disorders, and inherited thrombophilia (including antiphospholipid syndrome) were normal. Chest CTA demonstrated multiple bilateral pulmonary aneurysms. Further history revealed recurrent oral ulcers and a single episode of genitourinary ulcers, leading to a diagnosis of incomplete Behcets Disease, Hughes-Stovin variant. She was started on high dose methylprednisolone and cyclophosphamide to induce remission. Heparin was discontinued given the risk of bleeding from the pulmonary aneurysms, which is the most common cause of death in Hughes-Stovin Syndrome. After the second dose of cyclophosphamide, the genetic evaluation from her bone marrow returned revealing a heterozygous deletion of FANCA. Due to concern for possible Fanconi anemia and increased sensitivity of cells with FANCA mutations to DNA interstrand cross-linking agents, her treatment plan for Hughes-Stovin was altered to exclude further cyclophosphamide and azathioprine. Treatment continued with monthly infliximab for induction and low-dose methotrexate maintenance. Repeat CTA three months after infliximab initiation showed resolution of all pulmonary artery aneurysms.

Conclusion: We present a case of an 18-year-old female with newly diagnosed Hughes-Stovin Syndrome, a rare variant of Behcets Disease. Genetic evaluation revealed heterozygosity of the FANCA gene. Despite normal fibroblast breakage studies, conventional treatment with cyclophosphamide and azathioprine was abandoned due to the potential risk of secondary malignancy. Remission was achieved with infliximab, and at the time of the report, maintained with infliximab and methotrexate at six months.

Poster # 245

DEXTROMETHORPHAN ROLE IN THE FIRST TWENTY-FOUR HOURS OF METHOTREXATE-INDUCED-NEUROTOXICITY

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Background: Approximately five to twenty percent of patients after administration of high dose IV or intrathecal MTX can develop methotrexate (MTX) toxicity which is inevitable in the treatment of Acute Lymphocytic Leukemia (ALL) in children. Classification is determined by the onset of symptoms from the last MTX dose: acute, subacute, and chronic.
Methotrexate is a folic antagonist that inhibits dihydrofolate reductase which results in disruption of the conversion of folic acid to tetrahydrofolic acid.
This in turn causes impaired myelinization. Dextromethorphan is a non-competitive NMDA receptor antagonist and can aid in the treatment of MTX induced-neurotoxicity.

Objectives: To discuss the presentation, workup, and treatment of methotrexate-induced-neurotoxicity with dextromethorphan.

Design/Method: A single-study case report.

Results: Case Presentation: A seventeen-year-old male previously diagnosed with T-cell Lymphoma presented to the hospital five days after his last chemotherapy administration of Asparaginase and intravenous methotrexate. He also received IT (intrathecal) MTX seven days before the presentation. His symptoms were acute and involved right-sided weakness and facial droop, slurring of speech, nausea, and dizziness. Non-contrast CT and angiogram of the brain were initially performed and showed no evidence of thrombus or hemorrhage, however, the scans demonstrated mild enlargement of the ventricles, left more than the right side. Admission MRI without contrast revealed a focal area of restricted diffusion with corresponding low apparent diffusion coefficient within the left coronary radiata without flair hyperintensity or susceptibility artifact. Repeat MRI with contrast, eight hours later revealed a new area of restricted diffusion within the right corona radiata. These mild T-2 signal hyperintensity lesions are associated with methotrexate-induced encephalopathy.
This patient received dextromethorphan and leucovorin in the first twenty-four hours of treatment.
Dextromethorphan dose was 1-2 mg/kg. Aminophylline and dexamethasone were added after twenty-four hours of treatment.
There was a significant improvement in aphasia after the initial dose of dextromethorphan and the patient had complete resolution of symptoms after thirty-six hours of treatment.

Conclusion: This case report presents an example of the successful treatment of methotrexate-induced-neurotoxicity with dextromethorphan. The results of this case are comparable to previous reports with the improvement of symptoms by four-fold compared with patients who had delayed or no treatment with dextromethorphan. Also, an NMDA antagonist improves overall cognition in symptomatic patients. This case study supports the idea that dextromethorphan should be attempted in methotrexate-induced-neurotoxicity.

Poster # 246

UNCOMMON PEDIATRIC NON-HODGKIN'S LYMPHOMA: A CASE SERIES AND LITERATURE REVIEW

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Background: While pediatric lymphoma is generally well-studied, several uncommon subtypes of non-Hodgkin's lymphoma lack reliable, large-scale data due to their infrequency. These rarer subtypes comprise 5-10% of all pediatric lymphoma and include follicular lymphoma, cutaneous B-cell lymphoma, MALT lymphoma, nodal marginal zone lymphoma, primary mediastinal lymphoma, and hepatosplenic lymphoma, and peripheral T-cell lymphoma.

Objectives: Analyze cases of uncommon pediatric lymphoma at Nationwide Children's Hospital over 23 years in the context of existing literature to guide future research and evidence-based recommendations for patient treatment and surveillance.

Design/Method: Retrospective cohort study including chart and pathologic review of all cases of rare pediatric non-Hodgkin's lymphomas at Nationwide Children's Hospital over the past 23 years as well as a literature review on each subtype.

Results: Twenty cases of rare non-Hodgkin's lymphoma were discovered over a 20-year period at Nationwide Children's Hospital. Seven patients were treated with observation alone, four with surgical resection alone, and three with only topical skin therapy. Rates of chemotherapy, radiation, immunotherapy, and bone marrow transplant were much lower than in other types of pediatric malignancies. 55% of patients (11/20) achieved long-term remission with initial therapy, 15% (3/20) had isolated cutaneous recurrence, and 30% (6/20) had disease progression or recurrence and required increased therapy. Ten percent (2/20) of patients died, both of whom were diagnosed with peripheral T-cell lymphoma and treated with chemotherapy. Overall, these patients demonstrated a 90% survival rate, with 100% 5-year survival in all cases of marginal zone, cutaneous, follicular, and MALT lymphomas as well as mycosis fungoides.

Conclusion: Pediatric non-Hodgkin's lymphoma is a diverse group of heterogenous malignancies with widely variable incidence, clinical presentation, effective therapy, and outcomes. Rare subtypes of pediatric non-Hodgkin's lymphoma are vastly different from their adult counterparts and, with the exception of peripheral T-cell lymphoma, typically carry favorable prognoses even with conservative therapy. We hope that this clinical and pathological review aids pediatric oncologists in diagnosing and treating these rare entities.

Poster # 247

CHILDHOOD CANCER IN A TWIN SIBLINGS IN A REFERRAL CANCER CENTER IN CENTRAL CALIFORNIA

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Background: The causes of most childhood cancer remain elusive; some children clearly have a genetic predisposition, but in the majority the relative contributions of environmental and host factors are not established. The higher frequency of multiple pregnancies with assisted fertilization techniques may play a role in the future development of malignancies. It is known that the risk for cancer increases if a person has a relative who developed cancer. This risk is even higher in twin siblings. The lifetime familial risk of cancer for those whose co-twins were also diagnosed with cancer is reported to be 37% among fraternal twins and 46% among identical twins.

Objectives: To determine the incidence of twin siblings among children diagnosed with cancer at Valley Children's Hospital, and to determine the concordance rates for childhood cancer in twins.

Design/Method: Retrospective Review. Childhood cancers through age 21 diagnosed at Valley Children's Hospital from 2003 - 2020 were identified and those with twin sibling were identified.

Results: Over a 17 year period, 1,950 new cancer diagnosis were reported at Valley Children's Hospital; of those 29 patients were found to have a twin sibling, for an incidence of 1.5% among all pediatric malignancies. The average age at diagnosis was 7.8 years (range 0.6 – 17 years, median 13 years). 15 males and 14 females. The majority, 27/29 were same-sex twins of those 6 were dizygotic twins, 23 were monozygotic twins. Information on assisted fertilization type was not available. We found 34.5% (10/29) leukemia, 17% (5/29) lymphomas, 10% (3/29) brain tumors and 38% (11/29) solid tumors. Only on set of monozygotic twin pair developed concordant leukemia. They were diagnosed 9 months apart. The rate of concordant malignancies in our review was 3.4% among all malignancies in twins siblings. Patients have been followed from 6 – 15 years and none of the other twins have developed cancer.

Conclusion: Large and prospective studies of twins with cancer can provide further insight into the relative contribution of environmental factors in cancer development. Large population studies require linkage of birth registries and cancer registries.

Poster # 248

COMPLETE RESPONSE OF THERAPY RELATED MYELODYSPLASTIC SYNDROME TO ALISERTIB

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Background: Therapy related myelodysplastic syndrome (tMDS) is a secondary malignancy after treatment of a primary oncologic process. Prevalence is 5-11% after pediatric solid tumor therapy. Treatment guidelines focus on induction chemotherapy for cytoreduction and subsequent allogeneic hematopoietic stem cell transplant. Overall survival for tMDS is dismal. Atypical teratoid rhabdoid tumor (ATRT) is a highly aggressive class of CNS embryonal tumors. Treatment with surgery, chemotherapy and radiation is standard and may be associated with tMDS. Alisertib is an Aurora A Kinase inhibitor in phase II clinical trials used in the treatment of ATRT, now investigated for tMDS as well as AML.

Objectives: We report a 3 y/o female patient with tMDS after undergoing treatment for ATRT, with complete response to alisertib therapy.

Design/Method: Case study.

Results: Patient is a 3 y/o female, diagnosed with a posterior fossa ATRT and leptomeningeal spinal disease. Diagnosis was at 12 months of age after 2 weeks of progressive ataxia, lethargy and emesis. MRI showed a posterior fossa tumor without metastasis. A gross surgical resection was performed. Molecular testing confirmed a SMARCB1 mutation in tumor tissue and did not show germline mutation. Cytology on LP displayed tumor cells. She achieved complete remission after treatment as per the Dana Farber ATRT regimen and proton radiation. On re-evaluation 9 months off of therapy, new spinal lesions with leptomeningeal coating were observed. Intrathecal thiotepa/etoposide/topotecan via an Ommaya reservoir was started along with alisertib, as well as metronomic chemotherapy. Follow up bone marrow aspiration for prolonged thrombocytopenia showed MDS with excess blasts, 3.4% on flow cytometry. Cytogenetic studies showed t(11,16)(q23;p13.3) confirming tMDS. She underwent two rounds of 5-azacytidine treatment at 75mg/m^2/day x 7 days, after which bone marrow aspirate showed 0.1% residual blasts but 86% r-MLL/11q23 by FISH. Alisertib was re-started for recurrent spinal lesions, 3 cycles 40 mg/m^2/day x 7 days q21 days. Subsequent bone marrow aspirate showed an MRD down to 0%, and no r-MLL/11q23 rearrangement identified on FISH. There was a progressive improvement in blood counts with resolution of cytopenia and transfusions, with no major side effects.

Conclusion: Alisertib has been investigated for the treatment of ATRT, targeting propagation of the cell cycle. Response of tMDS to chemotherapy has been poor. We report a case of tMDS with complete response to alisertib. This could pose as a novel treatment in the arsenal against tMDS, improving morbidity and mortality. Further investigation is warranted.

Poster # 249

PEDIATRIC REFRACTORY SECONDARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS TREATED WITH EMAPALUMAB

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Background: Hemophagocytic lymphohistiocytosis (HLH) is a severe, life-threatening syndrome characterized by excessive immune activation, hyperinflammation, and end-organ failure amongst other diagnostic criteria. Primary HLH arises in patients with a genetic predisposition. Secondary HLH (sHLH) occurs as a result of inflammation-inducing events such as severe infection, malignancy, or rheumatologic conditions.

Objectives: Standard HLH therapy with dexamethasone and etoposide was established in 1994. However, it is associated with frequent treatment failure and significant toxicity, contributing to the high mortality rate of HLH. Emapalumab, an anti-interferon gamma (IFNγ) monoclonal antibody, is a novel targeted therapy approved for primary HLH with refractory, recurrent, or progressive disease. No such therapy exists for sHLH.

Design/Method: We describe a pediatric patient with refractory sHLH successfully treated with emapalumab. A 12-year-old male with Philadelphia chromosome (Ph+) pre-B acute lymphocytic leukemia (ALL) in remission with ongoing maintenance therapy presented with *Klebsiella pneumoniae* sepsis. He was critically ill with complications including pancytopenia with severe neutropenia, septic shock, acute respiratory distress syndrome with respiratory failure, acute renal failure, and invasive fungal disease. He met criteria for HLH and began dexamethasone and etoposide. After three weeks of standard therapy, he remained clinically unstable with persistent cytopenias and rising inflammatory markers. Salvage treatment with emapalumab was initiated, with escalation to full dose over 11 days.

Results: Emapalumab therapy resulted in an astonishing complete recovery with no evidence of sHLH to date without need for stem cell transplant. Emapalumab was later successfully weaned following a duration of approximately 12 weeks of therapy.

Conclusion: This is the first report of successful use of emapalumab in refractory sHLH and serves as an encouraging rationale for future applications of the novel agent in a broader patient population with potential for improved outcomes in this devastating, rapidly progressive disease.

Poster # 250

INCIDENTAL DIAGNOSIS OF CHRONIC MYELOID LEUKEMIA IN CHRONIC PHASE IN A PREVIOUSLY-HEALTHY 3 YEAR-OLD

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Background: Chronic myeloid leukemia (CML) is rare in children, encompassing less than 3% of pediatric leukemias (1). Many treatment guidelines are based on adult patient data as studies of CML in children are often limited in size. With a younger age at diagnosis, children may require years of treatment with tyrosine kinase inhibitors (TKIs) and monitoring for long-term side effects.

Objectives: Report a case of incidental diagnosis of CML in chronic phase in a previously-healthy 3 year-old male with leukocytosis. Demonstrate features of a rare pediatric leukemia, especially in this younger age group in which incidence is reported at 0.1 per 100 000 (2). Discuss treatment initiation and long-term monitoring of TKI side effects in a growing child.

Design/Method: Case report

Results: The child was seen in his pediatrician's office for follow up of anemia diagnosed almost 4 months prior. The new CBC was notable for WBC 117 K/mm3, hemoglobin 9.3 g/dL, and platelet count 300 K/mm3. Viral infectious workup was negative. Myelodysplastic syndrome extended panel was normal. Bone marrow flow cytometry showed a small population of CD7+ abnormal myeloblasts. Bone marrow biopsy revealed hypercellular left shifted trilineal hematopoiesis. Scattered small megakaryocytes and pseudo-Gaucher cells were noted. Peripheral blood BCR/ABL1/ASS1 FISH analysis detected t(9;22) BCR-ABL1 fusion. RT-PCR for BCR-ABL was positive for p210 transcript, 49.5% per international scale. Baseline thyroid studies, complete metabolic panel, and echocardiography prior to treatment initiation were within normal. Our patient was started on imatinib 300 mg/m2 daily. Nasogastric tube was placed as a temporary measure for antineoplastic agent administration because the patient refused to swallow oral medication in any form. Multidisciplinary efforts with nursing and child life specialists while inpatient provided the patient with tools to practice swallowing pills at home.

Conclusion: This case demonstrates potential presentations of pediatric CML, options for treatment administration, and unique social challenges in the diagnosis of childhood malignancy. For our patient, parental circumstances and his subsequent foster care placement delayed follow up of his initial anemia diagnosis. However, the regular medical care required by foster care helped facilitate an earlier CML diagnosis. Our patient will continue to be evaluated for medication-related toxicities and molecular and cytogenetic response, according to the Children's Oncology Group CML Working Group 2019 recommendations with attention to new guidelines.

1. Hijiya et al, Blood, 2016.
2. Surveillance Research Program, National Cancer Institute, available from https://seer.cancer.gov/explorer.

Poster # 251

A NOVEL ETV-6 VARIANT WITH THROMBOCYTOPENIA, NEUROBEHAVIORAL DISORDER, ESOPHAGITIS, AND ALLERGIES

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Background: The ETV6 gene encodes a transcriptional repressor of the ETS family that is essential for hematopoiesis. Germline pathogenic variants of ETV6 are responsible for chronic

thrombocytopenia and predisposition to hematologic malignancies such as acute lymphoblastic leukemia. Clinical presentation is variable and the extent of the clinical spectrum of ETV6-related disorders has not been well described. As research efforts are largely focused on understanding the role of ETV6 in hematopoiesis and oncogenesis, limited knowledge is available regarding ETV6 in the development of other systems such as the brain and its role in neurodevelopment. READ1 and ETV6 interaction have been described.

Objectives: To describe the clinical phenotype of a patient with a novel ETV6 pathogenic variant.

Design/Method: Case report.

Results: A 6-year-old boy with chronic thrombocytopenia was found to have the previously unreported c.1075_1086dup12:p.Arg359_Asp362dup *de-novo* pathogenic variant in ETV6 through whole exome sequencing family trio analysis. This variant is located in the critical and highly conserved ETS domain in exon-6 of the ETV6 gene (NM_001987.4). This variant has not been observed in population databases. Other genetic investigations included chromosome microarray, Fragile-X syndrome, and mitochondrial genome analysis. These studies were normal. Bone marrow biopsy was hypocellular (40%) and without evidence of malignancy. Additional clinical features included expressive language disorder, developmental delays, and multiple behavioral challenges. The patient also has severe food allergies, atopic dermatitis, allergic rhinitis, eosinophilic esophagitis, and distinctive facial features.

Conclusion: Germline pathogenic variants in ETV6 are consistently associated with thrombocytopenia and a predisposition to malignancy; however, other phenotypic associations are not well described. Prior case series of patients with ETV6 germline mutations have included patients with reading disability and with gastroesophageal reflux disease (suggestive of eosinophilic esophagitis). The ETV6 gene encodes a transcriptional repressor of the ETS family. The ETV6 protein is found in the nucleus of most cell types including brain cells, and it plays a key role in fetal development. ETV6 is essential for hematopoiesis and is involved in immune regulation, including interleukin-18 (IL-18), IL-10, and IL-4, cytokines involved in the clonal expansion of TH1 and TH2 subsets of CD4+ helper-T cells. Moreover, ETV6 and READ1 interaction has been studied and proposed as a regulator in language and reading development. Taken together, these findings suggest that our patient's distinct phenotype, with significant language disorder, severe atopy, and eosinophilic esophagitis, may be explained by this *de-novo* ETV6 pathogenic variant.

(AKM and WBF are employees of GeneDx, Inc.; GeneDx provided no financial support.)

Poster # 252

NOT SO "SWEET" - CASE OF SWEET SYNDROME IN PATIENT WITH MDS WITH EXCESSIVE BLASTS

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Background: Myelodysplastic Syndrome (MDS) is a group of disorders characterized by abnormal myeloid maturation resulting in peripheral cytopenia and bone marrow dysplasia. MDS with excess blasts (MDS-EB) is defined as the presence of 5-19% of blasts in the peripheral blood or bone marrow and may progress to AML, defined as a blast percentage >20%. Treatment options include chemotherapy, targeted drug therapy, and bone marrow transplant.

Sweet Syndrome (SS) is a rare inflammatory skin condition that can be secondary to chemotherapy or the underlying malignancy. SS is associated with AML and MDS in adults, however, is particularly rare in children. The pathophysiology is thought to include hypersensitivity reactions, cytokine dysregulation especially G-CSF and genetic susceptibility to the disease process. Major diagnostic criteria include abrupt onset of painful erythematous plaques/nodules and histopathologic evidence of sterile neutrophilic panniculitis. Minor criteria include excellent response to steroids, underlying malignancy and three of the following: ESR >20 mm/hr, CRP, >8,000 leukocytes and >70 percent neutrophils.

Objectives: We describe a case of a 4-year-old male with SS associated with MDS-EB undergoing chemotherapy.

Design/Method: Case report/literature review.

Results: Patient had previously failed therapy with Azacytidine now admitted for bridge chemotherapy with cytarabine and Erwinia L-asparaginase as per modified AAML1031. Despite morphine, pain associated with these lesions worsened, hindering ambulation. He had similar nodules during previous induction cycles starting around his ANC nadir. A biopsy showed patchy predominant lobular neutrophilic panniculitis and focal neutrophilic folliculitis without malignant infiltration. Laboratory remarkable for ESR 67, CRP 302, ferritin 1,398. These findings and the patient's clinical presentation course supported the clinical diagnosis of SS. Given his immunosuppressive status, steroid treatment was deferred. He was treated with ketorolac and supportive care, and the lesions and pain gradually improved as his ANC counts recovered with a similar pattern to prior cycles.

Conclusion: This atypical presentation of SS presents the first case report of a pediatric patient with SS secondary to MDS-EB. An abnormal response in this patient's endogenous G-CSF production for promoting bone marrow recovery is proposed to be the trigger that led to development of SS. This response observed with anti-inflammatory treatment poses the possibility of considering this treatment as an alternative for pain control during the peak of immunosuppressive state while undergoing chemotherapy.

Poster # 253

CHICKEN OR EGG: MYELOFIBROSIS ON ROMIPLOSTIM IN A PEDIATRIC PATIENT WITH MYH9-RELATED DISEASE

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Background: Individuals with myosin heavy chain 9-related disease (MYH9-RD) typically display a mild-moderate macrothrombocytopenia. Rarely, patients have severe thrombocytopenia and bleeding symptoms, requiring medical intervention. Thrombopoietin receptor agonists (TPO-RA) are used with great success to treat immune and non-immune thrombocytopenias. A rare complication is myelofibrosis, reported mainly in older adults on a TPO-RA for >2 years. There is little data on the risk of myelofibrosis in MYH9-RD, neither at baseline nor on TPO-RA treatment. We report the first case of a pediatric patient with MYH9-RD on romiplostim treatment for <1 year who developed moderate bone marrow fibrosis.

Objectives: Describe a treatment-related complication of romiplostim in MYH9-related disease.

Design/Method: Case report.

Results: A 14-year-old boy with MYH9-RD had longstanding severe macrothrombocytopenia ranging from 5-20 (10^9 cells/L) and frequent mucocutaneous bleeding. Secondary to decreased quality of life, the family opted to try a TPO-RA. He began romiplostim (1 mcg/kg/week) and eventually stabilized at 7 mcg/kg/week with sustained platelet counts 50-200 (10^9 cells /L). He experienced no adverse symptoms. In anticipation of remaining on romiplostim long-term, he underwent bone marrow examination after <1 year on romiplostim to provide a baseline for future surveillance. His marrow was hypocellular (60%) with moderate reticulin fibrosis (MF-2). Therefore, Romiplostim was discontinued, resulting in a return of his platelet count to a baseline of ~5 (10^9 cells/L).

Conclusion: We describe a 14-year-old boy with MYH9-RD with an appropriate response to romiplostim but who developed moderate bone marrow fibrosis on <1 year of therapy. Development of myelofibrosis associated with TPO-RA is rare in pediatric patients but is reported in adult patients with immune thrombocytopenia. Most had MF-1, and only one patient had MF-2 marrow. Consideration must be given to those who may be at increased risk of myelofibrosis in pre-clinical models. MYH9-deficient mice treated with romiplostim can develop myelofibrosis. Furthermore, it is unknown if patients with MYH9-RD are at increased risk of some myelofibrosis at baseline, as they do not typically get bone marrow surveillance. There is one published report of an untreated adult female with MYH9-RD with an MF-2 marrow.

Our case highlights either the development of TPO-RA-related myelofibrosis in a patient with MYH9-RD or a previously unknown risk of myelofibrosis at baseline. This raises whether a bone marrow exam is warranted for patients with MYH9-RD before initiating treatment with a TPO-RA and whether those on a TPO-RA should undergo more frequent surveillance.

Poster # 254

A UNIQUE CASE OF JUVENILE MYELOMONOCYTIC LEUKEMIA IN PATIENT WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Juvenile myelomonocytic leukemia (JMML) is a rare and aggressive myeloproliferative disorder of childhood. Gene mutations are involved in the activation of the RAS/MAPK signaling pathway. This is a case of a nine-month-old male initially diagnosed with infantile B cell acute lymphoblastic leukemia (ALL), who developed JMML about two months after induction.

Objectives: The objective of this case report is to highlight a unique presentation of JMML in a child with a confirmed diagnosis of ALL demonstrating the often difficult to establish diagnosis of JMML. There have been case reports initially thought to be ALL, thus delaying diagnosis of JMML. However, this is the first reported case of ALL and JMML found in the same patient.

Design/Method: Case report developed from chart review of patient's electronic medical record.

Results: This patient was initially diagnosed with infantile B-ALL. Bone marrow flow cytometry revealed CD19+, CD22+, CD10+, TdT+ B lymphoblasts consistent with B-Cell ALL. Cytogenetic and molecular diagnostics showed CDKN2A (p16) deletion, loss of ETV6, and trisomy 10. No MLL gene rearrangement was identified. He was induced per protocol AALL15P1 with no evidence of minimal residual disease at end of induction (EOI). However, EOI bone marrow biopsy pathology later returned with features suggesting monocytic leukemia. Repeat bone marrow biopsy did not show definitive evidence of neoplasm, thus he underwent induction intensification therapy. After count recovery, he had persistently rising leukocytosis prompting evaluation for JMML. Initial evaluation included a limited MPN/JMML NGS mutation panel and repeat bone marrow biopsy and aspirate, which were suspicious for JMML but non-diagnostic. Further evaluation with a more comprehensive NGS panel revealed a defining mutation in the RAS/MAPK pathway. He ultimately met all criteria for JMML with the absence of BCR-ABL1 fusion gene, monocytosis, <20% blasts in peripheral blood and bone marrow, splenomegaly, and a KRAS A146T mutation. As he was symptomatic from the leukocytosis, he was induced in order to bridge him to a bone marrow transplant. Currently, he remains well in morphologic remission, 3 years post-transplant.

Conclusion: JMML remains an interesting disease with its rarity and variable presentation. Other case reports discuss JMML presenting with symptoms of extramedullary involvement or with initial diagnoses of viral infections, hemophagocytic lymphohistiocytosis, or presumed ALL. This case of ALL and JMML in the same patient adds to the variability in presentation and raises awareness to maintain a high clinical suspicion for JMML.

Poster # 255

DELAYED MARROW ENGRAFTMENT AS AN ATYPICAL PRESENTATION OF HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

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Background: Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening hyperinflammatory syndrome that results from impaired cytotoxic T and NK cell activity producing uncontrolled macrophage activation. HLH can occur primarily from genetic causes or secondarily as a complication of viral infection or chemotherapy.

Objectives: We herein describe the case of a patient who experienced delayed engraftment following a second tandem autologous SCT that failed to respond to a stem cell boost.

Design/Method: Clinical history was extracted retrospectively from medical records.

Results: The patient is a 10-year-old Caucasian female who underwent a second tandem autologous stem cell transplant (SCT) for high-risk neuroblastoma following CEM conditioning. The stem cell dose administered was 9.6 x 10^6 CD34 cells/kg. The patient developed severe mucositis and glossitis, and had HSV1 reactivation and HHV-6 viremia. She experienced delayed neutrophil engraftment and a stem cell boost was administered on Day +29. Patient continued to be pancytopenic after the boost and was noted to have fever, hyperbilirubinemia, coagulopathy, and marked non-tender hepatomegaly.

A bone marrow biopsy performed on Day +56 showed marrow aplasia and hemophagocytosis, which led to the suspected diagnosis of HLH. While the patient had elevated ferritin and triglyceride levels, these predated the diagnosis of HLH and were attributed to iron overload and lipid infusion. While coagulopathy with hypofibrinogenemia is common with HLH, our patient had a prolonged prothrombin time from factor VII deficiency with normal fibrinogen levels. sIL2R and CD163, a marker of macrophage activation, however, were both elevated, consistent with the diagnosis of HLH. The above atypical presentation was what initially led to delayed diagnosis of this entity.

Treatment of HLH was instituted on Day +57 with high-dose i.v. dexamethasone 10 mg/m2/day. high dose i.v. anakinra 8 mg/kg/day and IVIG 2 g/kg every 2 weeks. Etoposide was withheld because of liver dysfunction and concern for marrow suppression. Our patient's fever, hepatomegaly, liver dysfunction and coagulopathy responded promptly to treatment. A second stem cell boost was given on Day +66. Neutrophil engraftment was achieved on Day +113 and transfusion requirements significantly improved. Although ferritin remains elevated, sIL2R and CD163 have normalized. Genetic testing for familial HLH was negative.

Conclusion: Our report emphasizes the need for clinical vigilance for HLH as a possible cause

for unexplained delayed engraftment following autologous SCT. A bone marrow biopsy should be strongly considered before a stem cell boost. sIL2R and CD163 can aid in the diagnosis of HLH cases with baseline hyperferritinemia or an atypical presentation.

Poster # 256

CASE SERIES OF CHILDREN PRESENTING WITH CHRONIC MYELOID LEUKEMIA IN BLAST PHASE

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Background: Chronic myeloid leukemia (CML) is rare among children and adolescents, which constitutes up to 3% of pediatric leukemia. Among the pediatric CML patients, it is even rarer to diagnose in blast phase (BP) at the initial presentation. Given the rarity of CML-BP in children, standard pediatric-specific management has not been established. The current treatment regimen for CML-BP in this age group is based on adult data and includes first or second-generation tyrosine kinase inhibitors (TKI), as well as hematopoietic stem cell transplantation (HSCT). However, the biology, clinical presentation, disease progression, as well as possible response to therapeutics in pediatric CML are different from those in adult CML, which poses additional challenges in extrapolating adult practice to children.

Objectives: We expand on the clinical findings and course of disease of CML-BP as the initial presentation in pediatric patients.

Design/Method: We 1) collected patient demographics, clinical, morphological, and genetic findings at initial presentation; 2) followed their disease course and treatment response via medical chart review; and 3) conducted a literature review of pediatric CML-BP cases.

Results: We describe three children who initially presented with hyperleukocytosis, basophilia, and left-shifted myeloid precursors in peripheral blood suggestive of CML-BP: a 15-year-old male and a 13-month-old female presenting with B-lymphoblastic precursors, and a 10-year-old male presenting with biphenotypic blasts. All had t(9,22) (q34; q11.2) on chromosome analysis and fluorescence in situ hybridization (FISH); and molecular studies confirmed BCR-ABL1 major (p210) transcript in two patients and minor (p190) breakpoint in one patient. They underwent four-drug induction therapy for acute lymphoblastic leukemia (ALL) plus a TKI. All achieved minimal residual disease (MRD) negativity with 0.01% for ALL at the end of Induction. There was an adequate decrease in the BCR-ABL1 transcript achieving major molecular remission (MMR2) with four additional months of TKI treatment, consolidation chemotherapy with cytarabine, cyclophosphamide, mercaptopurine, and high-dose methotrexate prior to haploidentical in two patients and matched-unrelated HSCT in one patient. They are currently in various phases: recent HSCT, 2 months post-HSCT, and 12 months post-HSCT, respectively.

Conclusion: Due to the rarity of pediatric CML-BP as the initial presentation of CML, there are no existing universal guidelines to monitor and treat patients in this age group. Our case series contribute to the knowledge of presentation and response to current treatment options. Future research and collaborative studies are needed to guide the diagnosis, management, and timing of HSCT for children presenting in CML-BP.

Poster # 257

REMDESIVIR THERAPY IN ACUTE LYMPHOBLASTIC LEUKEMIA: A CASE SERIES

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Background: A novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has emerged as a cause of severe lower respiratory tract disease, termed coronavirus disease 2019 (COVID-19). While initial reports suggested that SARS-CoV-2 is typically milder in children, insufficient data exist regarding whether immunocompromised children are at greater risk of severe COVID-19 infection compared to healthy children or those with other comorbidities. However, literature in adults points to particular risk for cancer patients and recipients of solid organ transplants. This creates a unique challenge in determining treatment for these patients.

Objectives: We present the successful use of antiviral remdesivir in two pediatric patients with acute lymphoblastic leukemia (ALL), one with the additional comorbidty of Down Syndrome (DS).

Design/Method: A case series presentation.

Results: Patient 1: A 15-year-old female with DS and ALL in maintenance therapy, admitted with a 4-day history of fever, hypoxia, and respiratory distress. No history of recent travel or known direct exposure however mother worked in a meat packing plant with confirmed SARS-CoV-2 outbreak. The patient presented with fever of 38.8°C, hypoxemia with blood oxygen saturations of 70% on room air, and respiratory distress. A chest x-ray showed diffuse, bilateral interstitial and airspace opacities. SARS-CoV-2 RNA was positive. Remdesivir was approved on D+1 and first dose received on D+2. The patient had 6 days of fevers with fluctuating respiratory status, however on D+6, was placed on room air and had repeat chest x-ray (CXR) showing improved lung consolidation. She ultimately clinically recovered from COVID-19 symptoms and discharged on D+10.
Patient 2: A 14-year-old male with ALL in maintenance therapy, admitted for respiratory distress and sepsis. He presented with fever, respiratory distress, and hypotension. A CXR showed patchy bilateral pulmonary opacities and SARS-CoV-2 PCR was positive. On arrival to the intensive care unit he was electively intubated due to cardiac compromise and severe metabolic acidosis. He was started on remdesivir on D0 and completed a 10 day course. He required mechanical ventilation through D+6 and weaned to room air on D+7 with CXR showing

improved bilateral pulmonary opacities. He ultimately clinically recovered from COVID-19 symptoms and discharged on D+12.

Conclusion: These cases highlight the successful treatment of COVID-19 infection with remdesivir without side effects in immunocompromised patients with ALL, illustrating the importance of initiating remdesivir therapy early in this high risk population to prevent prolonged ICU stay.

Poster # 258

A NOVEL CASE OF CONCURRENT T-CELL AND EARLY T-CELL LYMPHOBLASTIC LYMPHOMA IN AN ADOLESCENT FEMALE

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Background: Early T-cell precursor acute lymphoblastic leukemia/lymphoma is a subgroup of T-cell acute lymphoblastic leukemia/lymphoma with a distinct gene expression profile and immunophenotype that confers higher risks of induction failure, progression, and relapse, especially when treated with standard chemotherapy. Given its rarity and specificity of antigen profiling required for diagnosis, a paucity of literature exists regarding prognostic implications and therapy response.

Objectives: In the context of an evolving understanding of early T-cell precursor (ETP) lymphoma and leukemia, we present a case of concurrent T-cell lymphoblastic lymphoma and ETP lymphoma in an adolescent female to improve understanding of ETP acute lymphblastic leukemia/lymphoma as its own entity.

Design/Method: Review of existing literature as well as patient chart, imaging, and pathology.

Results: The patient remains in remission 4 years post allogeneic matched sibling donor bone marrow transplant. Our patient represents a unique case of pure ETP lymphoma without peripheral blood or BM involvement, which to our knowledge has not been described in the literature. She exhibited two unique populations of neoplastic cells—T-LBL and ETP-LBL—on initial biopsy.

Conclusion: To our knowledge, this represents the first reported case of both lymphoblastic lymphoma and ETP lymphoma as distinct and conjoined components of the same neoplasm. As an exception to current literature, our patient had only ETP lymphoma with no marrow involvement. This may suggest some yet-unknown aspect of these malignancies, like bi-directionality of lymphopoiesis or a complex ability of neoplastic T-cells to evolve or rearrange. It is possible that her initial biopsy captured an in vivo malignant reversion of more mature T-cells to a less differentiated phenotype, as has been described in mouse models. Finally, the

selective survival of the ETP population after intense chemotherapy concurs with reports suggestive of ETP-ALL/LBL resistance to standard chemotherapy.

Poster # 259

BLINATUMOMAB USE AS NOVEL BRIDGING THERAPY IN RELAPSED PEDIATRIC ALL WITH ACTIVE INVASIVE INFECTION

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Background: Invasive bacterial and fungal infections are a major cause of treatment-related morbidity and mortality in pediatric Acute Lymphoblastic Leukemia (ALL). Treatment options during life-threatening, invasive infections are limited by the immunosuppressive nature of most chemotherapy regimens. Blinatumomab, a bispecific monoclonal antibody, has previously been reported as salvage therapy after patients with relapse, a bridge to stem cell transplant, and for chemotherapy-related toxicity. Here we report the use of Blinatumomab as bridging therapy for two pediatric patients with invasive, life threatening infections (inonotus tropicalis rhinosinusitis and central nervous system (CNS) tuberculosis) requiring extended antimicrobial therapy.

Objectives: To describe the novel use of Blinatumomab as bridging therapy for two patients with relapsed ALL with invasive infections requiring extended antimicrobial therapy.

Design/Method: Case report of two patients with chart abstraction and literature review.

Results: Patient 1: 17-year-old female with relapsed ALL who developed invasive inonotus rhinosinusitis during re-induction with vincristine, dexamethasone, pegaspargase, mitoxantrone, and intrathecal methotrexate (Block 1). Imaging revealed fungal invasion of sinuses, facial and cranial bones, nerves, and muscles but not the CNS. Initial treatment of the infection led to a one-month delay in chemotherapy and an MRD of .5%, but MRD negative remission was achieved after blinatumomab cycle 1 completion. After 8 blinatumomab cycles, multiple surgical procedures and treatment with liposomal amphotericin, voriconazole, and subsequently posaconazole, the infection was cleared, and the patient remained in MRD negative remission. Blinatumomab was held on two non-consecutive days for neurotoxicity, but was otherwise tolerated.
Patient 2: 13-year-old female with relapsed pre-B ALL and history of treatment delays from vincristine-associated peripheral neuropathy, pancreatitis and bacterial infections. She presented with fever and severe abdominal pain after transitioning to palliative chemotherapy following hepatotoxicity from AALL0433-like therapy at an outside hospital. Imaging demonstrated uncal and subfalcine herniation with marked left frontotemporal lobe edema. An open biopsy was positive for mycobacterium tuberculosis complex consistent with vaccine reactivation. She received 12 Blinatumomab cycles primarily outpatient with no neurotoxicity and achieved negative MRD (0%) remission post cycle 1. Her CNS TB infection was treated with Rifampin, Isoniazid, Pyrazinamide, Ethambutol and Levofloxacin. After completing blinatumomab, the

patient returned to the outside hospital and remains in remission.

Conclusion: Blinatumomab may be a bridging therapy for relapsed leukemia control while treating acute invasive infections. This treatment allowed for leukemia control during infection resolution and was well tolerated by both patients with minimal complications.

Poster # 260

BLINATUMOMAB WITH DASATINIB AND INTRATHECAL THERAPY FOR RELAPSED PH-POSITIVE ALL WITH CNS RELAPSE

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Background: Philadelphia chromosome-positive B-cell acute lymphoblastic leukemia (Ph+ ALL) is a distinctive subtype of ALL associated with a reduced event free survival and overall survival compared with Ph-negative ALL. Tyrosine kinase inhibitors (TKIs) that target BCR-ABL have become essential in improving the prognosis of patients with Ph+ ALL, though these patients still remain at high risk of relapse. Children and Adolescents/Young Adults (AYAs) with Ph-negative ALL that experience a first relapse within 36 months from diagnosis receive reinduction therapy with the goal of achieving negative minimal residual disease (MRD; <0.01%) prior to allogeneic hematopoietic stem cell transplant (HSCT). Recent data suggests that the addition of blinatumomab prior to HSCT is likely to improve MRD clearance and improve outcomes. For AYA patients with Ph+ ALL that experience relapse there is no standard approach to achieve MRD negativity prior to HSCT.

Objectives: Describe the treatment course and outcome for a young adult with relapsed Ph+ ALL, including new CNS involvement, soon after completing initial therapy on Children's Oncology Group (COG) AALL1631.

Design/Method: Case report

Results: A 16-year old female was diagnosed with Ph+ ALL (CNS1) in 2017 and initiated therapy on COG AALL1631 (EsPhALL arm). After completion of therapy, her BCR/ABL1 p190 transcript increased and her bone marrow aspirate eventually showed relapsed disease based on multiparameter flow cytometry. Lumbar puncture revealed CNS3 disease. She was started on dasatinib 100 mg daily, blinatumomab, and received triple IT chemotherapy twice weekly until the CSF had no evidence of leukemia and then transitioned to weekly for the remainder of the first cycle. She achieved complete remission by flow cytometry after the first cycle of blinatumomab. Another course of blinatumomab was given in addition to three doses of triple IT chemotherapy with each dose approximately 2 weeks apart. After 2 cycles of dasatinib, blinatumomab, and intrathecal chemotherapy the BCR/ABL p190 decreased from 6.36 to 0.014%. She had no major complications from this salvage regimen and subsequently proceeded to matched unrelated donor HSCT. Day +30 and +100 bone marrow p190 was undetectable.

Conclusion: There is increasing evidence regarding the benefits of blinatumomab when combined with TKI therapy for adult patients with Ph+ ALL in the relapsed setting, as well as for upfront therapy. However, data for this combination is scarce for AYA patients with relapsed Ph+ ALL, especially when CNS disease is present. In this case, blinatumomab plus dasatinib and triple intrathecal chemotherapy was a feasible and efficacious bridge to HSCT.

Poster # 261

THE ADDITION OF DARATUMUMAB & BRENTUXIMAB IN A CASE OF PEDIATRIC ANGIOIMMUNOBLASTIC T-CELL LYMPHOMA

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Background: Angioimmunoblastic lymphoma is an aggressive peripheral T-cell lymphoma often characterized by autoimmune cytopenias and hypergammaglobulinemia. There is no standard treatment for this lymphoma in pediatrics with very few pediatric cases previously reported.

Objectives: To report a pediatric case of angioimmunoblastic T-cell lymphoma where daratumumab and brentuximab were combined with chemotherapy resulting in favorable response.

Design/Method: Single subject case report.

Results: A 17 year old male presented with septic shock and respiratory distress. His physical exam was most significant for cervical lymphadenopathy and hepatosplenomegaly. His initial labs identified an anemia, thrombocytopenia, leukocytosis with abnormal lymphocytes present, pan positive coombs test (IgG, anti C3b, eluate positive, indirect positive), and hypergammaglobulinemia (EBV IgM positive, negative EBV PCR, Mycoplasma IgM and IgG positive, HIV screen positive with confirmatory testing negative). The patient was diagnosed with autoimmune hemolytic anemia thought to be secondary to a mycoplasma infection and was thus started on a course of steroids. Given his abnormal CBC, flow cytometry was performed on his peripheral blood which identified an aberrant, monoclonal T-cell population (CD4+) of unclear significance. The decision was made to proceed with a bone marrow aspirate and biopsy where results were consistent with a peripheral T-cell lymphoma of T-follicular helper cell origin; angioimmunoblastic T-cell lymphoma. His initial imaging with PET MRI revealed his disease to include cervical, supraclavicular, axillary, mediastinal, retroperitoneal, and inguinal lymphadenopathy, all of which were FDG avid. Chemotherapy was initiated with cyclophosphamide, doxorubicin, prednisone, and etoposide (CHPE). In addition, brentuximab and daratumumab were added to the treatment regimen given the lymphoma expressing both CD30 and CD38. The patient completed two cycles of chemotherapy, following which a repeat PET MR showed complete remission of his disease (Deauville score of 2). The combination therapy was well tolerated without any significant side effects or complications to date. The patient is proceeding to a third cycle prior to Consolidation with allogeneic hematopoietic stem

cell transplant.

Conclusion: Although angioimmunoblastic T-cell lymphoma is exceedingly rare in pediatrics, it should be considered in cases of autoimmune cytopenias, especially when presenting with lymphadenopathy and hypergammaglobulinemia. This case illustrates the effectiveness of targeted therapies in brentuximab and daratumumab, which should be considered in cases of angioimmunoblastic T-cell lymphoma.

Poster # 262

PROLONGED REMISSION IN MULTIPLE RELAPSED MLL-REARRANGED INFANT B-ALL WITH INOTUZUMAB OZOGAMICIN

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Background: Inotuzumab Ozogamicin (InO) is a CD22-targeted antibody approved to treat relapsed acute lymphoblastic leukemia (ALL). It is typically used as a bridge to curative therapy. MLL-rearranged (MLL-r) infant ALL has a poor prognosis with poor response to conventional therapy. There are no reports of the use of InO for palliative treatment of MLL-r infant ALL.

Objectives: We report a case of prolonged MRD negative remission using InO in a patient with multiple relapsed, MLL-r, infant ALL.

Design/Method: Case Report.

Results: A 9-month-old infant presented with a subcutaneous nodule and leukocytosis. Bone marrow studies were diagnostic of MLL-r pre-B ALL. He was CNS2. He was enrolled on COG AALL15P1. End of Induction bone marrow showed MRD negative remission. His first relapse occurred only 5 months into therapy. He was then enrolled on AALL1331 protocol and was randomized to the chemotherapy arm. His second relapse occurred 4 months later after block 3 therapy. He had 2 additional relapses in the following 4 months (bone marrow, CNS and extramedullary) despite treatment with Blinatumomab, and CD-19 CAR-T cells.
He first received InO as bridge to CAR-T therapy, and had an excellent response (CR4) with negative MRD after two cycles. However, after CAR-T cell infusion was complete, a CNS and extramedullary relapse occurred only 28 days later.
After having 4 relapses in only 12 months, InO therapy was then resumed for palliative purposes. Cranial radiation was given (1200Gy) for CNS disease. He received 8 cycles of InO over the course of one year and surprisingly, maintained MRD negative complete remission (CR5) during this time. Dosing was given weekly for 3weeks/month, and then spaced to bi-weekly and then monthly. Complications included moderate but persistent pancytopenia (not requiring transfusions), mild mucocutaneous bleeding and one admission for pseudomonas cellulitis. The bleeding and the cytopenias improved with increased dosing intervals. Our patient had an excellent quality of life with few hospitalizations during this time. Because of his prolonged

remission, parents have since elected to pursue curative stem cell transplant.

Conclusion: This is the first reported case of prolonged MRD negative remission using Inotuzumab, in a patient with heavily treated, multiple relapsed, MLL-r infant ALL. InO should be considered as an alternative therapy for relapsed/refractory CD22+ infant ALL, either as a bridge to curative therapy, or for longer term palliative treatment.

Poster # 263

ACUTE LYMPHOBLASTIC LEUKEMIA IN A CHILD WITH HEREDITARY MULTIPLE EXOSTOSIS AND TP53 MUTATION

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Background: Hereditary multiple exostoses (HME) is an autosomal dominant disorder characterized by multiple osteochondromas, caused by inactivating mutations of the EXT1 or EXT2 genes. While malignant transformation of benign osteochondromas to chondrosarcomas and osteosarcomas is well documented in HME, there are also reports of occurrences of Non-Hodgkin Lymphomas, and acute leukemias in this population, albeit rare.

Objectives: To report a case of Acute Lymphoblastic Leukemia (ALL) in a child with HME.

Design/Method: Case report.

Results: A 13-year-old boy with HME presented with progressive pallor and fatigue and was diagnosed with pre-B cell ALL. His past medical history was significant for development of multiple bony swellings since the age of 6 years. He received induction chemotherapy and achieved remission (end of induction minimal residual disease <0.01%). While in consolidation, he underwent a hereditary cancer panel testing. Targeted gene testing of 92 known cancer driver genes revealed a heterozygous four base pair deletion in exon 2 of the EXT2 gene and a heterozygous three base pair deletion in exon 4 of the TP53 gene. The former has been previously reported in patients with HME while the latter is documented as variant of uncertain significance in Li-Fraumeni syndrome in the ClinVar database. The patient is continuing chemotherapy for ALL.

Conclusion: To our knowledge, this is the first report of ALL in a child with HME and EXT2 mutation. EXT group of genes have putative tumor-suppressor activity, but little is known of their association with malignancies other than bone sarcomas. Whether the coexistent TP53 mutation led to multistep carcinogenesis in this patient is uncertain.

Poster # 264

SIGNIFICANTLY DELAYED METHOTREXATE CLEARANCE IN A PATIENT WITH PRE-B ALL AND COVID-19

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Background: Coronavirus disease 2019 (COVID-19) has affected more than 85 million people worldwide. Children typically experience a less severe disease course, but not much is known about COVID-19 in pediatric oncology patients. As a result, treatment and changes in therapy are constantly evolving and institution specific. Methotrexate is an important chemotherapeutic agent in the treatment of acute lymphoblastic leukemia (ALL), and impairments in renal function can delay clearance.

Objectives: Describe a case of significantly delayed methotrexate clearance in a patient with high risk (HR) pre-B ALL and asymptomatic COVID-19 infection.

Design/Method: Case report.

Results: An 8-year-old white male with Hispanic ethnicity and HR pre-B ALL being treated per COG AALL1732 tested positive for COVID-19 prior to admission for Interim Maintenance I, Day 15. He was asymptomatic but had a known close exposure. He did not have any myelosuppression, but his ferritin was elevated at >2,000 µg/L at that time. His oral mercaptopurine was held, and his admission for systemic chemotherapy was delayed 10 days. Upon admission for Day 15 therapy with vincristine and high dose methotrexate, his ferritin had down trended to 960 µg/L, and his creatinine was at his baseline of 0.31 mg/dL. He had remained asymptomatic. He had no history of delayed clearance, so he received standard hydration at 125 mL/m2/hr. His level at 24 hours was appropriate, but his creatinine increased to 0.47 mg/dL. His methotrexate level at 42 hours was substantially elevated at 6.36 µm (goal ≤1 µm), so his IV fluids were increased to 200 mL/m2/hr. When his level remained persistently elevated, his leucovorin rescue was increased to every 3-hour dosing at hour 60 and was continued until he cleared. He eventually cleared at hour 211, and his creatinine peaked at 0.54 mg/dL. During this admission, he developed pancytopenia requiring mercaptopurine discontinuation and multiple transfusions. He remained profoundly neutropenic at time of discharge. Of note, he appropriately cleared his methotrexate on Days 29 and 43 of Interim Maintenance without issues.

Conclusion: This is a case of significantly delayed methotrexate clearance in a patient with HR pre-B ALL in the setting of asymptomatic COVID-19 infection. Further research is needed to characterize the effect of COVID-19 on these patients in order to make recommendations for treatment modifications when these patients have COVID-19 infections.

Poster # 265

POLYOMAVIRUS BK NEPHROPATHY IN A NON-TRANSPLANT PEDIATRIC PATIENT WITH ACUTE LYMPHOCYTIC LEUKEMIA

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Background: Polyoma type BK virus (BKV) is a non-enveloped virus known to cause BKV-associated nephropathy after kidney transplantation and hemorrhagic cystitis after allogeneic hematopoietic transplantation. BKV is frequently contracted during childhood and remains latent throughout adulthood, manifesting disease in the immunocompromised.

Objectives: To describe a case of BKV nephropathy in a non-transplant pediatric patient undergoing treatment for B-cell acute lymphocytic leukemia and report on the drug interaction of oral chemotherapy with leflunomide.

Design/Method: A review of medical records and literature on BKV nephropathy in pediatric patients was completed.

Results: A 5-year old, ex 34-week preterm boy, with history of in-utero hydronephrosis secondary to posterior urethral valves requiring surgical repair and right nephrectomy at 1-year of age, was diagnosed with standard risk B-ALL at almost 3-years of age. He was treated per COG study AALL0932 and admitted for workup of pancytopenia, hypertension, and acute kidney injury during maintenance therapy. Leukemia relapse was ruled out and he underwent renal biopsy which showed diffuse tubulointerstitial inflammation. BKV was detected in the blood and urine with serum level > 7 million copies/mL. He was started on leflunomide loading dose of 50 mg PO x 5 days followed by treatment dose of 20 mg PO daily and IVIg every 2 weeks. Oral chemotherapy was decreased to 50% once his counts recovered. Steroids and vincristine were briefly omitted from treatment to minimize immunosuppression. Two weeks into treatment oral chemotherapy was held again due to pancytopenia and transaminitis. Leflunomide was decreased and maintained at 10mg daily and oral chemotherapy was ultimately tolerated at doses between 10-30%. He received one dose of IV cidofivir and IVIg was spaced out to every 4 weeks. Five months after start of leflunomide patient completed oral chemotherapy and BKV levels became undetectable one month after. His creatinine remains elevated above baseline with close monitoring and strict hydration parameters.

Conclusion: This is a case report of a child who developed hypertension and AKI secondary to BKV nephropathy while undergoing maintenance chemotherapy for B-ALL. He received treatment with IVIg and leflunomide daily for control of BK viremia. Leflunomide given concurrently with oral 6-mercaptopurine resulted in significantly increased thiopurine metabolites and severe myelosuppression. We recommend starting with lower doses of leflunomide and reducing dose of 6-mercaptopurine/methotrexate by at least 25% of current dose with frequent monitoring of blood counts, thiopurine metabolites, liver enzymes, and BKV levels when treatment is given concurrently.

Poster # 266

CROSSING OUR T'S: AN UNUSUAL PRESENTATION OF INFANTILE T-CELL LEUKEMIA

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Background: Leukemia is the most common childhood cancer, with T-cell acute lymphoblastic leukemia (T-ALL) comprising 10-15% of pediatric leukemia diagnoses. T-ALL is commonly diagnosed in adolescents with a median age of diagnosis of 9 years old, yet rarely reported in children less than 12 months of age. The paucity of data regarding infantile T-ALL's clinical presentation, management, genomics, and outcomes results in difficult treatment decisions including potential use of agents such as Nelarabine, at a young age.

Objectives: We aim to supplement the literature with our management and clinical course for this unique diagnosis of infantile T-ALL with unusual genomic findings.

Design/Method: Single subject case report

Results: We present the case of a previously healthy 4-month-old Caucasian female with initial presentation of hepatomegaly, with leukocytosis (WBC 770 k/cumm) comprised of 94% peripheral blasts, anemia (hemoglobin 6.3GM/dL), and thrombocytopenia (platelets 43k/cumm). Physical exam was notable for marked hepatosplenomegaly, and ~1cm subcutaneous nodule of the right thigh. Initial treatment consisted of hyperhydration and rasburicase for a uric acid of 12.9mg/dL. She was initially on oxygen and quickly weaned to room air with negative chest X-ray. Peripheral flow confirmed a diagnosis of T-ALL, CNS1. Foundation One testing demonstrated *MLL* not rearranged, an *LM02* rearrangement, and variants of unknown significance, most uniquely *CSF3R* (R698H). She began induction therapy per COG protocol AALL0631. She had complications including bacteremia, mucositis, and required parenteral nutritional support. End of induction bone marrow aspirate demonstrated a minimal residual disease (MRD) of 4.1%. She continued AALL0631 and tolerated induction intensification without infections, minimal mucositis and nutritional support. MRD at end of re-induction was 3.1%. Considering her continued disease burden, we changed protocols and she received a combination of nelarabine and Intermaintenance therapy as per AALL0434, in hopes that nelarabine would improve her disease burden, and planned for stem cell transplant.

Conclusion: We report a unique case of infantile T-ALL, treated initially per COG protocol AALL0631. With *CSF3R*mutations association to GCSF, being an unusual finding. Additionally, *LMO2* overexpression is a common driver of T-Cell malignancies, however, has not been reported in infantile T-ALL. Persistence of disease posed challenges in treatment options, with needing to utilize Nelarabine in an infant. In addition, her genomic findings have not yet been reported in the literature. Future research should focus on reporting rare infantile leukemia cases, to better guide care for these patients.

Poster # 267

ACUTE LYMPHOBLASTIC LEUKEMIA PRESENTING WITH HYPEREOSINOPHILIC SYNDROME

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Background: Acute B-lymphoblastic leukemia (ALL) with hypereosinophilia is a rare diagnosis involving overproduction of mature, reactive, nonmalignant eosinophils that infiltrate and cause end organ damage. The presence of hypereosinophilia and its clinical manifestations may complicate standard approaches to the diagnosis and treatment of ALL.

Objectives: We describe a patient with ALL presenting with hypereosinophilic syndrome.

Design/Method: Case report

Results: A 13-year-old Hispanic male presented with four days of fever and cough. Initial physical exam was notable for tachycardia and scattered petechiae. Complete blood count showed eosinophilic hyperleukocytosis (white blood cell count 142 thousand/mm^3, absolute eosinophil count 113 840/mm^3) with mild thrombocytopenia and normocytic anemia. Peripheral blood smear revealed mature-appearing eosinophils. Lactate dehydrogenase was 589 units/L without other evidence of tumor lysis syndrome.

He was admitted to the pediatric intensive care unit where he became increasingly encephalopathic with dysmetria. Neuroimaging showed multifocal cerebral and cerebellar infarcts in multiple vascular distributions. Echocardiogram demonstrated normal ventricular function and no embolic source. Troponin I was elevated at 19.517 ng/mL and continued rising as cytoreductive therapies were initiated. Cardiac MRI revealed subendocardial late gadolinium enhancement consistent with the acute necrotic stage of eosinophilic myocarditis, along with left apical mural thrombus.

Bone marrow biopsy confirmed the diagnosis of B-lymphoblastic leukemia. The patient received hyperhydration with addition of steroids, hydroxyurea, and leukapheresis as his neurologic abnormalities evolved. He started chemotherapy with a four-drug induction and addition of Dexrazoxane prior to anthracyclines. As his clinical status stabilized, therapeutic anticoagulation was also initiated.

Conclusion: We present an adolescent with ALL and eosinophilic hyperleukocytosis resulting in multifocal ischemic strokes, myocarditis, and thrombosis. Hypereosinophilia is present in less than 1% of patients with ALL. The most common cytogenetic abnormality, t(5;14), drives lymphoblast overproduction of IL-3, a potent eosinophilopoietic cytokine, and is rarely found in other ALL subtypes. Identification of this pathognomonic translocation is sufficient when an overwhelming number of eosinophils and low percentage of bone marrow blasts preclude the diagnosis. Patients often have clinical manifestations of hypereosinophilia, as seen, to a more severe extent, in this case. Systemic steroids serve dual purposes in reducing eosinophil-driven inflammation and treating the underlying leukemia. Our patient tolerated intensive chemotherapy without additional complications. He had complete recovery from his neurologic and cardiovascular injuries. Consistent with published reports on ALL with hypereosinophilia, however, he had refractory leukemia after induction and consolidation. He achieved MRD-

negative remission after Tisagenlecleucel and ultimately underwent a matched sibling hematopoietic stem cell transplant.

Poster # 268

ISOLATED CNS RELAPSE IN TWO HIGH-RISK B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS AFTER SARS-COV-2

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Background: B-cell acute lymphoblastic leukemia (B-ALL) is the most common pediatric malignancy with a highly favorable overall prognosis. Central nervous system (CNS) relapse of B-ALL is rare and is associated with inferior survival outcomes. The effect of infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on outcomes in patients with B-ALL remains unknown.

Objectives: We present two patients with high-risk (HR) B-ALL who developed isolated CNS relapse following infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Design/Method: We reviewed the charts of two patients described below.

Results: 16-year-old Hispanic male diagnosed with HR B-ALL without CNS disease. He had evidence of minimal residual disease (MRD) by flow cytometry (0.4%) at the end of induction (EOI) and no evidence of MRD at the end of consolidation. During the maintenance phase of therapy, he tested positive for SARS-CoV-2 on routine asymptomatic screening. Chemotherapy was continued, although intrathecal chemotherapy was delayed one month. 56 days after SARS-CoV-2 diagnosis, cerebrospinal fluid (CSF) analysis demonstrated 198 nucleated cells/microliter, with 100% leukemic blasts. Bone marrow evaluation showed no evidence of leukemia.

14-year-old Hispanic male diagnosed with HR B-ALL without CNS disease. He had no evidence of MRD at EOI. During the maintenance phase of therapy, he developed fever, cough, and chest pain and tested positive for SARS-CoV-2. He was admitted and remained overall well despite nine days of persistent fevers and leukopenia. He was evaluated for Multisystem Inflammatory Syndrome – Children (MIS-C) due to elevated inflammatory markers, although this was felt to be consistent with acute coronavirus disease 2019 (COVID-19) infection. All chemotherapy was held 29 days. CSF analysis 56 days after SARS-CoV-2 infection revealed 109 nucleated cells/microliter, with 75% leukemic blasts. Bone marrow evaluation showed no evidence of leukemia.

Conclusion: The significance of SARS-CoV-2 infection in pediatric B-ALL patients is unknown. While few patients have severe complications from acute infection, there are multiple ways that COVID-19 might indirectly affect outcomes, such as delays in initial presentation,

postponement of chemotherapy, or isolation requirements resulting in delays in scheduled procedures. Alterations in the immune system are also described in patients with COVID-19 and given the known interplay between the immune system and malignancy, immune dysregulation must be considered as an effect as well. We postulate that in addition to known individual and disease factors, the potential interplay of delays in therapy together with immune system modulation due to COVID-19 may account for this cluster of B-ALL CNS relapse cases.

Poster # 269

TARGETED THERAPY USE IN RARE MUTATION IN T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA (ALL)

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Background: The NUP214-ABL1 gene fusion has been reported in approximately 6% of patients with T-cell ALL and is the second most prevalent fusion gene involving ABL1. The formation of episomal structures resulting from the fusion between ABL1 and NUP214 have been identified as a novel mechanism of tyrosine kinase activation. In adults with this gene fusion, the use of targeted tyrosine kinase inhibitor (TKI) therapy has dramatically improved outcomes

Objectives: To discuss the potential activity of TKIs against NUP214-ABL1 positive cell lines and consider the potential role for TKIs in the treatment of pediatric patients with T-cell ALL carrying this transcript.

Design/Method: We performed a retrospective chart review of patients with T-cell ALL at our center over the last 10 years to evaluate the frequency of this mutation and determine outcomes.

Results: There were 31 pediatric patients including both T-cell ALL and T-cell lymphoma treated at our center in the last 10 years. There were 3 patients positive for 9q34 fusion gene. Two of these had no specific fusion gene identified, as searching for NUP214-ABL1 fusion protein had not been established as an important practice at the time. One patient diagnosed within the past year was identified as having the NUP214-ABL1 gene fusion. None of these patients were treated with TKIs. Of the 31 patients in remission, approximately 60% of them suffered from treatment related complications such as recurrent infections and other toxicities. They were treated successfully per COG protocol AALL1231 and are currently in remission.

Conclusion: All ABL1 rearrangement-associated leukemias have a poor prognosis due to increased tyrosine kinase activity causing cell transformation. There is evidence that patients with NUP214-ABL1 gene fusion have increased risk of treatment failure. The development of targeted therapy with specific TKIs have dramatically modified outcomes. Human T-cell ALL cells with NUP214-ABL1 fusion show in-vitro sensitivity to TKIs, but the clinical experience is limited to several case reports of successful treatment in adult patients with T-cell ALL. It is time

to consider the usage of TKIs in pediatric patients with NUP214-ABL1 gene fusion. T-cell ALL has poor outcomes in comparison to B-cell ALL. Using TKIs may improve T-cell ALL outcomes in children. We may also be able to minimize side effects resulting from long term intensive chemotherapy regimens currently used in T-cell ALL treatment. Further studies are needed to investigate this possibility.

Poster # 270

THE USE OF NEXT GENERATION SEQUENCING IN THE DETECTION OF AN ELUSIVE CAUSE OF EOSINOPHILIC LEUKEMIA

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Background: Hypereosinophilia can be due to primary or secondary (reactive) causes. A rare reactive cause is acute lymphoblastic leukemia (ALL) (4). Eosinophilic leukemia is exceedingly rare with only 61 pediatric patients described (1). One particularly uncommon subtype is *IGH-IL3* B-ALL caused by t(5;14)(q31;q32). This translocation results in upregulation of interleukin 3 (IL3) expression and unregulated maturation and release of eosinophils into the bloodstream. To date, only 24 cases have been reported, 71% of which were children (2). The extent of eosinophilia in these patients poses unique challenges in diagnosis and management. Here we present a puzzling case of an adolescent boy with hypereosinophilia.

Objectives: Discuss the utility of next generation sequencing (NGS) in the diagnosis of eosinophilic leukemia.

Design/Method: Case report.

Results: An 11-year-old healthy male presented with facial paralysis in the setting of fever, myalgia, chest pain, and abdominal pain. Bloodwork demonstrated leukocytosis of 129,000/µL with 80% eosinophils and thrombocytopenia. Imaging revealed multifocal cerebral infarcts, pulmonary infiltrates, and cardiomyopathy with myelofibrosis. He developed acute respiratory failure and cardiogenic shock requiring mechanical ventilation and vasoactive support. Extensive testing with flow cytometry of the peripheral blood and bone marrow aspirate were negative for leukemia. Furthermore, chromosome analysis, FISH, and B-cell rearrangement studies were inconclusive. Bone marrow biopsy with immunostaining, however, was suspicious for patchy increase in B-lymphoblasts. Given the diagnostic conundrum, NGS was performed showing an *IGH-IL3* rearrangement and confirming B-ALL. Treatment consisted of leukapheresis and hydroxyurea with resulting drop in leukocytosis and eosinophilia, followed by a modified high-risk chemotherapy regimen as per Children's Oncology Group AALL1732.

Conclusion: *IGH-IL3* B-ALL is a rare cause of hypereosinophilia seen in adolescent males and is associated with restrictive cardiomyopathy, pulmonary infiltrates, and thromboembolic events

attributable to eosinophil infiltration (2). Due to the extent of IL3 upregulation, peripheral eosinophilia precedes the appearance of blasts (1). The combination of undetectable peripheral blasts and their partial bone marrow infiltration makes lymphoblast detection via standard methods particularly challenging (2). The result is a delay in diagnosis of a disease with already poor prognosis at baseline. This case emphasizes the utility of sensitive new technology such as high-throughput NGS to assist in *IGH-IL3* B-ALL diagnosis so as to reduce disease lead time and associated morbidity and mortality (3).

(1) Ferruzi V et al, *Int J Environ Res Public Health*, 2018. (2) Fournier B et al, *Front Oncol*, 2019. (3) Gagan J et al, *Genome Med*, 2015. (4) Yu et al, *Am J Hematol*, 2016.

Poster # 271

ACUTE MYELOID LEUKEMIA WITH MYELODYSPLASIA PRESENTING AS MULTISYSTEM INFLAMMATORY SYNDROME

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Background: Complex karyotype in children with advanced myelodysplastic syndrome (MDS) is associated with poor prognosis. Disruption of the bone marrow microenvironment through immune activation and proinflammatory signaling can promote transformation of MDS to acute myeloid leukemia (AML).

Objectives: Describe a patient presenting with multisystem inflammatory syndrome who was diagnosed with AML with myelodysplasia-related changes.

Design/Method: Case report, karyotype, whole genome sequencing, whole exome sequencing, RNA sequencing.

Results: A previously healthy 13-year-old female presented with two-week illness consisting of malaise, abdominal pain, and acute development of nausea, vomiting, and fever. She was found to be hypotensive, tachycardic, and febrile. She quickly decompensated with multiorgan failure and shock. Blood cell counts showed a hemoglobin level of 3 g/dL, white blood cell count of 5 $x10^3/mm^3$, a platelet count of 108 $x10^3/mm^3$ with immature myeloid cells on the differential. Inflammatory markers were elevated including CRP of 8.1 mg/dL (normal <1) and interleukin 6 of 1073 pg/mL (normal <2). She was treated with antibiotics, vasopressors, and was intubated. She received tocilizumab and intravenous immunoglobulin. There was no evidence of past or current COVID-19 infection. Bone marrow examination revealed hypercellular marrow with multilineage dysplasia, fibrosis, and increased myeloblasts (32%) with complex karyotype detected (monosomy 7/del7q; 91% of 58 metaphases). Next-generation sequencing revealed *RUNX1*, *TP53* (homozygous), and *ZBTB7A* abnormalities. Diagnosis of AML with myelodysplasia-related changes was made. Due to persistent multiorgan dysfunction she was ineligible for standard AML treatment and subsequently received treatment with Vyxeos (CPX-351), anakinra, and methylprednisolone which led to clinical improvement. Induction day 22

marrow revealed hypocellularity (5%-10%) and 1% blasts detected by flow cytometric analysis with evidence of persistent inflammation. She was transitioned to decitabine, venetoclax, and triple intrathecal chemotherapy leading to complete morphologic remission. She received haploidentical hematopoietic stem cell transplantation. Prior to initiating conditioning (antithymocyte globulin/cyclophosphamide/fludarabine), MRD was 0.173% with abnormalities detected 1/21 metaphases. Transplant course was complicated by cardiac dysfunction requiring brief course of milrinone. She is clinically well without evidence of leukemia or GVHD, now over 100 days from transplantation. Ultimately, genetic testing did not reveal a germline predisposition syndrome.

Conclusion: Rarely, MDS/AML with complex karyotype presents as a rapidly evolving clinical picture with multiorgan failure and elevated inflammatory markers. Management should focus on anti-leukemia treatment, steroids, and interleukin inhibition. Autoinflammatory disruption of the bone marrow microenvironment may impact tumor immune surveillance, predisposition to clonal evolution, promotion of genomic instability, and release of chemo attractants that promote trafficking of leukemic cells.

Poster # 272

CRYPTIC t(6;11) KMT2A-REARRANGEMENT IN A CHILD WITH AML DETECTED BY NEXT GENERATION SEQUENCING

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Background: Risk stratification per AAML1831 is based on identifying alterations including *FLT3*, *NPM1* and *CEBPA* bZIP status, RAM immunophenotype and minimal residual disease (MRD) after Induction I. These alterations are detected by cytogenetics, fluorescence in situ hybridization (FISH), flow cytometric immunophenotyping and next-generation sequencing (NGS). While FISH is better at detecting translocations such as *KMT2A* rearrangements (*KMT2A*-R), polymerase chain reaction (PCR) and sequencing methods including NGS are better at detecting MRD and cryptic translocations. Since risk stratification impacts treatment and the potential need for hematopoietic stem cell transplantation (HSCT), detection of clinically significant alterations is crucial.

Objectives: We report a rare pediatric case of AML where initial karyotyping and *KMT2A* breakapart FISH were negative for routine AML associated genetic changes including *KMT2A*-R; however, NGS demonstrated a t(6;11), *KMT2A*-*AFDN* (previously *AF6* or *MLLT4*) fusion both by DNA and RNA sequencing. This result was confirmed by dual probe FISH for each gene partner (*KMT2A* and *AFDN*), confirming the NGS result and changing risk stratification and subsequent treatment.

Design/Method: Single subject case report.

Results: Our patient was a 20-month-old male who presented with fatigue, bruising and bleeding. Flow cytometric immunophenotyping confirmed a diagnosis of AML with 80% bone marrow blasts. He had no CNS involvement and initially responded to treatment with ADE + GO.

The bone marrow had a complex cytogenetic pattern with multiple alterations but was negative for del(5), del(7), t(8;21), inv(16), and *KMT2A*-R on both karyotype analysis and FISH. NGS results, however, demonstrated a t(6;11) *KMT2A-AFDN* fusion, along with mutations in *FLT3*, *TP53*, *KRAS* and *NRAS.* Given the discrepancy between cytogenetics, FISH and NGS, a dual-probe FISH test specific for *KMT2A-AFDN* fusions was performed and confirmed its presence. Given his MRD-negative status after Induction I, it was solely the presence of this particular *KMT2A*-R that made him high risk, requiring HSCT for cure. Unfortunately, he had an early relapse prior to HSCT, was unable to achieve a second remission despite multiple salvage regimens and eventually succumbed to AML.

Conclusion: NGS plays an important role in detecting genetic alterations. NGS that includes fusion detection can help identify clinically significant cryptic translocations such as *KMT2A*-R that can greatly affect treatment decisions. Even though breakapart probes are generally considered superior, a negative breakapart *KMT2A* FISH does not rule out the presence of a *KMT2A*-R as shown in this case. The use of NGS including NGS-based fusion detection should be part of the standard diagnostic work-up for all AML patients.

Poster # 273

THE CHALLENGES IN MANAGEMENT OF ACUTE MYELOID LEUKEMIA IN A PATIENT WITH EMANUEL SYNDROME.

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Background: The t(11;22)(q23.3;q11.2) is the most common recurrent balanced translocation in humans. Carriers of this translocation are phenotypically normal and are usually identified after investigation for multiple miscarriages, infertility, or after the birth of a child with supernumerary derivative 22 syndrome also known as Emanuel syndrome (ES). This translocation results from 3:1 malsegregation of the parental derivative 22. ES is extremely rare and is characterized by multiple congenital abnormalities including severe developmental delays, craniofacial abnormalities, and congenital heart defects. Despite its distinctive features being well described, information regarding the natural history and course is lacking.

Objectives: To describe a case of Acute Myeloid Leukemia (AML) in a patient with ES and challenges in management.

Design/Method: Case Report

Results: A 20-year-old male with a complex medical history presented with fever and fatigue. He was known to have global developmental delay, epilepsy, repaired ventricular septal defect, gastrostomy-tube dependence, and had a history of hypogammaglobulinemia requiring infusions of intravenous immunoglobulins.
On examination, he had dysmorphic facies and was pale. His laboratory investigations showed leukocytosis, anemia, thrombocytopenia, and 58% circulating blasts. Further evaluation showed myeloblasts that were CD33+, favorable cytogenetics (NPM1+), and microarray confirmed ES. The literature regarding the risk for the development of cancer and the outcomes of patients with ES is limited. There exist conflicting studies regarding the risk of breast cancer in balanced carriers of the translocation, but no reported cases of leukemia in patients with ES have been described. The risk for increased toxicities with the administration of chemotherapy is also largely unexplored in this group. He was started on a standard regimen for AML with Gemtuzumab (AALL0531) after multidisciplinary discussions. He attained remission at the end of Induction I, but his course was complicated by multiple bacterial and fungal infections despite appropriate prophylaxis. Hypogammaglobulinemia is a well-recognized feature of ES and could have contributed to his increased susceptibility to infections. He also experienced a 20% decrease in his left ventricular ejection fraction with a total anthracycline dose of 150mg which led to discontinuation of anthracyclines for the remaining duration of his therapy. He proceeded with Intensification I but given the severity of toxicities and parental concern for the patient's quality of life, treatment was discontinued after 2 cycles of chemotherapy and a year later he has remained in remission.

Conclusion: Further research is needed to understand the complexities behind ES and if there exists an increased risk for toxicities associated with chemotherapy.

Poster # 274

VENETOCLAX AND LIPOSOMAL CYTARABINE-DAUNORUBICIN IN REFRACTORY AMKL WITH CBFA2T3-GLIS2 FUSION

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Background: Pediatric acute megakaryoblastic leukemia (AMKL) is a heterogeneous disease which, in the absence of trisomy 21, portends a particularly poor prognosis. The CBFA2T3-GLIS2 fusion oncogene underlies 15-20% of these cases, which are associated with young age, extramedullary disease, and refractoriness to traditional treatment regimens. Overall survival in these patients is consistently shown to be between 14-38%.

Objectives: To describe a 17-month-old girl with primary refractory AMKL with CBFA2T3-GLIS2 fusion and RAM phenotype who developed a complete marrow response to salvage

therapy with liposomal daunorubicin-cytarabine and venetoclax.

Design/Method: Case report.

Results: A 17-month-old girl with a subacute history of fever and emesis was found to be pancytopenic with 80% peripheral blasts. Flow cytometry confirmed AMKL with strong CD56, CD33, CD41, and CD61 expression while FISH demonstrated CBFA2T3-GLIS2 fusion. There were no coinciding cytogenetic or molecular abnormalities detected by G-banding, FISH, and next generation sequencing, although two secondary copy number abnormalities were noted on DNA microarray. Cerebrospinal fluid (CSF) was positive at diagnosis. Her induction included cytarabine, daunorubicin, etoposide, gemtuzumab ozogamicin, and repeated intrathecal cytarabine until her CSF had cleared on three consecutive occasions. During induction, she developed a pathologic fracture of the left femur with MRI findings suggestive of chloromatous disease. Following induction, her marrow demonstrated a 2.1% population of cells with RAM phenotype and FOLR1 presence by flow cytometry. PET/CT showed an enlarged FDG-avid right paratracheal node. Her second course included epigenetic modification with decitabine and vorinostat, gemtuzumab ozogamicin, fludarabine, high-dose cytarabine, and idarubicin. Follow up marrow evaluation showed 44% blasts by flow cytometry with PET/CT revealing increased size and FDG avidity of the right paratracheal node. Bcl-2 immunostain was diffusely positive. Her subsequent treatment included liposomal daunorubicin-cytarabine (CPX-351) and a 21-day course of venetoclax provided as an oral suspension. Treatment complications included prolonged neutropenic fever, bacteremia, and typhlitis. Her subsequent marrow assessments were negative by immunohistochemistry, MRD, and FISH evaluations. CT chest showed a smaller right paratracheal node with extensive central necrosis. PET/CT showed ongoing FDG avidity in the right paratracheal region, which is currently being investigated prior to proceeding with allogeneic hematopoietic stem cell transplant.

Conclusion: AMKL with GLIS2 fusion and RAM phenotype is exceptionally difficult to treat with conventional therapy. Innovative solutions are desperately needed for this grave disease. Assessing Bcl-2 status and incorporating venetoclax and liposomal daunorubicin-cytarabine into initial therapeutic planning should be strongly considered in these patients.

Poster # 275

A PEDIATRIC CASE OF TREATMENT-RELATED MYELODYSPLASTIC SYNDROME WHILE ON THERAPY FOR PRE-B ALL

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Background: Treatment-related myelodysplastic syndrome (t-MDS) is a known, but rare, late effect of cancer therapy, specifically radiation, alkylating agents or topoisomerase II inhibitors. When secondary to treatment with alkylating agents, t-MDS typically occurs 4 to 7 years after therapy, and common cytogenetics include chromosomes 5 and 7 abnormalities. Treatment in children with t-MDS is typically allogeneic stem cell transplant, but the prognosis remains poor.

Objectives: To describe a rare case of a pediatric patient who developed t-MDS while receiving treatment for Pre-B Cell Acute Lymphoblastic Leukemia (pre-B ALL) and to outline the treatment regimen that he received.

Design/Method: Case Report

Results: The patient is a 17-year-old male who was diagnosed with high risk pre-B ALL (CNS2) in November 2017. He received a standard 4-drug induction with negative MRD by flow cytometry at the end of induction. He continued the standard high-risk arm of AALL1131 and received 3000 mg/m2 cyclophosphamide.

While in cycle 6 of maintenance therapy, a routine CBC had 2.8% blasts. A bone marrow aspirate demonstrated severe erythroid and megakaryopoietic dyspoiesis with 13% myeloblasts by flow cytometry. There was no abnormal immature B-cell population. Chromosome analysis showed a reciprocal t(3;3)(q21.3;q26.2); GATA2, MECOM translocation with monosomy 7, consistent with diagnosis of t-MDS.

He completed 4 cycles of azacitidine prior to transplant and his blast percentage in the marrow decreased to 2%. His peripheral blast count cleared after completion of all 4 cycles of azacitidine. He received fludarabine, busulfan, melphalan and rabbit ATG as myeloablative conditioning for haplo-identical allogeneic bone marrow transplant. He received a CD34-selected, T-cell depleted transplant. On day +30 his marrow was negative for disease by flow cytometry and cytogenetics. On day +60 he started post-transplant decitabine maintenance therapy to prevent relapse. He completed 6 cycles of decitabine. Follow-up marrow evaluations after 2, 4 and 6 cycles have demonstrated no evidence of myelodysplasia or leukemia.

Conclusion: Alkylating agents, such as cyclophosphamide, are a known cause of t-MDS which can progress to AML. Generally, this occurs years after completion of therapy, however, this case demonstrates a rare instance of t-MDS developing on-therapy. There is room for improvement in treatment of t-MDS. Hypomethylating agents should be considered for use in patients with t-MDS prior to transplant, to limit additional chemotherapy in already heavily-treated patients. Maintenance therapy with hypomethylating agents post-transplant should be considered in patients at high risk of relapse.

Poster # 276

HIDDEN LYMPHOMA: VANISHING BILE DUCT SYNDROME PRECEDING HODGKIN RELAPSE BY 10 MONTHS

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Background: Vanishing bile duct syndrome (VBDS) is a rare form of liver injury characterized by progressive destruction of intrahepatic bile ducts leading to cholestasis, confirmed by

ductopenia on liver biopsy. It can be seen with multiple conditions: infection, ischemia, drugs, autoimmune disorders, allograft rejection and malignancy. It is an uncommon presentation of Hodgkin lymphoma (HL), thought to be a paraneoplastic phenomenon, with only case reports of patients presenting with VBDS found to concurrently have HL on the diagnostic work-up. However, there are no reports of VBDS preceding HL relapse.

Objectives: Describe the case of a 19-year-old male with HL in remission who presented with VBDS and no evidence of underlying HL activity and then relapsed 10 months later.

Design/Method: Chart review.

Results: 19-year-old male diagnosed with stage 4B HL in 8/2013, off therapy since 05/2014, presented in 03/2019 with fever, jaundice, direct hyperbilirubinemia and transaminitis. PET-CT showed hyperactive paratracheal and left inguinofemoral lymph nodes, latter was biopsied without evidence of HL. Aspirin and acetaminophen levels normal. Infectious work-up including viral hepatitis panel, HIV, and EBV and CMV serum PCRs negative. Autoimmune hepatitis work-up negative, alpha-1 anti-trypsin and copper levels normal. MRCP and HIDA scan normal. Liver biopsy showed cholestasis with ductopenia, he was started on ursodiol and hydroxyzine. However, pruritus worsened, bilirubin uptrended and he developed liver failure. Methylprednisolone 40 mg BID was added but weaned over 18 days due to lack of improvement, added ciprofloxacin/metronidazole briefly with transient improvement. Repeat MRCP unchanged. Serum and urine CMV PCR positive. Repeat liver biopsy showed cholestatic hepatitis with ductopenia, tissue CMV PCR positive but no histologic signs of active infection. He was started on valgancyclovir. Repeat PET-CT showed hyperactive paratracheal lymph nodes and moderate colitis of ascending colon and cecum. Paratracheal lymph node biopsy negative for lymphoma, colonoscopy negative for lymphoma or inflammatory bowel disease. Valgancyclovir discontinued after two negative CMV serum PCRs (4 weeks of treatment) but continued on ursodiol, bilirubin and LFTs normalized. He then presented in 7/2020, 6 years off-therapy, with fever, pancytopenia, hepatosplenomegaly and pulmonary consolidations. Bone marrow biopsy showed classical HL infiltration. PET-CT confirmed stage 4B HL relapse.

Conclusion: VBDS is a well recognized but poorly understood and rare presentation of HL. Etiologic work-up should include screening for underlying lymphoma. Here we present the first case to our knowledge of VBDS with no evidence of underlying active lymphoma preceding HL relapse by 10 months.

Poster # 277

ANTI-N-METHYL-D-ASPARTATE RECEPTOR ENCEPHALITIS AS INITIAL PRESENTATION OF HODGKIN LYMPHOMA

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Background: Anti-N-Methyl-D-Aspartate receptor (NMDAR) encephalitis is an autoimmune encephalitis which can occur as a paraneoplastic syndrome. Paraneoplastic anti-NMDAR encephalitis is most commonly seen in females of reproductive age with ovarian teratomas and rarely seen in pediatric cancers. Clinical presentation includes viral-like prodromal symptoms, followed by psychiatric symptoms, short-term memory loss, language disturbance, and ultimately, decreased responsiveness associated with agitation, catatonia, abnormal movements, and autonomic instability. First line therapy includes tumor directed treatment and may also include steroids, IVIG, and/or plasma exchange depending on severity of symptoms.

Objectives: We describe the case of a 10-year-old female who was found to have nodular sclerosing Hodgkin lymphoma with paraneoplastic anti-NMDAR encephalitis.

Design/Method: Case report and literature review

Results: A previously healthy 10-year-old female presented with acute on subacute changes in mental status including confusion, aggressive behaviors, short-term memory loss, and psychosis, oral automatisms, and urinary retention. At an outside hospital she had a normal head CT and laboratory workup and was initially provided psychiatric care recommendations. Further workup due to persistence of symptoms showed CSF pleocytosis, encephalopathy on EEG, and an incidental anterior mediastinal mass on spine MR, which was confirmed by chest CT measuring 5x4 cm and raising concern for paraneoplastic encephalitis. Labs were notable for mild leukocytosis, thrombocytosis and LDH elevation. CMP, uric acid, urine HVA/VMA, alpha-fetoprotein, and beta-HCG were normal. While awaiting biopsy results, she received methylprednisolone (discontinued after tumor identified), two rounds of plasma exchange (discontinued after patient pulled line), and three doses of IVIG for treatment of presumed paraneoplastic encephalitis. Biopsy of mass demonstrated nodular sclerosing Hodgkin lymphoma. PET and CT scans showed an enlarged right paratracheal lymph node in addition to the known mass. Paraneoplastic encephalitis workup revealed positive CSF NMDAR antibodies. She was treated per COG AHOD0031 protocol for intermediate risk Hodgkin disease. She received IVIG every four weeks while undergoing chemotherapy for total six months. After cycle 2 of chemotherapy, she was approaching her baseline, with only minor episodes of agitation. End of therapy imaging showed a 67% reduction in size of mass with negative PET scan. She is now 8 months off therapy and remains in remission and at her neuropsychiatric baseline.

Conclusion: In children who present with unexplained neuropsychiatric symptoms, paraneoplastic anti-NMDAR encephalitis should be considered. This case demonstrates a rare presentation of paraneoplastic anti-NMDAR encephalitis in a common pediatric cancer diagnosis with successful treatment involving standard of care chemotherapy including steroids, plasma exchange, and IVIG.

Poster # 278

WHEN A LUMP IS MORE THAN JUST A LUMP: ANAPLASTIC LARGE CELL LYMPHOMA PRESENTING AS A BREAST MASS

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Background: Anaplastic Large Cell Lymphoma (ALCL) is a rare non-Hodgkin T-cell lymphoma characterized by cluster of differentiation (CD) 30 positivity. Four major entities have been described: anaplastic lymphoma kinase (ALK) positive or negative, primary systemic ALCL, cutaneous ALCL which is ALK negative, and a subtype related to breast implants. More than 90% of the pediatric cases are ALK positive. We report a rare case of pediatric systemic ALK negative ALCL with an atypical presentation as a painful breast mass.

Objectives: To describe an uncommon lymphoma with a rare presentation and protracted course, and highlight the importance of including such pathologies in the differential diagnosis and evaluation of breast masses in pediatric patients.

Design/Method: Chart review, with pathology and radiology departments providing additional review and comments of original pathology and imaging findings.

Results: A 14-year-old Hispanic female presented with a firm, tender breast mass without systemic symptoms. Initial ultrasound showed a hypoechogenic complex cyst.; Ffine needle aspiration (FNA) reflected inflammatory characteristics. Due to persistent swelling and pain, further work up was done, remarkable for elevated inflammatory markers. CT scan revealed a hyperdense region corresponding to the previous ultrasound findings. Core-needle biopsy showed large, atypical, CD30 positive cells, negative for lymphoid or epithelial markers. Empiric antibiotic treatment for a presumed infectious cause was given, with good response and shrinkage of the mass. However, it later recurred, with subsequent ulceration of the skin and serosanguinous drainage. This prompted an excisional biopsy, showing a mixture of inflammatory and scarred large cells with abundant cytoplasm, large nuclei and prominent nucleoli. Immunochemical stains were positive for CD30 and MUM1 and negative for epithelial, B cell and histiocytic markers, and ALK. Findings were consistent with ALK-negative ALCL. Stage work up with PET-CT showed vertebral body involvement and bone marrow sparing, consistent with stage 3 anaplastic large cell lymphoma.

Conclusion: Despite the generally benign features of most pediatric breast masses, it can be challenging to consider additional, more systemic diagnoses like the one reported here. The rarity of ALCL in the pediatric population increases the difficulty of timely diagnosis. With the limitation of fine needle biopsy, excisional biopsy should be considered in suspected cases.

Poster # 279

FOLLICULAR LYMPHOMA PRESENTING AS HYPERTENSIVE URGENCY AND PELVIC MASS IN AN 18-YEAR-OLD FEMALE

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Background: Follicular lymphoma (FL) is an indolent form of Non-Hodgkin's lymphoma, typically presenting during the seventh to eight decades of life. It is extremely rare in pediatrics. Here we describe an unusual case of follicular lymphoma initially presenting as hypertension in an 18-year-old female.

Objectives: We describe the diagnosis and management of a case of FL involving the female genitourinary system in an adolescent.

Design/Method: Authorization for release of health information pursuant to HIPAA was obtained and chart review done to obtain relevant history, laboratory values, imaging, and pathology.

Results: An 18-year-old female with a medical history of obesity presented with new onset frontal headaches and photophobia. She was found to be hypertensive and admitted to the PICU for management and further investigation. MRI revealed a 6.1 x 6.0 x 5.5 cm mass in the right pelvis. The mass infiltrated the urinary bladder, urethra, right sided parenchymal tissues, vaginal wall, and vesiculo-uterine space. An open biopsy and partial excision of her pelvic mass with dissection of the bilateral pelvic lymph nodes and obturator nodes was performed.

Pathology of the pelvic mass was found to be consistent with a low-grade FL. Histologic sections showed diffuse and infiltrative proliferation of predominantly centrocytic cells with the immunophenotype: CD20+, PAX5+, BCL6+, CD10 dim, and BCL2-. The background consisted of abundant T-cells and fibrosis. The proliferation index was difficult to evaluate in the B-cells given the abundant admixed T-cells. FISH studies for IGH/BCL2 gene rearrangement was negative. Lymph nodes showed reactive follicular hyperplasia.

The patient exhibited no other symptoms, including fevers, weight loss, pain or local symptoms from the mass. Staging PET/CT showed hypermetabolic irregular mass encasing the cervix and inseparable from the posterior bladder and anterior rectal wall with an SUV max of 11.7.

The decision was made to treat with low-dose proton beam radiation, with follow up PET scans to assess response, due to the infiltrative nature of the tumor and its attendant side effects that included hypertension.

Conclusion: FL involving the female genitourinary system with clinico-pathologic features similar to our case have been rarely reported. They may represent a distinct subtype of FL similar to those presenting at other extranodal sites. The initial presentation of hypertension and headaches is unusual and highlights the importance of maintaining a broad differential. Coordination between adult and pediatric oncological practices is essential in the management of children/ adolescents with tumors typically seen in adults.

Poster # 280

MANAGEMENT OF PRIMARY HIGH-GRADE B-CELL LYMPHOMA OF THE PARASPINAL REGION WITH SPINAL INVASION

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Background: High-Grade B-cell lymphoma (HGBCL) is a rare entity in the pediatric population. Common sites of extra-nodal occurrence are in the gastrointestinal tract, followed by bone marrow, with central nervous system being the least common site. We present a 15-year old male with Primary paraspinal High-Grade B-Cell Lymphoma with spinal invasion involving the L4 vertebral body, who is being treated with chemotherapy as per ANHL1131.

Objectives: The objective is to describe a case of pediatric paraspinal HGBCL, NOS, with CNS invasion and discuss our management strategy for this rare malignancy that otherwise bears a good prognosis.

Design/Method: A retrospective chart review is performed to gather relevant data.

Results: Patient presented to pediatric neurosurgery with rapidly progressive low back pain, right lower extremity numbness and foot drop. MRI of the spine shows an infiltrative mass involving the L4 vertebral body and paravertebral soft tissue with severe epidural compression of the thecal sac and neural foramina. Emergent surgical decompression via debulking of spinal portion of the mass was performed with L4 laminectomy, but the paraspinal portion of the mass was not resected. Pathology confirmed a diagnosis of HGBCL, not otherwise specified, strongly CD20 positive. Fluorescence in situ hybridization was negative for MYC-N, BCL-2 and BCL-6. Bone marrow biopsies/aspirates and cerebrospinal fluid were negative for disease. Per the St. Jude's (Murphy) Staging and revised pediatric NHL staging system, patient was Stage IV and treated on the Group C1 arm of ANHL1131. Given the altered lumbar anatomy and frequency of intrathecal chemotherapy administrations, patient received an Ommaya reservoir in addition to a Broviac central line.

Conclusion: Pediatric paraspinal HBCL, NOS, with CNS invasion is a rare but aggressive pathology that historically has the worst outcome. Adult regimen employing R-CHOP has shown statistically significant improvement in event free survival. Our patient tolerated treatment as per ANHL1131 Group C1 arm with Rituximab, without significant complications, with only Grade 3 mucositis. The use of an Ommaya reservoir facilitated therapy for the CNS compartment greatly, without need for sedation. Imaging obtained after cytoreductive therapy, and after one cycle of induction, showed radiographic and clinical response of the portion of tumor not initially resected in the paraspinal region. The current literature is limited in terms of other treatment options and highlights the need for perhaps targeted therapy that minimizes the acute and chronic impact to the immune system as a result of Rituximab.

Poster # 281

CNS LCH AND NEURODEGENERATIVE SYNDROME RESPONDING TO MEK INHIBITOR AFTER BEING REFRACTORY

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Background: Langerhans cell histiocytosis (LCH) is rare myeloid neoplasia of CD1a+/CD207+ dendritic cells. The incidence in children is 2–9 per million/year with peak age 1-4 years. The presentation can vary from isolated skin or bone lesions to life-threatening multisystem disease. Central nervous system (CNS) LCH can present as headache, ataxia, dysmetria, learning disabilities, or behavioral issues. Five percent of the patients will develop neurodegenerative disease. Radiologically identified by the presence of T2 and FLAIR hyperintensity lesions. BRAFV600E mutations were reported in 60% of the patients. The standard therapy for CNS LCH is a combination of Vinblastine and steroids but the management of non-responders or neurodegenerative disease remains an ongoing challenge.

Objectives: We report a pediatric patient with CNS LCH, neurodegenerative syndrome and BRAF Exon 12 Deletion who responded to MEK inhibitor Trametinib and Cytarabine after being refractory.

Design/Method: A previously healthy 13-year-old girl initially presented with headaches, memory lapses, hallucinations, and behavior issues. She was diagnosed with low-grade glioma after ventral hypothalamic mass biopsy showed glial tissue with rare atypical cells. Mass was BRAFV600E, H3k27M, and IDH 1 negative. She was treated with Carboplatin and Vincristine for 15 months and the size of the brain lesion improved. One year later she presented with frequent falling events and repeat imaging showed that the hypothalamic lesion had grown in size. Later she developed fever, and PET scan showed lytic FDG-avid lesions in the right acetabulum, right inferior pubic ramus, and ribs.

Results: Immunohistochemical stains showed that the lesional cells were strongly positive for CD1a and S100 protein, characteristic for LCH. BRAF Exon 12 Deletion was also detected. She was started on Vinblastine and steroids for 3 cycles but she developed numerous endocrine complications. She was switched to Cytarabine and Trametinib, and completed 7 cycles with an outstanding response to therapy.

Conclusion: There is no established optimal therapy for refractory CNS LCH or neurodegenerative syndrome. Our case demonstrates that molecular targets could lead to effective and maintained response in these patients.

Poster # 282

A RARE CASE OF SOLITARY CUTANEOUS ALK-POSITIVE HISTIOCYTOSIS IN AN INFANT

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Background: ALK-positive histiocytosis is a rare form of histiocytic proliferation characterized by ALK immunoreactivity. The initial cases, first described in 2008 by Chan *et al.*, comprised three female infants who presented with pallor and were subsequently found to have disseminated disease, manifesting as hepatosplenomegaly, anemia, and thrombocytopenia. Since then, 18 cases have been reported in the literature with a variety of clinical presentations across diverse age groups, highlighting the heterogeneity of this disease entity. Of note, two distinct phenotypes have emerged: infants and toddlers with systemic disease; and localized disease in older children and adults. Treatment regimens include excision, chemotherapy, or targeted therapy, with choice of therapy dependent on the extent of disease and the organs involved. In the majority of cases, good clinical outcomes have been achieved.

Objectives: We report a unique case of an infant with localized ALK-positive histiocytosis confined to a lesion of the skin.

Design/Method: Case report

Results: A seven-month-old male infant presented with a cutaneous lesion on his back, first noticed at three months of age, which grew to an erythematous pea-sized lump. The infant was otherwise well with no other physical exam findings and he underwent excision of the lesion. Gross examination of the skin biopsy showed a papular tan lesion measuring 0.9 x 0.5 cm. Histopathological examination revealed a multinodular dermal lesion consisting of plump spindle and large epithelioid cells, extending from the dermoepidermal junction with some infiltration into the underlying subcutaneous adipose tissue at the deep resection margin. The lesional cells were large and pleomorphic with irregular infolded nuclei, vesicular chromatin, and abundant eosinophilic cytoplasm. Infiltrating collagen fibers, mitotic activity, and multinucleated giant cells were seen. An initial immunohistochemistry panel was consistent with a histiocytic neoplasm, and further immunohistochemical workup revealed strong ALK positivity. Taken together, these findings were consistent with ALK-positive histiocytosis. Importantly, due to the possibility of disseminated disease, investigations were carried out to rule out multi-organ involvement. Physical exam, bloodwork, abdominal ultrasound, and skeletal survey revealed no abnormalities. The patient underwent secondary excision, which demonstrated presence of ALK-positive histiocytosis in the resected material with negative margins. The patient has no signs of recurrence and is doing well six months post-secondary excision.

Conclusion: ALK-positive histiocytosis is a rare disease entity, with no standard course of treatment. Due to the potential for systemic involvement, it is an important differential to consider when evaluating patients with similar histopathological features.

Poster # 283

LANGERHANS CELL HISTIOCYTOSIS MIMICKING POTT'S PUFFY TUMOR IN A CHILD WITH SICKLE CELL DISEASE

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Background: Langerhans cell histiocytosis (LCH) is a rare clonal disorder caused by the abnormal proliferation of CD1a+/ CD207+ dendritic cells. Incidence of LCH is approximately 5 cases per million pediatric patients. LCH can affect a single organ or present as a multisystem disease. It commonly affects skin and bone, including skull lesions, cutaneous eruptions and cervical adenopathy.

Objectives: Case of a 12-year-old African American male with HBSC genotype, positive for COVID-19 who presented with forehead swelling thought to be from osteomyelitis of the frontal bone. Cytology of the aspirate confirmed presence of Langerhans cells excluding all infectious etiologies.

Design/Method: Single case report and literature review.

Results: Patient initially presented with a midline swelling of the forehead with right eyelid swelling, recurrent nosebleeds and headaches. He failed outpatient treatment with Amoxicillin for a presumed sinus infection. Initial CT brain showed destruction of calvarial bone in the right frontal region which led to clinical diagnosis of Potty's puffy tumor, hence broad-spectrum antibiotics were initiated. Repeat CT noted formation of an abscess ~3 x2 cm located anterior to the frontal sinus with bony erosions and periosteal reaction. The frontal swelling increased despite antibiotics and down trending inflammatory markers. As antibiotics failed to improve the clinical picture, osteomyelitis/osteonecrosis was thought to stem from underlying sickle cell disease process. MRI showed fluid collection with enhancement of dura. Ultrasound guided aspiration of the swelling was then performed. Cytopathologic examination revealed abundant inflammatory cells composed of large histiocytic-like cells with irregular, kidney-shaped nuclei in a background of eosinophils, neutrophils and lymphocytes with immunohistochemistry positive for CD1a and S100. Metastatic disease workup including bone marrow biopsy and skeletal survey was negative. Patient underwent bifrontal craniectomy and complete resection of the lesion with cranioplasty.

Conclusion: Clinical presentation of LCH is highly variable and reaching an appropriate, timely diagnosis can be challenging. Sickle cell disease (SCD) is a common disorder predominantly in people of African American descent. We do not postulate a causative link between these two diseases but rather a rare co-occurrence which may have led to delay in management. LCH should be considered in patients presenting with bone lesions evident on imaging especially when infectious etiology has been excluded. Per LCH trials data, there is no role for chemotherapy in the management of uncomplicated single bone lesion when adequate excision is performed and prognosis is favorable. The patient will be followed closely with skeletal surveys over next few years.

Poster # 284

CONCURRENT HEPATOBLASTOMA AND WILMS TUMOR LEADING TO DIAGNOSIS OF BECKWITH-WIEDEMANN SYNDROME

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Background: Beckwith-Wiedemann syndrome (BWS) is an epigenetic overgrowth disorder and cancer predisposition syndrome caused by imprinting defects of chromosome 11p15.5-11p15.4. Phenotypic features include macroglossia, abdominal wall defects, nephrourological anomalies, hypoglycemia, hemihyperplasia, and organomegaly. About 10% of affected children develop embryonal tumors in early childhood [1], including Wilms tumor (WT) (52%) and hepatoblastoma (14%), among others [2]. Patients with segmental uniparental disomy (UPD), upd(11)pat, and IC1 gain-of-methylation (GoM) classified by methylation analysis have a higher tumor risk [3,4].

Objectives: To report the first case of concurrent WT and hepatoblastoma in a child, leading to the diagnosis of BWS with UPD epigenetic classification and describe the approach to management.

Design/Method: Methylation-sensitive multiplex ligation-dependent probe amplification (MLPA) was used to identify defects in IC1 GoM and IC2 loss-of-methylation (LoM) critical regions on chromosome 11p15. Additional molecular testing included tumor-normal whole exome sequencing (WES) and single-nucleotide polymorphism (SNP) microarray of patient only buccal sample.

Results: A one-year-old male ex-29-week fraternal twin presented with abdominal distension with no syndromic features. A 6.6x5.6cm right renal mass and a 9.3x6.4cm hepatic mass were identified by abdominal CT. Alpha-fetoprotein (AFP) was 437,665ng/ml. Initial liver biopsy confirmed hepatoblastoma, mixed fetal and embryonal type, PRETEXT III P-positive, V-negative by imaging. Due to the unusual nature of concurrent tumors, a subsequent biopsy of the right renal mass revealed favorable histology WT. MLPA identified IC1 GoM and IC2 LoM, consistent with paternal imprinting pattern of UPD. WES and SNP microarray showed germline heterozygosity across the entire chromosome 15.

The patient received four cycles of cisplatin, 5-fluorouracil, vincristine, and doxorubicin (C5VD), with dual effect of vincristine and doxorubicin on both tumors. He underwent left hepatectomy and right radical nephrectomy, achieving negative margins and is currently undergoing adjuvant chemotherapy.

Conclusion: This is the first reported case of a child presenting with concurrent hepatoblastoma and WT prompting diagnosis of BWS, UPD subtype. Despite lacking cardinal phenotypic features, his atypical presentation triggered genetic workup. A treatment plan involving chemotherapy and surgery tailored to address both tumors resulted in complete remission.

Upon diagnosis of BWS, molecular genetic testing should be performed for risk stratification, tumor surveillance, and family planning. BWS and other cancer predisposition syndromes should be considered in unusually young patients presenting with WT or concomitant tumors.

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Poster # 285

USING TARGETED THERAPY TO ACHIEVE TUMOR CONTROL IN A PATIENT WITH RELAPSED PANCREATOBLASTOMA

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Background: Pancreatoblastoma is the most common malignant pancreatic tumor in children, occurring with an incidence of 0.004 per 100,000 cases. It has slight male predominance and, in children, the average age at diagnosis is 5 years old. AFP is elevated in ~ 68% of cases and biopsy is imperative for definitive diagnosis. Patients most commonly present with abdominal pain and obstructive symptoms (loss of appetite, jaundice, nausea/vomiting). The mainstay of treatment is complete surgical resection, with administration of neoadjuvant or adjuvant chemotherapy +/- radiation. There is a high rate of recurrence even with resected tumors.

Objectives: Demonstrate successful tumor control utilizing targeted oral therapy in a patient with relapsed pancreatoblastoma.

Design/Method: We describe a patient with relapsed pancreatoblastoma who responded well to targeted therapy based on a BRAF V600E mutation. This mutation has not been previously described in patients with pancreatoblastoma.

Results: A 3-year-old male presented with two weeks of jaundice, decreased appetite, abdominal pain, and hepatomegaly. Evaluation demonstrated an elevated AFP (1 308 ng/ml), hyperbilirubinemia and a pancreatic head tumor. The patient underwent complete surgical tumor resection and pathology demonstrated pancreatoblastoma with duodenal wall invasion and regional lymph node metastasis. Hence the patient was diagnosed with an AJCC Stage 3 (T3N1M0) pancreatoblastoma. Post-operatively he received 4 cycles of cisplatin and doxorubicin after which axial imaging confirmed complete remission. Routine surveillance 11 months later demonstrated an elevated AFP to 142 ng/ml. Imaging at this time revealed retroperitoneal and hepatic disease consistent with tumor recurrence which was confirmed by histology evaluation of the hepatic metastasis. Recurrent disease progressed despite 2 cycles of irinotecan, temozolomide + Palbociclib on an early phase clinical trial. Next generation sequencing on the hepatic metastasis revealed a BRAF V600E mutation. Consequently the

patient was started on a combination of BRAF and MEK inhibition (dabrafenib and trametinib) with sustained clinical and radiological response one year later.

Conclusion: Pancreatoblastoma is a rare tumor in children treated primarily with surgery and chemotherapy but with high rates of recurrence. This case demonstrates the utility of genetic testing in such a rare tumor and reports a BRAF V600E mutation for the 1st time in this disease.

Poster # 286

DIAGNOSTIC AND THERAPEUTIC CHALLENGES IN INFANTILE INFLAMMATORY MYOFIBROBLASTIC TUMOR OF THE LIVER

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Background: Inflammatory myofibroblastic tumors (IMTs) are low grade neoplasms characterized by myofibroblasts in a myxoid/collagenous stroma with infiltrates of lymphocytes, plasma cells, and eosinophils. Oncogenic gene fusions involving receptor tyrosine kinases (RTKs) drive the pathogenesis of IMTs. Anaplastic lymphoma kinase (ALK)-rearrangements are a type of RTK fusion detected in up to 50% of IMTs by immunohistochemistry (IHC). Next generation sequencing is a more powerful technique used to identify oncogenic fusions not captured by IHC, further characterize aberrantly-expressed RTKs, and guide selection of RTK inhibitor.

Objectives: Describe a newborn infant misdiagnosed with an IMT mimicking congenital hepatic hemangioma (CHH).

Design/Method: Case Report

Results: A premature newborn female presented with an abdominal mass. Ultrasound identified a 2.6 x 2.5 x 3.9 cm mass in the left hepatic lobe. MRI demonstrated progressive filling on delayed images which favored CHH as opposed to hemagioendothelioma, hamartoma, or hepatoblastoma. After no response to propranolol, triple therapy with propranolol, prednisolone, and sirolimus was initiated. By three months of age, MRI showed a peripherally enhancing mass measuring 9.7 x 3.6 cm. Ultrasound described a hyper-vascular lesion. She also developed feeding intolerance due to a mass-effect. She also developed hypercalcemia refractory to hydration, furosemide, and calcitonin. Parathyroid hormone-related peptide (PTHrP) was elevated. Sub-optimal response to triple therapy prompted core biopsy to re-evaluate the diagnosis which showed vascular lumina, many of which appeared collapsed, and abundant fibromuscular stroma. The findings supported CHH with treated-related changes. Ultimately, complete resection was not feasible, but subtotal resection alleviated her feeding intolerance and hypercalcemia. Pathology confirmed IMT with an ALK-rearrangement on IHC. Fluorescent in-situ hybridization found an unbalanced ALK-rearrangement with loss of the 5' ALK region. Molecular genetic testing identified a TPM4-ALK gene fusion. PET-CT obtained for staging identified peritoneal sites of enhancement concerning for metastases. Due to her age and

unknown consequences on development, observation for progression with serial imaging was preferrable to upfront targeted therapy.

Conclusion: IMT can be misdiagnosed as CHH based on its overlapping pathologic and radiographic features with other spindle cell, vascular, and inflammatory infiltrative lesions. Thus, consider IMT after treatment failure with standard therapy for CHH. Furthermore, a paraneoplastic syndrome is atypical for hemangioma and suggests underlying malignancy. Resection is the only known cure, but local recurrence is common. In patients with un-resectable disease, ALK-inhibitors such as crizotinib or ensartinib potentially help achieve complete response, resectable disease, or eligibility for liver transplantation.

Poster # 287

PEXIDARTINIB FOR UNRESECTABLE DIFFUSE TENOSYNOVIAL GIANT CELL TUMOR IN CHILDREN: A CASE REPORT

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Background: Tenosynovial giant cell tumors (TGCT) are uncommon benign tumors that usually affect adults and rarely children. By MRI, two clinically different subtypes are distinguished: localized and diffuse. Though seldomly lethal, TGCT cause significant loss of function of joints and overall quality of life. Standard treatment is surgical resection. However, especially in diffuse TGCT which has high recurrence rates, initial and subsequent resections frequently lead to worse functional outcomes and overall quality of life. Systemic therapies are being investigated to reduce this burden. In TGCT, cells overexpress CSF-1. Pexidartinib, a selective CSF-1R oral tyrosine kinase inhibitor, is the first FDA-approved therapy for adult patients with TGCT and severe morbidity or functional limitations not amenable to surgical resection. However, it has yet to be approved for pediatrics.

Objectives: Describe the case of a 15-year-old male with left knee diffuse TGCT not amenable to resection effectively treated with pexidartinib.

Design/Method: Chart review.

Results: 15-year-old male presented with 2-month history of left knee swelling, warmth, pain and limited range of motion. X-ray showed a fibro-osseous lesion in the distal femur metadiaphysis. MRI showed a large joint effusion, severe synovial thickening with frond-like projections, contrast enhancement and blooming artifact, and superficial erosion of articular cartilage, consistent with diffuse TGCT. After 4 months, pain and limitation of range of motion had worsened, repeat MRI showed new erosive changes in tibia. Complete resection carried high risk for loss of function and recurrence so he was referred to Oncology. He was treated with pexidartinib 400 mg twice daily. After four weeks, he reported resolution of symptoms. After 12 weeks, MRI showed >50% tumor reduction with decreased contrast enhancement, near-complete resolution of joint effusion, and improved bone marrow edema. Has now completed 24 weeks of

therapy and remains asymptomatic. He developed depigmentation of hair, no other side effects. He has experienced no liver toxicity.

Conclusion: TGCT are rare in children. Surgery is the primary treatment, but especially in diffuse TGCT, can lead to poor functional outcomes and recurrence. In the near future, systemic therapies targeting the CSF-1R, such as pexidartinib, may play crucial roles as preoperative regimens to reduce surgical morbidity, postoperative therapies to reduce recurrence rates, and may even replace surgical management completely in some cases. Here we present the first case of a child with diffuse TGCT of the knee causing significant functional impairment not amenable for surgery that was effectively treated with pexidartinib.

Poster # 288

UNIQUE PATHOLOGY OF A KIT-MUTATED, SDH DEFICIENT GASTROINTESTINAL STROMAL TUMOR (GIST) IN A 15-YEAR-OLD PATIENT: A CASE REPORT

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Background: Gastrointestinal stromal tumors (GIST) are rare sarcomatous tumors in the pediatric population, with an estimated incidence of 0.08-0.11 cases per million. Adult GIST are predominantly associated with KIT mutations, whereas approximately 85% of pediatric cases are wild-type GIST and demonstrate SDH deficiency or germline SDH mutations. Previous literature and case reports have shown KIT mutations and SDH deficiency to be mutually exclusive pathophysiologic causes of gastrointestinal tumors in the pediatric population.

Objectives: To report a unique case of coexisting KIT-mutated, SDH deficient gastrointestinal stromal tumor in a pediatric patient.

Design/Method: Case report.

Results: A previously healthy 15-year-old female presented with one week of fatigue, pallor, decreased appetite, lightheadedness, abdominal pain and melanotic stool. Laboratory evaluation showed a hemoglobin of 3.7, mean corpuscular volume (MCV) of 88, ferritin of 8, an absolute reticulocyte count of 282, and a positive fecal occult blood test. Upper endoscopy demonstrated multiple gastric lesions with ulceration and a polypoid-like mass at the duodenal bulb. Abdominal CT revealed a lobular extraluminal mass along the greater curvature of the stomach with intraluminal extension. She underwent a partial gastrectomy to remove the multifocal tumor, which was 10.2x4.5x3.0cm in size. Tissue pathology revealed a mixed spindle and epithelioid tumor morphology consistent with a GIST. Surgical margins were positive. Immunostaining was positive for DOG1 and CD34, and negative for SDH-B. Molecular tumor testing identified a c-KIT mutation (exon-11 L576P), no mutations in SDH-A/B/C/D, but nearly absent RNA expression of SDH-C in the setting of high levels of SDH-A/B/D RNA expression. There were no identified germline mutations. Given the rarity of this patient's molecular tumor

testing results, her case was discussed at the National Institute of Health/Life Raft Group's Virtual GIST Tumor Board. There was consensus that, given this patient's co-existing KIT mutation, she would benefit from at least 3 years of imatinib therapy per adult GIST National Comprehensive Cancer Network guidelines.

Conclusion: The patient is currently receiving 400mg of imatinib daily with surveillance CT scans of her abdomen and pelvis as well as chest X-rays every 3 months. The patient is currently 7 months from her tumor resection without evidence of local recurrence, pulmonary chondroma, or paraganglioma. This case report represents the first, known, published description of a pediatric patient with a combined SDH-deficient and KIT-mutated GIST.

Poster # 289

EXTRARENAL MALIGNANT RHABDOID TUMOR OF THE HEART: AN EXTREMELY RARE DIAGNOSIS IN AN INFANT

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Background: Malignant rhabdoid tumors are rare, very aggressive malignancies of infancy, accounting for a high number of relapses and deaths, and an overall survival rate of less than 20%. They can occur at every location in the body; however, localization to the heart is extremely rare, with very few cases reported in the literature.

Objectives: To depict the unusual case of a 5-months-old male diagnosed with extrarenal malignant rhabdoid tumor in the heart after presenting with respiratory distress.

Design/Method: Case Report

Results: A 5-months-old African-American male presented with respiratory distress, fever, and vomiting. Evaluation revealed cardiomegaly, a pericardial effusion with tamponade, and bilateral pleural effusions. He underwent intubation, pericardiocentesis, and bilateral chest tubes placement, as well as pediatric ICU admission after suffering a cardiac arrest. A cardiac MRI showed an ill-defined mass infiltrating the mediastinum and superior pericardium, also involving the interventricular septum. A median sternotomy for tumor biopsy was performed; the mass was deemed unresectable due to its complexity and major vessels involvement. The diagnosis of extrarenal malignant rhabdoid tumor was confirmed by loss of SMARCB1 and negative FISH EWSR1 gene rearrangement. Treatment was begun under COG Protocol AREN0321, Regimen UH-1, omitting the anthracycline-containing cycle 1 given concern for cardiomyopathy in the setting of cardiac instability. After two cycles, no significant change in tumor size was achieved, so an intensified individualized rhabdoid tumor therapy consisting of Vincristine, high-dose Cyclophosphamide, and Doxorubicin was initiated. A 75% decrease in tumor size was attained after three cycles of therapy. One month later, an echocardiogram was performed prior to sedation for a line replacement procedure. Results, confirmed with chest CT, showed disease progression. Another tumor biopsy was performed and genomic studies confirmed loss of

SMARCB1. Arrangements for participation in a Phase I trial began; however, worsening of respiratory distress and pleural effusions deemed the patient unsuitable to travel. He was given one dose of Ipilimumab and Nivolumab in an effort to prolong quality of life. Unfortunately, despite all efforts, he died four days later.

Conclusion: Cardiac malignant rhabdoid tumor is extremely rare and has a very dismal prognosis. To date, there are only 3 patients reported in the literature. Two of them died secondary to disease progression, while the third survived after complete tumor resection. Early diagnosis and intensive treatment are necessary to prolong quality of life. However, further research with new treatment modalities is essential to improve survival in patients where complete tumor resection is not possible.

Poster # 290

PAZOPANIB FOR TREATMENT OF REFRACTORY MALIGNANT PERIPHERAL NERVE SHEATH TUMOR (MPNST), A CASE REPORT

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Background: Malignant peripheral nerve sheath tumor (MPNST) are rare, aggressive sarcomatous tumors that arise from peripheral nerve sheaths. They commonly arise among patients with neurofibromatosis type I (NF1). Definitive treatment is surgical excision. Post operative radiotherapy plays an important role in disease free survival rates and Chemotherapy is offered to people who have systemic disease.

Objectives: Majority of MPNST are not sensitive to chemotherapy, progression after chemotherapy and radiation is common. Currently there is no clear guidelines on what to offer patients with metastatic disease that progress or become refractory after chemotherapy, radiation or surgical excision.
Pazopanib is a well tolerated oral medication, that inhibits growth factor receptors associated with angiogenesis and tumor cell proliferation.

This case report is on a 17 years old lady, with Neurofibromatosis type 1, who had a near complete response with monotherapy Pazopanib after progressing post chemotherapy with Iphosphamide and Doxorubicin, radiation and multiple surgical resections.

Design/Method: 17 years old female, with Neurofibromatosis type 1, who complained of a left foot swelling. Physical examination revealed a hard mass, which was confirmed to be Malignant Peripheral Sheath Tumor (MPNST) on biopsy, Unfortunately, disease staging revealed bilateral multiple lung metastases.
Patient underwent below knee amputation of the primary tumor, 6 cycles of Ifosphamide and Doxorubicin chemotherapy, followed by radiation to the remnant lung metastases.
4 months off therapy evaluation showed multiple new lung nodules, one of the nodules was invading the right pulmonary artery, causing tumor thrombus, patient underwent surgical

resection of the lung metastases followed by radiation.
2 months later, new lung nodule was detected on a follow up scan, patient was then started on Pazopanib maximum dose of 800mg daily.

Results: While on Pazopanib Treatment, the solitary lung nodule regressed more than 80%, patient ultimately stopped Pazopanib after 12 months due to recurrent diverticulitis, a known side effect of Pazopanib.
Off therapy follow up Computerized Tomography follow ups continued to show stable solitary lung nodule ~ 3mm, belevied to be fibrotic tissue at this point as patient is currently 12 months off Pazopanib.

Conclusion: Pazopanib led to a durable near complete response in a patient with MPNST who progressed through heavy chemotherapy, radiation and multiple surgical resections.

Poster # 291

COEXISTING ARTERIOVENOUS FISTULA IN A CHILD WITH SUPRASELLAR GERM CELL TUMOR - CASE REPORT

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Background: While the coexistence of an arteriovenous malformation with astrocytoma is well documented in the literature, coexistence of vascular malformations with concurrent germ cell tumor has rarely been reported, especially in children. Early detection and prompt management of this manifestation can prevent devastating permanent neurologic sequalae in affected children.

Objectives: To report a case of a pediatric patient with an arteriovenous (AV) fistula coexisting adjacent to a suprasellar mixed germ cell primary tumor.

Design/Method: Case report

Results: An 8-year-old previously healthy, African American female presented with acute-onset right-sided hemiparesis, right facial paresis and left third nerve palsy with a preceding history of nausea and vomiting for 3 weeks, and progressive headache for 1 week. Magnetic resonance imaging (MRI) demonstrated a hypervascular, suprasellar mass with intra-tumoral hemorrhage and left anterior thalamic infarct. Dynamic MR angiogram (MRA) and computer tomography angiogram (CTA) of the brain demonstrated intracranial AV shunting in the suprasellar and parasellar regions. Diagnostic cerebral angiogram confirmed erosion of the left posterior communicating artery by the tumor as the cause of AV shunting. Transarterial embolization with coils and n-butyl cyanoacrylate glue of the left posterior communicating artery AV fistula was performed to prevent further tumoral hemorrhage and protect against subarachnoid hemorrhage. A second embolization was required to completely close the fistula seven days later. Elevated

serum α-fetoprotein (AFP; 41 ng/mL) and serum β-human chorionic gonadotropin (β-hCG; 168,552 milli IU/mL) along with an elevated cerebrospinal fluid AFP (2.4 ng/mL) and β-hCG (>9000 milli IU/mL) suggested the diagnosis of a mixed germ cell tumor. She was additionally found to have pulmonary metastases. She underwent chemo-radiation therapy and remains disease free 2.5 years since diagnosis. Repeat MRA 1.5 years from diagnosis showed complete resolution of the AV fistula with appearance of asymptomatic radiation-induced cavernomas. She had marked neurologic recovery with only mild, residual, right-sided weakness and no cranial nerve deficits.

Conclusion: We report the first case of a pediatric patient with a primary suprasellar germ cell tumor and coexisting adjacent AV fistula. While the pathophysiology of the AV fistula is unclear and may be related to tumor secretion of β-hCG, this case report highlights the need to consider and recognize this rare manifestation so that timely, lifesaving neurovascular intervention may be undertaken to prevent catastrophic neurologic deficits.

Poster # 292

UNDER THE RED SEA OF SYNOVIAL SARCOMA: CASE OF A PRIMARY SYNOVIAL SARCOMA PRESENTING AS A HEMOTHORAX

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Background: Synovial sarcomas are tumors of possible mesenchymal origin, named after their histologic similarity to synovial cells. They are more common in adolescents and young adults and can be associated with a t(X;18)(p11.2q11.2) translocation, resulting in fusion of the SS18 and SSX genes. Pleural synovial sarcomas represent <0.5% of pulmonary malignancies. Few cases have been described, more so in the pediatric population. There is no consensus in treatment, but surgery is the gold standard; chemotherapy and adjuvant radiotherapy have been used in unresectable tumors, however their efficacy is unknown.

Objectives: We describe the case of a 14-year-old female with massive hemothorax found to have a primary pleural synovial sarcoma.

Design/Method: Chart and literature review.

Results: Our patient is a 14-year-old female who presented with a 1-month history of episodic shortness of breath and left shoulder pain with acute worsening of her symptoms 1 day prior to arrival. Upon examination, she was noted to have shallow respiration and hypoventilation of the left lung. Chest XR showed a massive left sided fluid collection with mass effect on the mediastinum, for which she underwent emergent thoracentesis draining 1L of sanguinous fluid. CT angiography of lungs revealed extensive consolidation of the left upper and lower lobes with hypoenhancement of the latter lobe which raised concern for necrotizing pneumonia versus malignancy. As her infectious workup returned negative and she failed to improve after a course

of antibiotics, she underwent a VATS procedure with bronchoscopy which revealed a mass in the posterior lower lobe. Hemothorax fluid cytology was positive for histiocytes. Full body MRI showed irregular thickening of the entire left hemithorax pleura and a basal heterogeneous mass, but no metastatic disease. Biopsy yielded spindle cells (TLE-1, OSCAR, BCL-2, and EMA positive, and S100, desmin, and myogenin negative); karyotype and tumor FISH detected t(X;18)(p11.2q11.2) and SS18/18q11.2 rearrangement with 3'SS18/18q11.2 deletion, confirming the diagnosis of synovial sarcoma. She was started on chemotherapy with ifosfamide and doxorubicin per protocol ARST0332. To date, she has completed 4 cycles with significant decrease in tumor size and resolution of her hemothorax.

Conclusion: Hemothorax may be the first sign of pleural synovial sarcoma. Cytology is positive in up to 50% of malignant effusions; when clinical suspicion is high but cytology is negative or non-conclusive, a thorough workup including pleural biopsy should be performed to achieve final diagnosis.

Poster # 293

STERILIZATION OF PEDIATRIC PATIENT TO MINIMIZE RISK OF SMALL CELL OVARIAN CARCINOMA

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Background: Thirteen-year-old female with cancer predisposition syndrome of pathogenic mutation in the SMARCA4 gene underwent bilateral salpingoophorectomy to minimize her risk of developing small cell carcinoma of the ovary, hypercalcemic type (SCCOHT).

Objectives: The goal of this case report is to highlight the medical and ethical complexity surrounding sterilization of a pediatric patient with limited safe fertility preservation options to decrease lifetime risk of an aggressive cancer.

Design/Method: This is a case report developed from patient's chart review.

Results: Small cell ovarian carcinoma, hypercalcemic type is an extremely aggressive cancer with poor five-year survival rates, no targeted therapies, and ineffective surveillance options. Surveillance consists of labs and ultrasounds, though early detection does not affect outcome. Expert consensus is to perform prophylactic oophorectomy upon diagnosis in adults; though there are no clear recommendations in children. This patient's family history suggests that penetrance is quite high as four family members developed ovarian cancer, with youngest at age 16 with death within one year of diagnosis. Fertility preservation in this prepubertal patient posed an issue as there would be risk of ovarian cancer in preserved ovarian tissue and concern for inducing tumor growth with ovarian stimulation for preservation. Given the patient's age, her understanding of her oncologic risks and the implications of the surgery was unclear. Following multidisciplinary visit with Adolescent Gynecology, Oncology, Genetic Counseling, and Psychology, as well as Ethics Committee review of the case, decision was made to recommend

bilateral salpingoophorectomy in the prepubertal stage. However, patient underwent menarche within the next month, which allowed for successful fertility preservation prior to surgery.

Conclusion: Presence of pathologic mutation of SMARCA4 gene portends a high risk for SCCOHT. Prophylactic oophorectomy in a pediatric patient with this cancer predisposition and strong family history should be considered with care by a multidisciplinary team. Ethical evaluation should take place prior to sterilization of a pediatric patient.

Poster # 294

SMALL CELL OVARIAN CARCINOMA OF THE OVARY HYPERCALCEMIC TYPE IN A 12 MONTH OD FEMALE

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Background: Small Cell Carcinoma of the Ovary Hypercalcemic Type (SCCOHT) is a highly aggressive neoplasm that primarily affects young adults and adolescents. SCCOHT is a rare tumor accounting for less than 1% of all ovarian cancers. Since it was first described in 1982 less than 500 cases have been reported. Floral and colleagues have described a case in a 14 month old female which is believed to be the youngest known case until now. Here we present the case of a 12 month old female recently diagnosed with SCCOHT.

Objectives: To describe the presentation and genetic findings of SCCOHT in a 12 month old patient.

Design/Method: The patient is a previously healthy 12 month old female who for a well-child examination. During screening laboratories she was found to be anemic. Within a week the patient's abdomen was distended and firm to the touch with early satiety and vomiting and irability. She returned to her primary care provider's office where she was found to have a worsening normocytic anemia thrombocytosis and hypertension. Abdominal ultra sound revealed an 8.6 cm mass inferior to the right kidney.
She was urgently referred for further evaluation of a presumed renal mass. At presentation to the pediatric oncology service, labs confirmed a normocytic anemia, elevated blood urea nitrogen, and hypercalcemia. The patient was admitted for transfusion and hydration to correct electrolyte abnormalities prior to computerized tomography scans.
CT scans were notable for a large abdominal mass with central calcifications originating from the left adnexa extending into the right upper quadrant, and scattered enlarged lymph nodes. The patient underwent exploratory laparotomy with excision of the left adenexal mass. Surgical procedure was complicated by severe bradycardia which required atropine, epinephrine and four minutes of cardiopulmonary resuscitation.

Results: Genetic testing revealed a germ line mutation of the SMARCA4 protein which IS found in 43% of SCCOHT. SMARCA4 is an important component in the SWI/SNF complex. Loss of function of the SWI/SNF complex interrupts regulatory function and is key in development of

SCCOHT. As of this time therapeutic approaches aimed at restoring expression of inactive tumor suppressor genes has not been identified. Some studies have shown that Tazemetostat a selective inhibitor of Enhancer of Zeste Homolog 2 expression can serve as a promising therapeutic agent in SWI/SNF deficient cancers such as SCCOHT.

Conclusion: Small Cell Carcinoma of the Ovary Hypercalcemic Type can present at any age and is often associated with SMARCA4 mutations.

Poster # 295

AGGRESSIVE APPROACH TO PRIMARY RENAL MYOEPITHELIAL CARCINOMA

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Background: Myoepithelial carcinoma (MEC) is a rare malignancy arising from soft tissues and less often, from viscera such as the kidney. Primary renal MEC (PRMEC) appears to follow the same aggressive clinical course as other sites, with frequent metastases and high risk of recurrence.

Objectives: We present a patient with PRMEC and treatment sequelae.

Design/Method: Case report

Results: A 6-year-old South Asian male presented with gross hematuria for 2 weeks. On physical exam, a firm abdominal mass was palpated. Imaging revealed a large heterogeneous mass with internal calcifications arising from the left kidney. No renal vein thrombosis or distant metastases identified. The patient underwent a left radical nephrectomy with lymph node sampling; no tumor rupture or intra-abdominal spread was noted. The identification of an EWSR1-KLF15 fusion aided in the diagnosis of PRMEC with metastases to regional lymph nodes.

Following complete resection, he received neoadjuvant radiation to the left flank and para-aortic nodes and chemotherapy as described by the Italian Tumori Rari in Etá Pediatrica project: 4 cycles of Ifosfamide, Cisplatin, and Etoposide (ICpE) followed by 3 cycles of Ifosfamide, Vincristine, and Etoposide (IVE). Intravenous (IV) fluids were given before and after chemotherapy, along with Mannitol for renoprotection. His course was complicated by multiple admissions for febrile neutropenia and non-oliguric acute kidney injury after each chemotherapy cycle without other signs of renal dysfunction. He was initially responsive to IV hydration but less so with later cycles. Upon completion of therapy, he had glomerular filtration testing consistent with chronic kidney disease, stage 3b. He continues to have normal blood pressures and urine output.

Conclusion: MEC tends to follow an aggressive clinical course with poor outcomes. The diagnosis itself may be difficult to establish due to diverse histopathologic features. A unique

EWSR1-KLF15 fusion has been described in PRMEC and was crucial in confirming our patient's diagnosis. A wide array of systemic and targeted therapies has been used to treat MEC with varying responses. The Italian experience with ICpE/IVE had encouraging results, though the cohort was small without any primary renal tumors. Balancing the higher risk of renal injury in a patient with solitary kidney with the curative potential of this nephrotoxic regimen, we proceeded with treatment as described. To date, six months after completing treatment, he has no evidence of residual or recurrent disease. Our experience demonstrates an aggressive approach to PRMEC and the need for improved supportive measures to limit long-term toxicities.

Bisogno, Ped Blood Cancer, 2014

Poster # 296

SYNOVIAL SARCOMA AND SUBSEQUENT PAPILLARY THYROID CARCINOMA IN A PEDIATRIC PATIENT

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Background: Synovial sarcoma (SS) is a translocation driven tumor (t(X;18)) resulting in a fusion of the SYT and SSX genes. SS represents the most common non-rhabdomyosarcoma soft tissue sarcoma in children. Papillary thyroid carcinoma (PTC) is relatively rare in children and is often associated with mutations in the mitogen activated protein kinase pathway (MAPK). There are case reports of both synchronous and metachronous presentations of SS and PTC, but no such report has been made in children.

Objectives: We report the first metachronous presentation of synovial sarcoma followed by papillary thyroid carcinoma in a pediatric patient.

Design/Method: Case Report and Literature Review

Results: An 8 year old male with a history of in vitro conception, asthma, and allergic rhinitis presented with 3 months of right lower limb gait abnormality. MRI demonstrated an iliotibial (IT) band tear, and he was initially diagnosed with right IT band tendonitis.

Twenty-eight months after initial presentation, the patient presented with a 2.5 x 1.5 x 1.3 cm mass at the site of the prior IT band tear. Pathology confirmed Grade I synovial sarcoma. The patient was treated with a complete surgical resection, and no chemotherapy or radiation was administered. Forty-seven months after initial presentation, the patient was noted on surveillance imaging to have a right thyroid nodule. Pathology evaluation after thyroidectomy demonstrated papillary thyroid carcinoma.

Somatic next generation sequencing demonstrated a t(X;18) SS18-SSX2 and BRAF p.V600e mutation in the SS and PTC respectively. The PTC also had two variants of unknown clinical

significance: XPC p.Ala483Thr and KPNB1 p.Lys211Glu.

Conclusion: Prior reports in 2 of 4 adult patients with SS and PTC have been confounded by radiation therapy potentially precipitating the subsequent SS or PTC. Although the somatic mutations in our patient suggest no obvious relationship between the two malignancies, we suspect there may be a link that is yet to be elucidated. Prior studies have postulated that SYT–SSX chimeric proteins may be involved in the transcriptional deregulation of currently unknown specific target genes; and both SSX1 and SSX2 are expressed in low levels in normal thyroid. Potential relationships to other somatic driver events are unknown but represent an interesting area for future investigation.

Poster # 297

ATYPICAL PRESENTATION AND MANAGEMENT OF JUVENILE XANTHOGRANULOMA

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Background: Juvenile xanthogranuloma (JXG) is the most common type of non-Langerhans cell histiocytic disorder of childhood. Typically, 15-20% of patients have lesions at birth with 75% presenting during the first year of life[1]. Adults comprise 10% of cases usually presenting in twenties or thirties with solitary lesions[1]. Cutaneous, subcutaneous and soft tissue JXG typically resolve spontaneously. Symptomatic systemic JXG requires treatment with excision, radiotherapy or systemic chemotherapy.

Objectives: Describe a patient with an atypical initial presentation of JXG that required several cycles of various treatments to achieve complete remission.

Design/Method: Case report

Results: A 24-year-old male was diagnosed with JXG at 21years of age after one year of recurring episodes of worsening headaches, photophobia, diplopia, right V1 and V2 paresthesia, right eye ptosis and orbital swelling. A brain MRI showed a 2.9 cm x 1.6 cm x 1.5 cm right cavernous sinus/parasellar mass with some right cranial nerve V enhancement into Meckel's cave. A lumbar puncture showed a high opening pressure of 26 mmHg. CT imaging showed multiple lytic bone lesions and peritoneal carcinomatosis. Pathology of peritoneal biopsy showed histiocytic proliferation indicating JXG without malignant cells. On initial physical exam presented with cutaneous lesions on scalp. Had a negative comprehensive genetic panel (*NF1, NF2, KRAS, LZTR1, PTPN11* and *SMARCB1*). Six weeks of chemotherapy treatment with vinblastine, methotrexate, leucovorin rescue and high dose prednisone was initiated. Due to refractory disease, 10 cycles of cladribine with maintenance chemotherapy was planned. Eight cycles of cladribine were administered, with the last 2 cycles omitted due to thrombocytopenia in the setting of complete remission. Two weeks of maintenance therapy with 6-mercaptopurine and methotrexate were tolerated before discontinuing systemic therapy due to worsening

pancytopenia and clinical side effects. Continued surveillance with bone marrow evaluation, PET and brain MRI have continued to demonstrate complete remission.

Conclusion: This patient had an unusual clinical presentation of adult onset JXG which required a variety of different treatment cycles to achieve remission. Atypical clinical cases such as this should be reviewed to help clinicians understand the disease course and provide better care for patients.

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Poster # 298

RESISTANCE TO PLATINUM-BASED CHEMOTHERAPY IN A MYOEPITHELIAL CARCINOMA WITH A NOVEL ARID1A MUTATION

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Background: Soft tissue myoepithelial carcinomas are rare, aggressive tumors in the adolescent and young adult (AYA) population. Molecular testing of this rare tumor has identified recurring genetic mutations, including *EWSR1* rearrangements in up to 45% of cases and deletions in *SMARCB1*. *SMARCB*1 is a subunit of the larger chromatin remodeling complex, Switch Sucrose Non-Fermentable (SWI/SNF), a key epigenetic regulator. *ARID1A* regulates gene expression by controlling gene accessibility, and mutations in this gene have been reported in multiple neoplasms such as hepatocellular carcinoma, gastric and gynecologic cancers. Specifically, in ovarian clear cell carcinoma, loss of *ARID1A* is associated with resistance to platinum-based therapy and overall decreased survival. The optimal treatment approach in patients with soft tissue myoepithelial carcinoma has yet to be defined as there is a high rate of recurrence after surgical resection and variable sensitivity to systemic chemotherapy.

Objectives: Describe an AYA patient with treatment-resistant soft tissue myoepithelial carcinoma found to have a novel inactivating *ARID1A* mutation.

Design/Method: The design is a case report of an AYA patient.

Results: This case describes a 23-year-old male who presented with progressive right flank pain. Chest imaging identified a pleural-based lesion extending from the anterior chest wall to the thoracic cavity. The tumor was confirmed to be a myoepithelial carcinoma based on histologic and immunohistochemistry criteria. Genomic testing identified an inactivating *ARID1A* mutation, microsatellite stability, and low tumor mutational burden. The patient completed four rounds of neoadjuvant therapy with ifosfamide, carboplatin, and etoposide in combination with 50 Gy radiation. Surgical resection pathology was significant for limited tumor necrosis (< 5%) consistent with treatment resistance. The patient was followed

closely with surveillance imaging and relapsed five months after surgery. He had considerable disease progression despite pembrolizumab and investigative therapies on early phase clinical trials. The patient elected to pursue hospice care and died six months later.

Conclusion: This case describes an AYA patient with a treatment-resistant soft tissue myoepithelial carcinoma and a previously unreported *ARID1A* mutation. *ARID1A* mutations have been described as potent oncogenic drivers in other tumor types and are reportedly resistant to platinum-based chemotherapy regimens. While we cannot establish clinical guidelines from a single case, our finding expands the molecular phenotype of this tumor, provides a potential mechanism for the observed resistance to platinum-based chemotherapy in a subset of cases, and highlights the need for a new therapeutic approach to this challenging diagnosis.

Poster # 299

RARE CASE OF A PEDIATRIC INTRACRANIAL INFLAMMATORY MYOFIBROBLASTIC TUMOR WITH DCTN1-ALK FUSION

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Background: Inflammatory myofibroblastic tumor (IMT) is a rare, primarily pediatric cancer associated with anaplastic lymphoma kinase (ALK) gene rearrangement in approximately 50% of cases. There are roughly 100 reported cases of intracranial IMT in the literature. This is the first report of intracranial IMT with a DCTN1-ALK fusion, and 1 of only 4 reported IMTs with this fusion.

Objectives: We aim to demonstrate the importance of gene sequencing in diagnosing tumors and the use of entrectinib as an alternative therapy due a hypersensitivity reaction to alectinib.

Design/Method: We followed the patient's therapy and present his progress.

Results: A 17-year-old male presented with a 2-month history of headaches, blurry vision, and slowed mentation with acute onset of difficulty walking.
MRI of the brain revealed a heterogenous mass (7.9 * 5.2 * 5.0 cm) located in the left parietooccipital lobe with internal hemorrhage, vasogenic edema, and hydrocephalus.
A craniotomy with partial surgical resection of the mass, due to excessive bleeding and location, was performed. Histopathology was consistent with a hypercellular, high grade spindle cell neoplasm diagnosed as an undifferentiated spindle cell CNS sarcoma. Next generation gene sequencing discovered a DCTN1-ALK fusion. This led to a supplemental pathology review from a soft tissue sarcoma expert who confirmed a diagnosis of IMT.
He was initially treated with intensive chemotherapy for a presumed diagnosis of high grade undifferentiated sarcoma, but he was switched to targeted immunotherapy with alectinib, an oral ALK inhibitor with good CNS penetration, once the DCTN1-ALK fusion was identified. After starting alectinib, he developed a diffuse rash without anaphylaxis. He was then switched to entrectinib, a multi-kinase inhibitor that also has excellent CNS penetration, instead of

undergoing intensive desensitization therapy to alectinib. He has tolerated entrectinib well without issues. Follow-up MRI of the brain at 6 months showed a marked decrease in tumor size (1.5 * 1.2 cm) with no new enhancing lesions. Clinically, he has been progressing well and has regained significant strength, with very mild residual right arm weakness.

Conclusion: IMT is a rare but important diagnostic consideration when evaluating an intracranial mass in a pediatric patient as it has a better prognosis than most other CNS tumors. Gene sequencing is crucial for confirming the correct diagnosis and guiding treatment with targeted immunotherapy. The patient's tolerance and response to entrectinib after developing a hypersensitivity to alectinib supports alternative ALK inhibitor use as a substitute to desensitization therapy, which can be time intensive and carry risk.

Poster # 300

ATYPICAL PRESENTATION OF JUVENILE XANTHOGRANULOMA: TUMOR OF THE INTERNAL CHEST WALL

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Background: Juvenile xanthogranuloma (JXG) is a benign histiocytic tumor of infancy and early childhood. JXG typically presents as an asymptomatic, solitary skin papule or nodule on the face, neck, or upper torso that typically regresses spontaneously over several years. There can also be systemic JXG, involving one or more organs, with or without cutaneous involvement, and a much more varied clinical course. The lungs are often involved in systemic JXG, however isolated JXG chest wall lesions have rarely been reported in the literature. The few reported cases had no systemic involvement and while some presented with pulmonary symptoms, others were asymptomatic and mass was incidentally detected on imaging.

Objectives: To present a rare case of JXG of the internal chest wall with pleural metastasis and review the literature of extra-cutaneous JXG.

Design/Method: Case report

Results: A 6-month-old female presented with a one-day history of tachypnea and poor breastfeeding. Chest CT with contrast revealed a large right pleural effusion and a 3.4 x 2.2 cm hyperdense soft tissue mass eroding into the 7th rib. Labs were nonspecific. Video assisted thoracostomy (VATS) showed the mass was attached to the pleura of the right lateral chest wall along with multiple metastatic nodules within the pleural space. A biopsy of the primary tumor confirmed the diagnosis of juvenile xanthogranuloma (JXG). Lesions were isolated to the internal chest wall and did not involve the lung.

The patient's respiratory distress resolved upon drainage of the pleural effusion. Given the typically benign nature of JXG and likelihood to involute spontaneously over time, we decided to observe the patient clinically without further planned intervention. Three-month follow-up CT

chest revealed a slightly smaller primary tumor without radiographic evidence of pleural metastasis or effusion. Patient continues to do well.

Conclusion: Juvenile xanthogranuloma (JXG) is well characterized amongst the non-Langerhans cell histiocytoses, however, there is still much to be learned about its varied clinical presentations. Our patient's diagnosis of extra-cutaneous JXG adds to the growing evidence to consider this entity when evaluating pediatric chest wall masses. With a lack of management guidelines due to the limited number of cases, treatment approaches differ amongst isolated extracutaneous JXG lesions in the literature and is dependent on the location, symptomatology, and age of the patient. Remarkably, our patient experienced resolution of symptoms without complete excision of the tumor and there has been no progression of disease at the time of this publication.

Poster # 301

REFRACTORY PAPILLRY THYROID CARCINOMA RESPONSIVE TO SELPERCATINIB IN A PEDIATRIC PATIENT

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Background: Thyroid cancer currently accounts for over 6% of pediatric cancers and has increased in incidence by 3% annually from 1974 to 2013. When diagnosed in the pediatric population, it is typically more advanced than in adults. Papillary thyroid carcinoma (PTC) makes up 90% of pediatric thyroid cancer, and historically has been treated with surgical resection +/- radioactive iodine (RAI). It has also been found to have higher rates of gene fusion than its adult counterpart, with 25-30% of sporadic PTCs harboring a *RET*-fusion. While the use of *RET*-specific tyrosine kinase inhibitors (TKI) has been described in adults with PTC, there is little data describing their utility in pediatrics.

Objectives: To report the response of a RAI-refractory pediatric PTC to selpercatinib, a RET-specific TKI.

Design/Method: Case report and literature review.

Results: A 9-year-old female was incidentally found to have innumerable small pulmonary nodules on chest x-ray, favored to be miliary tuberculosis, along with a right-sided neck lesion most consistent with hemangioma on ultrasound. When undergoing an MRI at 11 years of age, profound hypoxia was noted which prompted further work-up; open lung biopsy confirmed a diagnosis of metastatic PTC. She then underwent emergent total thyroidectomy and bilateral neck dissection, followed by RAI which was complicated by radiation pneumonitis. After 7 doses of RAI (cumulative dose of 280 mCi) she continued to have diffuse pulmonary uptake on I-131 total body scan and persistent oxygen requirement, and thyroglobulin level remained elevated at 810 ng/mL (down from initial value of 2850 ng/mL). Molecular testing performed on her initial resection revealed a *NC0A4-RET* chromosomal rearrangement. She subsequently

started selpercatinib (120 mg twice daily), a highly selective, small-molecule RET kinase inhibitor now FDA approved for pediatric patients ≥12 years with advanced or metastatic RAI-refractory *RET*-fusion positive thyroid cancer. Repeat CT evaluation after 2 cycles of treatment showed significant treatment response with improving partially calcified mediastinal lymphadenopathy and marked radiologic improvement in innumerable pulmonary metastases; thyroglobulin level 143 ng/mL. She has weaned off of supplemental oxygen and has not had any drug-related toxicity.

Conclusion: PTC in pediatrics is often metastatic at diagnosis and can be challenging to adequately treat with the current standard of care[MS1] . This case demonstrates the effectiveness of selpercatinib in a 13-year-old patient with RAI-refractory metastatic PTC with a *RET*-fusion and has been well tolerated. Upfront molecular sequencing of pediatric thyroid cancers with potential use of targeted agents early in treatment should be considered.

Poster # 302

PEDIATRIC GASTROINTESTINAL STROMAL TUMORS: A CASE REPORT

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Background: Gastrointestinal stromal tumors (GIST) are rare entities in the pediatric population and occur only 0.5 to 2.7% of patients below the age of 21. The median age at presentation is 13[1], with a female predominance[2]. Anemia is the most common presentation.The majority are located in the stomach, in particular the antrum[1]. GISTs may occur sporadically or associated with genetic syndromes. GISTs without a KIT or PDGFRA mutation are classified as wild type (WT). WT GIST may harbor succinate dehydrogenase (SDH) A, B, C, D mutations, which may represent a germline inactivating mutation in hereditary paraganglioma syndromes. Other tumors associated with these syndromes include pheochromocytoma, renal carcinoma, thyroid carcinoma and neuroblastoma[2]. Currently, surgery is the mainstay of treatment in pediatric GIST[4].

Objectives: Review the presentation of two pediatric patients presenting with GIST to the same institution within a one week time period.

Design/Method: Case Report

Results: An 18 year old female with a history of iron deficiency anemia accompanied by a history of hematochezia and emesis, presented with a 2 week history of fatigue, palpitations and weight loss. Patient was noted to have a Hgb of 5.7 and low iron; treated with a blood transfusion and iron replacement. An magnetic resonance enterography (MRE) revealed a 5.8 centimeter mass along the lesser curvature of the stomach. Resection of the mass and adjacent enlarged lymph nodes was tolerated well, and histology confirmed metastatic GIST, with low mitotic-karyorrhectic index (MKI).
A 12 year old male with a history of stage 1 Wilm’s tumor, initially diagnosed at 6 months of

age, s/p left nephrectomy and chemotherapy per CCG EE-4A presented with right lower quadrant pain. He had no associated symptoms, including fevers, chills, nausea, vomiting, diarrhea, blood in stool or urine. Physical exam was significant for abdominal distension and tenderness to palpation of the right lower quadrant and labs were significant for leukocytosis. A CT abdomen was performed for concern for appendicitis, and showed an exophytic mass of the lower curvature of the stomach. The patient underwent complete gastric tumor resection and histology confirmed SDH deficient gastrointestinal stromal tumor, with a high MKI.

Conclusion: This case series discusses a classical initial presentation of a GIST as well as a patient with a less common presentation and history of previous malignancy. Germline testing will further delineate possible associations between the discussed malignancies, which might then elicit a baseline for testing and monitoring.

Poster # 303

BILATERAL OVARIAN MASSES IN AN ADOLESCENT WITH CLOVES SYNDROME

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Background: CLOVES Syndrome (congenital lipomatous overgrowth, vascular malformations, epidermal nevi, scoliosis/skeletal and spinal anomalies) is a genetic disorder caused by somatic mutations in the PIK3CA gene. It belongs to the group of disorders collectively referred to as PIK3CA-related overgrowth spectrum (PROS). Complex ovarian cysts in patients with CLOVES, namely those not treated with sirolimus, have not been described.

Objectives: We describe the diagnostic workup and treatment of bilateral ovarian masses in a 14-year-old patient with CLOVES Syndrome who was not treated with sirolimus.

Design/Method: Case Report

Results: This is a 14 year-old female who was born with overgrowth of the face, chest, arm abdomen, and left lower extremity. She has a capillary malformation extending over her chest and left abdomen as well as lipomatous masses of her chest and back. At one year of age, she underwent toe amputation due to macrodactyly, and genetic evaluation from this tissue demonstrated a somatic mutation in PIK3CA (E109 del, variant allele frequency 23%). At 14 years of age, she developed left arm pain consistent with intralesional hemorrhage within a lymphatic malformation. The patient and her family chose not to pursue medical treatment with sirolimus. At 14 years of age, an MRI of her spine was performed due back pain. This showed lipomatous overgrowth and extensive vascular malformation involving her cervicothoracic spine. It also demonstrated a large right-sided complex cystic ovarian mass (8.1x 9.7 x 5.8 cm). Her back pain resolved without intervention and the cystic mass was followe d by abdominal ultrasound. After 6 months, she developed a cystic mass of the contralateral side. Tumor markers (AFP, b-HCG, Inhibin A/B, CA-125, CEA, estradiol, and testosterone levels) were normal. Both masses were surgically removed due to interval growth. She did well postoperatively. Pathology

demonstrated that her right ovarian mass was consistent with a mucinous cystadenoma. Her left ovarian mass was consistent with a corpus luteal cyst. Genetic testing of the mucinous cystadenoma demonstrated the patient's known PIK3CA mutation (E109 del, variant allele frequency 25%). The patient has enrolled in a clinical trial of the AKT inhibitor miransertib and has done well. She has had no recurrence of pain nor development of new cysts or masses.

Conclusion: Patients with CLOVES may be at risk for development of ovarian cysts. As clinical trials for CLOVES/PROS emerge, it is important for practitioners to consider the possibility that these lesions are manifestations of patients' underlying PROS disorder and may be responsive to targeted therapy.

Poster # 304

OSTEOCHONDROMAS MIMICKING LATE LUNG RELAPSE IN A TEEN FOLLOWING TREATMENT FOR WILMS TUMOR

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Background: Wilms tumor (WT) is associated with an excellent prognosis even when advanced. However, survivors may develop treatment-related adverse effects including cardiomyopathy, renal dysfunction, musculoskeletal growth disturbance, infertility, and secondary benign and malignant tumors. Osteochondromas, a relatively common benign bone tumor, have been linked to total body irradiation conditioning prior to hematopoietic stem cell transplant in children treated for high-risk neuroblastoma. Little is known regarding osteochondromas in wilms tumor survivors.

Objectives: To describe late-onset occurrence of osteochondromas that mimicked late Wilm's tumor relapse in a male teenager treated for stage IV Wilms tumor as a toddler, thus adding to the spectrum of late effects reported in this patient population.

Design/Method: Retrospective review of patient medical records, radiographic imaging, and literature review.

Results: A 16-year-old male diagnosed at age 23 months with stage IV favorable histology left renal Wilms tumor associated with five nodules within both lungs. He was treated with left nephrectomy, then chemotherapy per DD4a [vincristine, dactinomycin, doxorubicin] followed by 1200 cGy whole lung irradiation and subsequently evaluated with serial physical exam, laboratory tests, and radiographic imaging. Surveillance chest radiograph 13 years following treatment completion demonstrated a 1 cm soft tissue nodular density in the left lung base concerning for late pulmonary relapse. Follow-up chest computed tomography (CT) showed multiple bilateral rib and scapular lesions, including one corresponding to the nodule noted on the chest X-ray (CXR), that appeared consistent with osteochondroma, and no evidence of pulmonary metastases.

Conclusion: Although chest CT is not part of the routine surveillance studies in wilms tumor survivors, it could be used to help distinguish abnormal findings on CXR. Rib osteochondromas have uncommonly been reported in Wilms tumor survivors, are usually solitary in number, and associated with prior whole lung irradiation. Interestingly, osteochondromas have also rarely been reported in Wilms tumor survivors whose treatment did not include irradiation, possibly related to underlying hereditary multiple osteochondromas (HMO). There is no hereditary cancer predisposition syndrome associated with both Wilms tumor and osteochondromas, but multiple osteochondromas are associated with pathogenic variants in the *EXT1* and*EXT2* genes causing HMO. Radiation-induced osteochondroma carry a higher risk of malignant transformation than non-radiation induced osteochondroma, so ongoing radiographic surveillance is warranted once detected. Evaluation for HMO should be considered in patients who develop multiple osteochondromas and when treatment did not include irradiation.

Poster # 305

OVARIAN TERATOMA MASCARADING AS ENCEPHALITIS IN AN ADOLESCENT

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Background: N-methyl-d-aspartate receptor antibody encephalitis (NMDAR-E) is an autoimmune syndrome previously recognized as a frequent cause of encephalitis among young individuals and adults, most often in women. Teratomas as an etiology for NMDAR-E in adults are well described in close to 50% of the cases, however, this association is rare in children. NMDAR-E is treatment responsive, and tumor removal and immunotherapy are known to reverse the encephalitis.

Objectives: To report an adolescent female with psychosis found to have an ovarian teratoma.

Design/Method: Case report.

Results: A 17 year old Hispanic female with a history of depression, anxiety and self-cutting presented with a 2-week history of altered mental status and seizure-like activity. Her mother noted that 4 weeks prior to symptom onset her father was murdered and her grandfather was diagnosed with cancer. The patient reported an "out of body experience," and developed intermittent episodes of anxiety, giddiness, agitation, left sided paresthesias, decreased appetite, weight loss, auditory and visual hallucinations, with paranoid ideation. A week into the disease process, she experienced two seizure-like episodes for which she was hospitalized. On examination, she was afebrile with episodes of disorganized thoughts and visual and auditory hallucinations. Complete blood counts and comprehensive chemistry were normal; urine toxicology screen and pregnancy test were negative. A head CT and brain MRI with contrast were normal. She continued to have waxing and waning agitation, requiring lorazepam, diphenhydramine, halperidol and physical restraints. She was started on olanzapine with plans to transfer to a psychiatric unit. Cerebrospinal fluid (CSF) evaluation for infectious etiologies,

including HSV, were all negative. An electroencephalogram was suggestive of encephalopathy. Pulse steroids were initiated for presumed autoimmune encephalitis (AE). The CSF autoimmune panel was significant for anti-NMDAR titer of 1:20. Pelvic US and MRI revealed a right ovarian cystic mass. Clinically she developed progressive catatonia, autonomic instability and respiratory depression requiring intubation. An excisional biopsy revealed a mature teratoma confirming the diagnosis of ovarian teratoma-associated anti-NMDAR-E**.** Treatment consisted of steroids, plasmapheresis, IVIG and tumor resection, with gradual resolution of clinical and psychiatric symptoms**.**

Conclusion: NMDAR-E related teratomas may present with neuropsychiatric signs and symptoms, including memory loss, hallucinations, and decreased level of consciousness. Early recognition is important to prevent long term sequaeala. This case highlights the importance of a thorough clinical evaluation in young female patients with new onset neuropsychiatric manifestations and consideration for ovarian teratoma-associated NMDAR-E.

Poster # 306

ACUTE PSYCHOSIS AS AN INITIAL MANIFESTATION OF A PINEAL GERMINOMA IN AN ADOLESCENT MALE

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Background: Intracranial germ cell tumors can be classified as either germinomas or non-germinomatous germ cell tumors. Although psychiatric symptoms are known manifestations of central nervous system tumors, very few cases have been described in pineal germinomas, more so in the pediatric population. These symptoms can be present at onset, during the course or after completion of treatment. Proposed mechanisms include mass effect from the tumor itself or from the secondary obstructive hydrocephalus, presence of anti-brain antibodies, circadian rhythm disorders, and medication induced psychosis from hormone replacement therapy.

Objectives: We describe the case of a 19-year-old male with a pineal germinoma who presented with acute psychosis. His symptoms improved as the tumor decreased in size with chemotherapy.

Design/Method: Chart review of a patient with pineal germinoma.

Results: Our patient is a previously healthy 19-year-old male who presented with a 1-month history of behavioral changes (auditory and visual hallucinations, disorientation to place, and insomnia), with poor response to outpatient psychiatric management. Initial exam revealed flat affect, confused conversation, repetition, disorientation to time and place, and Parinaud syndrome. Neuroimaging revealed a pineal mass with associated hydrocephalus for which he underwent external ventricular drain and subsequent ventriculo-peritoneal shunt placement. Biopsy confirmed diagnosis of pineal germinoma (CD117, PLAP, and Oct 3/4 positive, hCG,

AFP, and CD30 negative, and a Ki-67 high proliferation index). He underwent chemotherapy with carboplatin and etoposide per protocol ACNS 1123, and after 2 cycles had significant decrease in tumor size, and resolution of his psychiatric symptoms. He completed a total of 4 cycles of chemotherapy, followed by whole ventricular proton radiation; to date he has had no recurrence in his symptoms.

Conclusion: Psychiatric symptoms may be the only presenting feature of a pineal germinoma in the pediatric population. A thorough history, physical exam, and high index of suspicion are required for early diagnosis and intervention. Imaging should be considered in patients with focal neurologic findings or atypical psychiatric symptoms. The timeline of symptom onset (initial presentation) and the fact that our patient's symptoms improved after initiation of treatment and decrease in mass size, suggest these behavioral changes were likely related to the tumor itself. Further studies are required to determine the exact mechanism by which pineal germinomas produce psychiatric symptoms, and could provide insight into the pathophysiology and treatment opportunities for psychiatric disorders.

Poster # 307

GIANT CELL TUMOR OF THE OCCIPITAL BONE: A CASE REPORT AND REVIEW OF LITERATURE

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Background: Giant cell tumors of the bone (GCT), also known as osteoclastomas, are locally aggressive primary bone neoplasms, which represent approximately 5% of all primary bone tumors. These tumors are rare in the pediatric population with a peak incidence in the third decade of life, the most common site of presentation is the knee followed by distal radius and proximal humerus. GCT tends to grow rapidly and destroy its primary site and even metastasize. Cranial GCT preferentially involves the sphenoid and temporal bone. There is limited data on the presentation and management when GCT involves the cranial bones.

Objectives: The occurrence of occipital GCT is exceedingly rare, we present the second known instance of a GCT in the posterior fossa of a pediatric patient causing cerebellar compression and a review of worldwide literature of this rare entity to aid with the diagnosis and management of this tumor.

Design/Method: A 9-year-old female presented with a 2- month history of frontal headache that had acutely worsened, blurry vision, and dizziness. An MRI brain showed multiloculated hemorrhagic and an intensely enhancing soft tissue mass arising from the right occipital bone with the expansion of the inner and outer table. There was a mass effect on the right cerebellum and mild effacement of the 4th ventricle noted, without associated hydrocephalus.

Results: The patient underwent occipital craniotomy with gross total resection of epidural midline skull base mass, with the resolution of posterior fossa mass effect. Immunostaining with

CD68 highlighted uniformly distributed osteoclastic multinucleated giant cells with intervening mononuclear dendritic-type stromal spindle cells. Post-surgical recovery was uncomplicated and radiotherapy was not required due to total resection.

Conclusion: Six cases of occipital GCT have been reported in the literature with only 1 pediatric case. There have been more females than males with a median age of 21 years. The main presenting symptom was a headache with other symptoms being neck pain, difficulty swallowing, blurry vision, or localized tenderness. Three patients had total resection of the tumor and only two received postoperative photon radiation. After total resection, local control was achieved in 85% of all cases, with a high rate of local recurrence within two years in incomplete resection cases. The outcome was favorable in most of the cases. Though rare, this case highlights the importance of consideration of GCT in the differential diagnosis in patients with headache and cerebellar symptoms.

Poster # 308

MORE THAN MEETS THE EYE: JUVENILE XANTHOGRANULOMA IN A CHILD WITH HYPERLIPIDEMIA AND BICYTOPENIA

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Background: Juvenile xanthogranuloma (JXG) is a non-Langherhans cell histiocytosis of unknown incidence and pathogenesis. It is usually a self-limited cutaneous disease of childhood presenting with a single raised, rubbery lesion; cases of disseminated skin and systemic involvement (including bone marrow) have been described in the literature. Although rare, an association between JXG and certain blood disorders (such as juvenile myelomonocytic leukemia, acute lymphoblastic leukemia, autoimmune lymphoproliferative disorder, and myelodysplastic syndrome) has been reported.

Objectives: We describe the case of a 6-year-old female with bicytopenia and giant cells on peripheral blood smear (PBS) found to have JXG.

Design/Method: Chart and literature review.

Results: Our patient is a 6-year-old female with past medical history of hyperlipidemia, referred by her pediatrician due to an abnormal routine CBC showing anemia (8.9 g/dl), thrombocytopenia (13,000/µl), and giant cells on PBS. Mother reported that anemia and thrombocytopenia had been noted during her WIC appointments. Denied fever, weight loss, bone pain, easy bruising, or bleeding. Initial exam revealed multiple soft nodules on bilateral auricles, elbows, and knees, previously attributed to her hyperlipidemia, but was otherwise unremarkable. Institutional CBC confirmed bicytopenia. Reticulocyte count (2.01%), triglycerides (276 mg/dl), and LDL cholesterol (222 mg/dl) were elevated. Infectious workup, iron studies, thyroid function tests, and Hemoglobin electrophoresis were unremarkable; lupus, acute leukemia, and FISH MDS panels were negative. Bone marrow aspiration (BMA) showed occasional histiocytes with

phagocytosis of fragmented cells, but no evidence of malignancy. Chromosome analysis of the bone marrow was unremarkable. Punch biopsy of the nodules showed foamy histiocytes (CD4, CD68, ALK, and FXIIIA positive, and S100, CD1a, and langerin negative) and scattered Touton cells with extensive fibrosis consistent with JXG. Although a specific trigger for her bicytopenia was not identified, she remained asymptomatic and with improved cell counts during the hospital course.

Conclusion: The presence of hyperlipidemia can make the distinction between JXG and tuberous xanthomas challenging. Although the diagnosis is usually made clinically, biopsy can be used to distinguish them (with the latter lacking Touton cells). Our patient had bicytopenia, giant cells on PBS, and hemophagocytosis on BMA, suggestive of possible bone marrow involvement. We highlight the importance of performing a thorough workup including BMA when abnormal blood cell counts are found in patients with JXG, as cases of bone marrow involvement and other associated blood dyscrasias have been reported.

Poster # 309

THE USE OF NIVOLUMAB ADJUVANT THERAPY IN A 5-YEAR-OLD WITH STAGE IIIC RESECTED SPITZOID MELANOMA

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Background: Melanoma is the primary skin cancer of pediatric patients, and accounts for 1-3% of pediatric malignancies. The prognosis for both adults and children with melanoma correlates with stage at diagnosis. Surgical management remains the definitive treatment for cutaneous melanoma in all patients, but the value of adjuvant systemic therapy with immune checkpoint inhibitors for improving event-free and overall survival in adults is established and has changed the treatment landscape of melanoma. The rarity of pediatric melanoma limits the robust study of the safety and efficacy of adjuvant therapy in children. Withholding this therapy in pediatric patients due to this lack of data may compromise pediatric melanoma outcomes.

Objectives: Describe a 5-year-old who presented with T3aN3cM0 spitzoid melanoma who was treated with nivolumab adjuvant therapy for 1 year per adult treatment guidelines.

Design/Method: Case report

Results: A 5-year-old boy presented with a 1 cm raised, red papule of his right scapula. Initial clinical diagnosis was a wart for which over-the-counter treatment was recommended. With no improvement after 4 months, he was referred to Dermatology and molluscum contagiosum was diagnosed based on the clinical appearance of the erythematous umbilicated papule with new surrounding smaller pink papules that were treated with cryotherapy. Two months later, biopsy was performed given persistence after cryotherapy. Biopsy revealed spitzoid melanoma with homozygous 9p21 loss associated with *in-transit* metastasis, AJCC 8th edition Stage IIIC

(T3aN3cM0), after complete diagnostic sentinel node mapping/biopsy work-up (2 involved regional lymph nodes). Kaplan-Meier melanoma-specific survival curves show survival rates of 52% at 5 years and 43% at 10 years for adult patients with N3c disease at diagnosis. The patient underwent wide local excision and right axillary completion lymphadenectomy. He was treated with nivolumab adjuvant therapy for 1 year. He tolerated this without dose-limiting toxicity or significant side effects. He remains disease-free 22 months following diagnosis.

Conclusion: Nivolumab is an immune checkpoint inhibitor that targets the programmed death 1 (PD-1) inhibitory receptor, with proven efficacy in treatment of adult metastatic and high-risk operable stage III melanoma. There is limited evidence for its use in treatment of pediatric melanoma, given the overall disease rarity. Recent studies in pediatric advanced solid tumors have shown evidence of safety of anti PD-1 therapy. Our case illustrates that the treatment of pediatric melanoma based on adult guidelines is feasible and may be best practice in the setting of limited pediatric data given robust adult efficacy data.

Poster # 310

HARLEQUIN SYNDROME: A RARE PRESENTATION OF THORACIC NEUROBLASTOMA

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Background: Harlequin syndrome (HS) is a dysautonomic condition involving disruption of hemifacial sympathetic innervation leading to unilateral anhidrosis and lack of facial flushing in response to heat, exercise, or emotional stimuli. Compensatory facial plethora and diaphoresis are apparent on the contralateral side. HS may be congenital, idiopathic, or caused by anesthetic or surgical intervention. Rarely, HS occurs secondary to structural lesions and malignancies. We present a case of HS with subsequent identification of metastatic paraspinal neuroblastoma.

Objectives: Inform clinicians about HS and disrupted sympathetic innervation to enable early screening and detection of occult malignancies

Design/Method: Case report

Results: At 7-months of age, a previously healthy boy showed signs suggestive of HS: he experienced left-sided anhidrosis with contralateral hemifacial flushing and sweating triggered by physical activity. At 12-months of age, he presented with fevers; SARS-CoV-2 PCR was positive. Shortly after defervescence, his mother noted a non-tender left lateral neck mass. Examination revealed supraclavicular lymphadenopathy. Despite the recent viral illness, nodal location was concerning for malignancy. Complete blood count, lactate dehydrogenase, and urine homovanillic and vanillylmandelic acid levels were within normal range. No mediastinal mass was identified on chest x-ray. Lymph node biopsy revealed poorly differentiated neuroblastoma with favorable histology, MYCN non-amplified. Biologic and genetic features were favorable, including no loss of heterozygosity of 1p or 11q. Bone marrow evaluation was

negative. Computed tomography of the chest, abdomen and pelvis demonstrated left upper thoracic paravertebral disease, right submandibular, as well as left cervical, supraclavicular, and axillary lymphadenopathy. Metaiodobenzylguanidine scan detected focal uptake in the corresponding areas of lymphadenopathy. Magnetic resonance imaging of the cervicothoracic spine confirmed left paraspinal neuroblastoma with minimal extension into T2-T3 neural foramina. The patient was treated with two cycles of chemotherapy per COG ANBL0531 with carboplatin and etoposide, followed by carboplatin, cyclophosphamide, and doxorubicin. Subsequent imaging demonstrated an approximate 50% reduction in paraspinal tumor volume. HS symptoms have slightly improved to date.

Conclusion: HS is rare; there are only three cases of HS secondary to neuroblastoma published in the literature to date. We describe a child with paraspinal neuroblastoma extending at T2-T3 causing HS. The anatomical location of the tumor correlates with the child's presenting signs as sympathetic facial vasomotor and sudomotor fibers emerge at this spinal level. This case brings attention to HS, a syndrome that can signal an underlying malignancy. An etiology should be sought in pediatric patients with HS without known cause, including consideration of neuroblastoma.

Poster # 311

MALIGNANT TRANSFORMATION OF PARAVERTEBRAL MASS FROM GANGLIONEUROBLASTOMA TO NEUROBLASTOMA

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Background: Neuroblastic tumors (NT) are the most common extra-cranial solid tumors in childhood and include neuroblastoma, ganglioneuroblastoma, and ganglioneuroma that vary on a spectrum from least differentiated to most differentiated tumors, respectively. It is well known that the nodular type of ganglioneuroblastoma portends risk for malignant behavior and outcome. There is limited literature of the biologic behavior of neuroblasts and ganglion cells in regards to their potential to dedifferentiate into immature tumors , leading to a neuroblastomatous malignant transformation.

Objectives: To describe a case of nodular ganglioneuroblastoma in a pediatric patient with genetically similar components in a new neuroblastic tumor after being disease free for 5 years, concerning for recurrence and malignant transformation of her previous tumor versus a new primary malignancy.

Design/Method: A PubMed search was conducted for queries including "ganglioneuroblastoma", "N MYC amplification", "differentiation" , "neuroblastoma", "transformation", "recurrence" and "Pediatrics." Relevant papers were selected for literature review.

Results: A 13-year-old female with a past medical history of localized retroperitoneal

ganglioneuroblastoma with complete resection in May 2016 was admitted for 2 month history of progressively worsening lower back, bilateral hip, and left lower extremity pain. Imaging showed a large right infiltrative paravertebral lumbar spine mass compressing the L4 Nerve root; the soft tissue component of the lesion measured approximately 5.0 x 2.0 x 3.9 centimeters. Metaiodobenzylguanidine (MIBG) scan showed findings compatible with multifocal osseous metastatic disease of the left shoulder, bilateral acetabula, lumbar spine and proximal left fibula. Biopsy of the paravertebral mass confirmed aggressive neuroblastic tumor, N MYC negative with molecular findings showing chromosome 2cen and N MYC locus probe signal gains as identified in a previous primary tumor interphase FISH study reported for this patient. Staging evaluation showed disease involvement of bone as well as involvement within the bone marrow. The patient was started on treatment per high risk neuroblastoma.

Conclusion: We present a suspected malignant transformation of a paravertebral mass from ganglioneuroblastoma to neuroblastoma after disease free survival of 5 years. This case raises the possibility of a dedifferentiating potential for ganglion cells in her nodular ganglioneuroblastoma of unfavorable type to neuroblastoma versus the presence of a long-term, quiescent form of neuroblastoma. If further cases are recognized, genetic analysis of the lesions might provide more insight into the molecular drivers of possible dedifferentiation into highly malignant neuroblastic tumors.

Poster # 312

ASYMPTOMATIC NEUROBLASTOMA IN A PATIENT WITH SH2D1A-DEFICIENT X-LINKED LYMPHOPROLIFERATIVE SYNDROME

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Background: X-linked lymphoproliferative (XLP) disorder is a primary immunodeficiency associated with increased risk for hematologic malignancies, particularly lymphoma. This case report discusses the unique management issues pertinent to incidental finding of an asymptomatic abdominal mass in these patients during evaluations for curative allogeneic hematopoietic stem cell transplantation (HSCT) for the primary immunodeficieny. This includes the potential for non-hematologic malignancies in these patients, associated with genetic defects in cytotoxic immune editing.

Objectives: We present this case to illustrate the importance of considering potential for non-hematologic malignancies in patients with XLP when determining the diagnostic approach to masses found in these children.

Design/Method: This is a retrospective case report. Informed consent was obtained from parents for communication of patient data.

Results: A 2-year-old male with persistent fevers, cervical lymphadenopathy, and bicytopenia was diagnosed with Epstein-Barr Virus (EBV) viremia and found to have a hemizygous *SH2D1A* mutation associated with XLP. He was referred to our facility for routine pre-HSCT evaluation. An incidental left adrenal mass and mild persistent peripheral lymphadenopathy were discovered on routine CT of the chest and abdomen. The mass was laparoscopically resected and initial frozen section was consistent with neuroblastoma. Multi-disciplinary discussion was held with decision that, if staging work-up revealed high-risk neuroblastoma, the previously planned curative *allogeneic* HSCT for *SH2D1A* deficiency would be preceded by chemotherapy and additional multimodal therapy for neuroblastoma. Final pathology revealed no *myc-n* amplification and metastatic evaluation, including bilateral bone marrow aspirates and biopsies as well as meta-iodo-benzylguanidine (MIBG) scan, was negative. This mass was therefore classified as low-risk ganglioneuroblastoma and he proceeded to matched unrelated donor allogeneic HSCT as previously planned for his underlying disease. He tolerated HSCT well and continues with surveillance screening for ganglioneuroblastoma and with no evidence of recurrence.

Conclusion: This case highlights the need to consider non-lymphoproliferative tumors and to pursue definitive excisional approaches rather than assume that asymptomatic intraabdominal masses are lymphoproliferative in patients with *SH2D1A* deficiency. Individuals with XLP who receive early curative allogeneic HSCT from a healthy donor have a lifetime risk of malignancy only at the background rate for the HSCT regimen itself. Allogeneic (rather than autologous) HSCT as normally pursued as immunotherapy for high-risk neuroblastoma, reduces the overall risk for future malignancies related to known natural killer and other cytotoxic immunosurveillance defects in XLP. The incidental finding of a ganglioneuroblastoma in this patient also suggests a potential role for cytolytic immune populations defective in XLP in neuroblastoma immuno-editing.

Poster # 313

A UNIQUE CASE OF CYSTIC PARTIALLY DIFFERENTIATED NEPHROBLASTOMA IN AN ADOLESCENT FEMALE

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Background: Cystic partially differentiated nephroblastoma (CPDN) is an uncommon renal tumor of childhood. It should be differentiated from other renal tumors such as cystic nephroma (CN) and Wilms tumor (WT) cystic type, as they can all present with an abdominal mass, abdominal pain, and hematuria. CPDN has a male predominance under two years of age. CPDN and CN are typically identical on radiological imaging, with pathology revealing CPDN having blastema cells in septa and a negative DICER1 mutation. WT is characterized by a solid component associated with necrosis, hemorrhage, and histologically consisting of blastema, epithelial, and stromal components. The following case presents an unusual presentation of renal tumor in a 17-year-old female.

Objectives: This is a case presentation of Cystic partially differentiated nephroblastoma in an adolescent female.

Design/Method: Case report

Results: Seventeen-year-old female presented with dysmenorrhea, and pelvic ultrasound (US) showed a didelphic uterus. Due to its known association to renal anomalies, a renal screening US was obtained, which revealed a right cystic renal mass with scant solid component (4.7 x 4.4 x 3.5 cm) in the lower pole. CT chest/abdomen/pelvis showed the lesion to be hypo-enhancing, a normal left kidney, patent vasculature, no lymphadenopathy, and no pulmonary nodules. The lesion was initially monitored with US as the family preferred a non-surgical approach, and the question was raised whether this could represent a hemorrhagic cyst. Follow-up imaging showed a persistent lesion with no changes, and the patient underwent a right partial nephrectomy. The pathology was consistent with CPDN showing cystic appearance with immature nephrogenic elements in septa, which stained positive for WT-1, with no necrosis, hemorrhage, or solid component. Molecular testing was negative for DICER1, ALK, ROS1, MYC, RET, PTEN, PD-L1, BRAF, BRCA1, BRCA2, EGFR, KIT, KRAS, NRAS, PDGFRA, PIK3CA. A post-operative PET scan showed no metastatic disease.

Conclusion: CPDN is a rare entity, which needs to be distinguished from CN and WT as the presentation can be similar, but treatment and prognosis differ. A pathologic diagnosis is imperative as the treatment for CPDN and CN is resection with negative margins, while in WT, it can also include chemotherapy and radiation. DICER1 testing is crucial as CPDN lacks this mutation, while CN has a high prevalence, and WT has been associated with the mutation. Lastly, the presence of DICER1 in a tumor should be followed by germline mutation testing and referral to a cancer predisposition program.

Poster # 314

LATE RELAPSE IN WILMS TUMOR: DOES INTENSE CHEMOTHERAPY IMPROVE SURVIVAL?

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Background: Wilms tumor (WT) is the most common primary pediatric kidney cancer. Five-year survival approaches 90%. High-risk features include age >2 years, higher stage, poor differentiation, anaplasia, and molecular findings like loss of heterozygosity in chromosome 16p, 1p, and 11p15. Relapse occurs in 50% of these high-risk patients, with most common sites being the lungs, original tumor bed, and liver. Among those who relapse, 95% do so within two years of initial diagnosis. Late recurrence (LR) is a relapse after five years in remission and is extremely rare for patients with WT, with only a few cases reported. Due to the rarity, there are no current treatment recommendations.

Objectives: Describe the case of an eighteen-year-old male diagnosed at three-years-old with stage IV WT who relapsed fifteen years after diagnosis.

Design/Method: Case report.

Results: Eighteen-year-old male, diagnosed at three-years-old with stage IV WT (liver and lung metastasis). Pulmonary nodule biopsy showed favorable histology and he received neoadjuvant therapy for ten weeks under NWTS Regimen DD4A with vincristine + doxorubicin. Then, he underwent left nephrectomy, partial hepatectomy, and lymph node biopsies. Pathology showed WT with rhabdomyomatous differentiation and diffuse anaplasia, with tumor extension into the renal sinus, but no lymph node or liver margin infiltration. Due to unfavorable histology, treatment was changed to NWTS5 relapse protocol stratum C alternating cyclophosphamide/carboplatin with etoposide, plus total lung irradiation. End-of-treatment scans showed subcentimeter bilateral pulmonary nodules, which remained stable for several years. Surveillance was followed per NWTS5 protocol. He remained disease-free for 15 years until he presented with a two-week history of progressive shortness of breath. CT showed several lung nodules, left-sided complex pleural effusion, and possible liver metastasis. Pulmonary nodule biopsy confirmed recurrence of WT with rhabdomyomatous differentiation but no anaplasia. He has received therapy alternating between ICE, vincristine + irinotecan, and vincristine + cyclophosphamide + doxorubicin. PET scan after 7 cycles showed decreased disease burden, yet still significant pleural-based nodules, making future gross total resection challenging.

Conclusion: LR in WT is rare. Primary high-risk patients receive more aggressive chemotherapy. Since time to relapse is prolonged, it is unclear if treatment with similar previous drugs would be effective or if a typical more intense relapse regimen is necessary. Local control can also be challenging as the utility of radiation is limited when many received radiation previously. Further research is needed to identify and improve treatment options for these patients.

Poster # 315

UNUSUAL PRESENTATION OF PATIENT WITH WILMS TUMOR AND OBSTRUCTING DUODENAL HEMATOMA

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Background: Wilms Tumors make up approximately 5% of pediatric malignant tumors with about 500 new cases annually in the United States. If unilateral, standard treatment involves complete surgical resection with associated nephrectomy after visualization with no mass on contralateral kidney. If unable to resect tumor due to risk of damaging other organs affected by tumor invasion or mass effect, treatment involves biopsy of the mass to confirm histology, followed by 6-9 weeks of chemotherapy to reduce tumor size and allow for resection with reduced risk of damage to other organs.

Objectives: Describe a pediatric patient with Wilms Tumor that did not have any direct duodenal tumor invasion, but presented with an obstructive duodenal hematoma.

Design/Method: Case Report

Results: A 5 year old female presented with five days of persistent vomiting, abdominal pain, and gross hematuria with a right renal mass visualized on MRI Abdomen/Pelvis along with concern for intestinal obstruction. The renal mass measured 9.1 x 9.3 x 8.4cm. Upon direct visualization via open laparotomy, the tumor was adherent to the duodenum and surrounding serosa and an intraluminal duodenal hematoma was noted. It was determined that to attempt to complete dissection of the tumor from medial tissues and duodenum would have increased risk of morbidity and mortality. The patient was subsequently closed after G-tube and J-tube placement to allow for bowel rest and gradual resorption of the duodenal hematoma. There was no evidence of direct duodenal invasion by the mass and etiology of the hematoma remains unclear. Possible causes include abdominal trauma, microscopic invasion, and direct mass effect on the duodenal vasculature. The pathology of the mass was consistent with favorable Wilms Tumor. After 6 weeks of chemotherapy with vincristine, dactinomycin, and doxorubicin, repeat imaging indicated that the tumor had grown since previous imaging to 9.7 x 12.2 x 12.5cm with cystic changes and central necrosis. The duodenal hematoma had resolved with no intestinal obstruction persisting. The patient returned to the operating room and underwent a right nephrectomy and tumor excision with minimal complication. Final pathology confirmed Wilms tumor.

Conclusion: Wilms Tumors often share presenting symptoms but can behave differently and present unique challenges. In this case, the tumor was strictly adherent to the duodenum, and had caused an obstructive intraluminal duodenal hematoma. The tumor grew despite chemotherapy, and the duodenal hematoma resolved. Skilled surgical resection was successfully performed without further signs of intestinal obstruction.

Poster # 316

TERATOID WILMS TUMOR PRESENTING AS BILATERAL RENAL TUMOR AND RECURRENCE AS TRIPHASIC WILMS

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Background: Teratoid variant of Wilms tumor was first described based on the presence of heterologous differentiation with presence of mature tissue types such as muscle, squamous tissue, bone, cartilage, glial, adipose and glandular tissue within the tumor. In majority of cases these tumors are chemotherapy and radiotherapy resistant.

Objectives: This case report describes a child with primary bilateral teratoid Wilms who had recurrent disease isolated to right chest pleural area.

Design/Method: Review of patient medical records, radiographic imaging, pathology and review of literature

Results: We describe a 3-year-old female who presented at 1 year of age with multiple bilateral renal masses, containing large amount of fat attenuation tissue and borderline enlarged left retroperitoneal lymph nodes on computerized tomography (CT). Right kidney demonstrated 2 renal masses measuring 10.3 x 11.5 x 11.0 cm and 3.8 x 2.6 x 3.1cm. Left kidney demonstrated 3 masses, largest measuring 5.5 x 5.7 x 4.9 cm. CT chest was negative for metastatic disease. Histopathology of right renal mass biopsy showed predominantly mature fat with scattered mature epithelial tubules and skeletal muscle indicative of teratoid Wilms tumor. Patient was treated with 2 drug chemotherapy (vincristine and dactinomycin) per children's oncology group (COG) protocol AREN0534 regimen EE4A. Patient had stable disease with minimal reduction in tumor sizes at week 6 and underwent surgical resection - partial right nephrectomy, total left nephrectomy, right ureteral stent. Pathology demonstrated teratoid Wilms tumor stroma predominant with muscle and adipose tissue differentiation. As expected for teratoid Wilms there was minimal necrosis and chemotherapy effect. Left kidney demonstrated focal anaplasia; all lymph nodes were negative for disease, and negative loss of heterozygosity (LOH) at 1q and 16q. She completed therapy per EE4A. Fifteen months off therapy there was recurrence of disease with a large 4.2 x 5.5 x 3.8 cm pleural based mass in the right posterior hemithorax with bony remodeling and no disease in abdomen/pelvis. Histopathology of the mass showed triphasic Wilms tumor - blastemal predominant. She began therapy per COG protocol AREN0532 regimen I with 5 drugs (vincristine, doxorubicin, dactinomycin, cyclophosphamide and etoposide). Resection was done at 6 weeks and demonstrated triphasic Wilms tumor with no anaplasia or teratoid component. Post resection she has continued on chemotherapy.

Conclusion: Though rare, bilateral teratoid Wilms tumors can have recurrence of disease. Here we report a unique case with recurrence of the disease presenting as triphasic Wilms tumor rather than the teratoid component.

Poster # 317

CLOFARABINE AS MONOTHERAPY AND SALVAGE THERAPY IN HISTIOCYTIC SARCOMA

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Background: Histiocytic sarcoma (HS) is an aggressive malignancy of histiocytic origin from a monocyte/macrophage lineage. The incidence of histiocytic malignancies is <0.5/million/year, with few case reports in children. While surgery, radiation therapy and chemotherapy based on Lymphoma/leukemia or Langerhans cell histiocytosis (LCH) protocols have been used to treat

HS, there is no standard of care due to lack of data. This is the first case series reporting Clofarabine for HS in a pediatric population.

Objectives: Describe two pediatric patients treated with Clofarabine for HS.

Design/Method: Descriptive retrospective case series.

Results: A 13 y/o female presented with a painless lump on the posterior right thigh enlarging for about three weeks. MRI of the right leg showed a 2.8 cm mass arising from the semimembranous muscle. A CT chest, PET-CT, bone marrow biopsy, MRI brain/spine and LP were negative. A biopsy showed discohesive sheets of large atypical epithelioid cells with abundant eosinophilic cytoplasm negative for pan-keratin, EMA, CD34 and desmin with normal INI-1 with positivity for CD163, CD68, and LCH and CD4. Sequencing identified DOC8-BRAF and AXON1-P314L fusions. Following complete resection, she was started on Clofarabine monotherapy. She is presently on cycle 4 with no clinical or radiographic evidence of disease.

Our second patient is a 15 y/o male who presented with supraclavicular and axillary adenopathy. Biopsy showed large atypical cells with spindled and epithelioid morphology positive for CD4, CD56, lysozyme, CD163, CD43 and vimentin with variable CD45, S100 and CD68 consistent with metastatic histiocytic sarcoma. Marrow and CSF studies were negative. He was treated with a modified version of the T-cell leukemia protocol AALL0434 with complete clinical resolution at the end of induction. Four weeks into consolidation, he developed palpable neck lymphadenopathy. PET-CT confirmed avidity at the primary site with new lesions in the mediastinum and liver consistent with refractory disease. Sequencing revealed mutations in NF-1, FBXW7, and CBL. While on salvage therapy of Clofarabine and Tremitinib, he had an aggressive recurrence, including liver metastasis. A third outside opinion favored a myeloid sarcoma (MS) over HS and patient was switched to an AML-based regimen. Unfortunately, patient ultimately died of his disease. Although diagnosis remains unclear, patient did show initial response to Clofarabine. Further data for its effectiveness is needed.

Conclusion: HS is a rare, highly aggressive cancer. Clofarabine has been used as a monotherapy and in combination with MAPK pathway inhibition and salvage therapy to treat HS and MS.

Poster # 318

A RARE CASE OF INDOLENT EWING SARCOMA AND ROLE OF THE TUMOR IMMUNE MICROENVIRONMENT

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Background: Ewing Sarcoma (ES) is a rare and aggressive primary malignant bone tumor, that can be osseous (75-85%) or extra-osseous. Presentation includes bone pain, swelling,

pathological fractures and some exhibit systemic symptoms.

Objectives: We present a case of indolent localized ES, diagnosed and treated as osteomyelitis at an outside hospital despite three biopsies over the course of three years.

Design/Method: Case report

Results: An 8-year-old previously healthy girl presented with left leg pain and limp in 2017. Imaging showed a "ball-like lesion" on her left tibia. Excisional biopsy was reportedly negative for malignancy, with features concerning for osteomyelitis. She was treated with Clindamycin with good response. Later in June 2020, patient presented with similar symptoms, with a needle biopsy again reportedly negative for malignancy and underwent another course of antibiotics for 6 months. Symptoms persisted and a MRI showed increased asymmetric osteoblastic activity contained within the tibial meta-diaphysis. Repeat biopsy showed characteristic small, round blue cells, with positive labelling for CD99 and NKX2.2, amidst an inflammatory backdrop, consistent with ES, FISH pending. On review of prior biopsies, the neoplastic cells were present however had undergone infarction, preventing a definitive diagnosis. Metastatic workup is negative.

Conclusion: The role of the immune system in sarcoma has been known for years, first described in 1800s when spontaneous tumor regression was noted following bacterial infections.[1] Several recent studies in solid tumors have described the role of tumor microenvironment (TME) and immune surveillance in arresting tumorigenesis as well as predicting response to therapy.[2] The behavior in our patient is highly unusual as the sarcoma cells were present in prior biopsies although necrotic, likely secondary to a robust immune response. Most cases of ES are driven by EWS-FLI1 fusion oncoprotein. Variability in EWS-FLI1 levels have been linked with the propensity of metastasis: low levels associated with higher metastasis secondary to upregulation of PDL1- and PDL2 resulting in tumor immune evasion.[3] It is unclear whether this had any role to play in our case. Additionally, a benign radiographic appearance and lack of viable cells on histology can lead to mis- or delayed diagnosis, as seen here.
This case highlights the role of the immune microenvironment as well as co-infection in containing a highly aggressive malignancy. Further insights into the sarcoma TME can help understand the behavior and identify potential novel immunotherapeutic targets for adoptive cellular therapy and cancer vaccines.
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Poster # 319

INTRACRANIAL EWING SARCOMA OF THE RIGHT LATERAL VENTRICLE IN AN ADOLESCENT FEMALE

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Background: Ewing sarcoma (EWS) usually arises in the long bones or axial skeleton with extension into soft tissue. Rarely it occurs as a primary soft tissue tumor, in which case it is referred to as extraosseous EWS. Very rarely, EWS arises intracranially, often from the dura. It is important to differentiate intracranial EWS from other CNS embryonal tumors as treatment and prognosis differ. Five-year survival rates are approximately 60% with surgical resection, chemotherapy and radiation therapy.

Objectives: To describe the presentation, diagnosis and treatment of an adolescent patient with primary, localized intracranial EWS arising within the lateral ventricle.

Design/Method: A 16-year-old Hispanic female initially presented with complaints of one week of headaches that resolved. One month later, she developed blurry vision in her left eye. Subsequent ophthalmologic evaluation revealed bilateral papilledema. CT and MRI of her brain revealed a 7 cm x 4 cm x 3 cm solid, cystic mass centered in the right lateral ventricle causing mass effect and without parenchymal extension. MRI spine was negative. She underwent an initial hemispheric craniotomy with tumor resection, which demonstrated a very firm, fibrous, vascular tumor with involvement of the choroid plexus and choroidal vasculature. Due to the vascularity, complexity of tumor and concern for surgical morbidity, a subtotal resection was performed. Pathology revealed features of small round cell sarcoma. Next generation sequencing showed fusion between the EWSR1 gene at chromosome location 22q12 and the FLI1 gene at chromosome location 11q24, confirming the diagnosis of EWS.

Results: CT of the chest, abdomen, and pelvis, PET/CT, and bilateral pelvic bone marrow aspirates and biopsies were negative for metastases. Patient began treatment with high-dose ifosfamide, carboplatin and etoposide (ICE). Repeat imaging demonstrated tumor response with shrinkage. Repeat craniotomy was performed with a gross total resection as tumor was less firm and more accessible. She is now six months status post initial resection and is continuing with radiation therapy and oral etoposide. She is clinically well-appearing without headache or vision changes. Plan is for six total cycles of high-dose ICE.

Conclusion: Primary, localized intracranial EWS is extremely rare. Here we present a case of an adolescent female with tumor arising within the lateral ventricle presenting with mass effect. Genetic sequencing revealed EWSR1/FLI1 gene fusion. Chemotherapy prior to repeat resection improved surgical results. Our recommendation is for biopsy and attempted surgical excision followed by chemotherapy, a second surgery to remove residual disease if necessary and feasible, and radiation therapy.

Poster # 320

PAZOPANIB MAINTENANCE IN AN UNUSUAL CASE OF RHABDOMYOSARCOMA WITH DIFFUSE BONY METASTASES

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Background: A fourteen-year-old male with high risk, stage IV, genitourinary primary, fusion negative alveolar rhabdomyosarcoma with diffuse bony metastatic disease (bony lesions throughout the calvarium, skull base, numerous vertebrae, sacrum, pelvis, and bone marrow) presenting in spontaneous tumor lysis syndrome achieved a sustained remission with a modified treatment regimen that included Vincristine, Actinomycin-D, and Cyclophosphamide (VAC) chemotherapy per COG ARST0531 Regimen A, who due to unusual circumstances received only orchiectomy for local control, no radiation, and a one-year pazopanib maintenance therapy following completion of VAC.

Objectives: To highlight a very unusual presentation of rhabdomyosarcoma that suggests a possible benefit of pazopanib-based maintenance therapy.

Design/Method: Case report developed from patient chart review.

Results: Metastatic rhabdomyosarcoma in adolescents historically holds a grim prognosis. A recent report found that fusion negative rhabdomyosarcoma patients with more than one metastatic site have an event free survival of 34%. However, the observations of Oberlin have demonstrated that outcomes progressively worsen as the number of metastatic sites increase, with bone and bone marrow involvement portending an even worse prognosis in metastatic rhabdomyosarcoma. This patient had an Oberlin score of three given his age, greater than three metastatic sites, and bone/bone marrow metastasis, with a striking presentation of diffuse bony metastasis. Rare cases of primary alveolar rhabdomyosarcoma of the bone or bone marrow without a soft tissue primary site mimicking an acute leukemia have been described. In contrast, our patient had an identifiable primary site and overt bony disease. Following standard chemotherapy, due to concerns of his high-risk disease that was not radiated due to the diffuse nature of the disease, his therapy was continued with one year of oral pazopanib. The patient is now currently four years off therapy without evidence of disease. While it is unknown if pazopanib changed the expected poor outcome for this patient, the pazopanib was well tolerated.

Conclusion: Rhabdomyosarcoma can present in unusual ways, such as in this patient with diffuse bony disease. While we expected a poor outcome for this patient, he is currently in a long-term remission after receiving a modified treatment regimen that included pazopanib maintenance therapy. Given the current ongoing debate regarding maintenance therapy in rhabdomyosarcoma, and the proven efficacy of pazopanib in non-rhabdomyosarcoma soft tissue sarcomas, further study of pazopanib as maintenance therapy in rhabdomyosarcoma could be beneficial and merits organized investigation.

Poster # 321

SECONDARY OSTEOSARCOMA HELPS IDENTIFY A PATIENT ON HOSPICE FOR 5 YEARS WITH CURED NEUROBLASTOMA

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Background: Neuroblastoma is a tumor of neural crest cells, commonly found in organs of the sympathetic nervous system. It is the most common extracranial solid tumor in children with an incidence of 10.5 cases per million in children 15 years of age and younger.[1] A unique characteristic of neuroblastoma is the variety of clinical and biological manifestations. Some tumors regress spontaneously or differentiate without treatment, while others metastasize despite aggressive interventions resulting in poor outcomes.

Objectives: The authors describe a unique presentation of secondary osteosarcoma in a 19-year-old male patient who had been on hospice for 5 years with suspected refractory, metastatic neuroblastoma.

Design/Method: This is a case report by which the authors used data, imaging, and documentation from the electronic health records of the various health care institutions where the patient received treatment.

Results: The patient was first diagnosed with high-risk stage 4 neuroblastoma in 2011. He participated in several clinical trials and subsequently, due to treatment toxicity, decided to enroll in hospice in 2014, at which time, serial MIBG scans revealed stable widespread osseous metastases. However, the patient's condition remained stable for the next five years aside from left knee pain, which was radiated for palliation. In early 2020, the patient's left knee pain worsened, at which time, he was ultimately referred to Pediatric Oncology and Orthopedic Surgery, at which time, this lesion was diagnosed as an osteosarcoma, likely secondary to previous radiation. The patient had surgery to resect the sarcoma and to repair a pathologic fracture due to the tumor. He is currently receiving Methotrexate, Cisplatin, and Doxorubicin (MAP) chemotherapy for osteosarcoma.

Conclusion: It is exceedingly rare for a patient to be on hospice for 5 years, especially without an oncology involvement. We suspect that the stability of the MIBG uptake over the last several scans was due to differentiation of neuroblastoma into ganglioneuroma after therapy, such as Isotretinoin.

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Poster # 322

A FAVORABLE RESPONSE TO TARGETED MOLECULAR THERAPY IN METASTATIC OSTEOSARCOMA: WHAT HAVE WE LEARNT?

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Background: Osteosarcoma is the most common primary malignant bone tumor in children and adolescents. It is estimated that 15-20% of patients present with clinically detectable metastases, with the lung being the most common site. Over the last three decades, improving survival outcome in metastatic osteosarcoma has remained stagnant with a survival rate of 25-30%, despite advances in therapy. Currently, there is no standard of care for relapsed/metastatic osteosarcoma. This case discusses a favorable response with the addition of a multi-targeted tyrosine kinase inhibitor (TKI), Sorafenib, to a chemotherapeutic regimen in a patient with relapsed osteosarcoma with an unfavorable histological response to neoadjuvant chemotherapy.

Objectives: To emphasize the promising therapeutic effect of multi-targeted TKIs in the management of relapsed or metastatic osteosarcoma.

Design/Method: Case report with literature review.

Results: 11-year-old male was diagnosed with Osteosarcoma of right distal femur, completed neoadjuvant chemotherapy with MAP (Methotrexate, Adriamycin and Cisplatin), and underwent limb sparing surgery with negative margins, showing 60% tumor necrosis in the resected tumor. He presented eleven months later in relapse with pulmonary metastatic nodules measuring 4.2 x 0.2 cm and received two cycles of Ifosfamide 2800mg/m^2/dose and Etoposide 100mg/m^2/dose (EURAMOS-1 study protocol). Subsequent imaging demonstrated disease progression despite treatment. Sorafenib was initiated with the third cycle of chemotherapy as an adjuvant, and then continued with 11 cycles of Gemcitabine and Docetaxel. Subsequent interval imaging showed a size reduction in the primary chest lesion to 3.4 x 0.9 cm along with improvement in the other pulmonary nodules. Patient tolerated the therapy with minimal tolerable side effects.

Conclusion: Receptor Tyrosine Kinases (RTKs) trigger multiple signaling pathways resulting in cell migration, differentiation, proliferation, and metabolic changes. Dysregulation of RTKs are related to tumor neovascularization, invasion, metastasis and chemotherapy resistance. As a result, RTKs have become a focus of research on antitumor drugs. Sorafenib, a TKI with broad activity against MAPK, BRAF, VEGFRs, and PDGFR, has proven effective against hepatic, renal and thyroid cancer and is the most studied TKI in osteosarcoma. In preclinical osteosarcoma models, Sorafenib demonstrated cell proliferation, restriction and reduction of metastasis formation which led to a phase II clinical trial where patients with relapsed, unresectable osteosarcoma following standard MAP therapy were administered Sorafenib. The result was a 46% progression-free survival after 4 months (16% increase from the primary endpoint of 30%). This new aspect of therapy has led to a favorable response in our case and this may serve as a gateway for further studies.

Poster # 323

EWING SARCOMA OF THE 9TH RIB SUBSEQUENT TO PEDIATRIC LEUKEMIA: A CASE SERIES

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Background: Ewing sarcoma (EWS) is a high-grade sarcoma described as a small round cell tumor of bone and soft tissue. EWS is an aggressive malignancy that accounts for approximately 2% of cases of childhood cancer, most commonly occurring in adolescent and young adult patients. The metastatic pattern is typically hematogenous, with lung, bone, and bone marrow being the most common sites of metastasis. Studies performed via the Childhood Cancer Survivor Study (CCSS) found that secondary neoplasms occur more frequently among females, patients older at time of cancer diagnosis, and those treated with radiation therapy. Overall, subsequent EWS was rare. Two pediatric cases of secondary EWS of the 9^{th} rib presented following surveillance visits for primary diagnoses of precursor B-acute lymphoblastic leukemia (pre B-ALL) and acute myeloid leukemia (AML) within northeast Pennsylvania.

Objectives: The purpose of this study was to evaluate for potential commonalities between two rare cases of subsequent EWS in older pediatric patients. Evaluation of risk factors and outcomes were performed.

Design/Method: Review of the electronic health records was completed for each patient. Patient characteristics at the time of diagnoses were detailed.

Results: Patient 1 was a 9-year-old female diagnosed with pre B-ALL and achieved complete remission with treatment. Almost 4 years later, she developed chest pain and dyspnea; imaging revealed a rib lesion. Biopsy diagnosed EWS. Patient 2 was a 14-year-old male diagnosed with AML. He achieved complete remission with treatment, including >300 mg/m^2 cumulative anthracycline dosage. Eight months later, he developed back pain; imaging revealed a rib lesion. Biopsy diagnosed EWS. Interestingly, both patients had tumor burden localized to the right 9^{th} rib without prior radiation therapy. Patient 2's anthracycline dosage may have increased his risk of secondary sarcoma [Friedman, 2010], otherwise there were no known risk factors for subsequent EWS. Two months prior to diagnosis, Patient 1 was at the 92nd percentile for body mass index; Patient 2 was at the 93rd percentile. Both patients resided in areas near hydraulic fracturing ("fracking") wells.

Conclusion: Childhood cancer survivors have a significantly increased risk of developing secondary sarcoma compared to risks in the general population. Further investigation is warranted to evaluate secondary malignancies within 5-years of treating primary cancer and environmental factors potentially predisposing to rare forms of EWS. This case series emphasizes the importance of continued surveillance and regular cancer screening for childhood cancer survivors.

Friedman, J National Cancer Inst, 2010.

Poster # 324

CASE REPORT: TP53 MUTATION IN A PEDIATRIC PATIENT WITH OSTEOSARCOMA AND LUNG ACINAR ADENOCARCINOMA

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Background: TP53 gene mutation, also known as Li-Fraumeni syndrome (LFS), is an autosomal dominant syndrome that leads to a hereditary cancer predisposition. It can involve multiple primary tumors and is associated with a broad spectrum of malignancies distinguishing it from other cancer syndromes[1]. Here we present the case of a 13-year-old male who presented with humeral osteosarcoma, known family history of LFS, who subsequently developed a second primary tumor of the lung. Upon literature review, no other cases of similar presentation have been reported.

Objectives: Describe a pediatric case of TP53 mutation presenting with lung acinar adenocarcinoma and discuss the importance of surveillance imaging in these patients.

Design/Method: Case report.

Results: The patient is a male who presented at 12 years old with persistent right upper arm pain for 6 weeks. X ray was performed which revealed a right humeral lesion. Pathologic evaluations confirmed the diagnosis of osteosarcoma of the right humerus and he subsequently initiated chemotherapy with cisplatin, doxorubicin and methotrexate per COG protocol AOST0331.

Prior to surgical resection, he had pre-operative imaging which included a PET CT Chest with contrast. This revealed a 5 mm subpleural nodule in the right upper lobe of unclear etiology but not determined to be metastatic disease. This lesion was monitored to determine if chemotherapy would have treatment effect.

After completing 21 weeks of chemotherapy and undergoing resection, he had a repeat CT chest which showed that the subpleural nodule did not demonstrate treatment. A thorascopic biopsy of the right upper lobe was performed to rule out metastatic osteosarcoma. Pathology revealed an acinar adenocarcinoma with positive margin.

Conclusion: Patients with LFS have a very high lifetime cumulative risk of developing multiple malignancies and strong family history of early-onset malignancies. The Toronto Protocol is a multi-modality protocol developed to detect tumors early and reduce morbidity and mortality in patients who are TP53 mutation carriers[2].
Currently, the surveillance protocols published do not include routine screening modalities for lung cancers[2]. Furthermore, at our institution it is not possible to order a full body MRI at this time.

The development of his lung acinar adenocarcinoma is not common in pediatric LFS patients. When specifically looking at lung cancer, one study found that there was no significant association with germline TP53 mutation[3]. This highlights the importance of performing full surveillance imaging to prevent missing a potential subtle finding as was seen in this case.

1. Giacomazzi CR, Rev Assoc Med Bras, 1992
2. Kratz CP, Clin Cancer Res, 2017
3. JM, Oncogene, 2001

Poster # 325

METASTATIC CLIVAL CHORDOMA SUCCESSFULLY TREATED WITH IMATINIB

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Background: Chordomas are extremely rare tumors, arising from notochord remnants, that primarily affect the spine and skull base with approximately 5% of all cases affecting pediatric patients. Chordomas are slow growing though can be locally aggressive and be associated with distant metastases. The primary treatment is surgical resection however this is not always feasible and is associated with high recurrence rates. Cytotoxic chemotherapy has historically been ineffective. Imatinib, a tyrosine kinase inhibitor, has been shown to successfully treat chordoma when combined with cytotoxic chemotherapy.

Objectives: A case report of a patient with metastatic chordoma of the clivus treated with Imatinib and Etoposide.

Design/Method: Case Report

Results: An 8-month-old female with metastatic chordoma of the clivus presented after treatment failure with cytotoxic chemotherapy. The patient presented at birth with a blueberry muffin rash, negative for TORCH infections, with bilateral lung and kidney lesions and a large unresectable clival mass (40x35x35 mm) causing compression of the brainstem. A skin lesion was biopsied and was consistent with metastatic chordoma. She was started on chemotherapy with carboplatin and etoposide alternating with ifosfamide, vincristine and actinomycin D (IVA) with the addition of doxorubicin (IVADo) for lack of response in cycles 3-6. While the metastatic lesions decreased in size the clival mass was unchanged. We initiated treatment with oral Imatinib (337 mg/m2/dose) and oral etoposide. Treatment was complicated by Grade 4 neutropenia which resolved with etoposide interruption and dose reduction. After 9 months of therapy the patient has had a complete response of the metastatic lesions and near complete response of the clival primary (15x12x10 mm) with resolution of mass effect on the brainstem.

Conclusion: We present a case of metastatic chordoma of the clivus previously unsuccessfully treated with cytotoxic chemotherapy, now with near complete response on follow up imaging after treatment with Imatinib and Etoposide. Imatinib, when paired with a second agent, may be

an effective therapy for patients with advanced chordoma.

Poster # 326

HIGH-GRADE ANAPLASTIC EPENDYMOMA AFTER LIVING RELATED KIDNEY TRANSPLANTATION IN A PRESCHOOLER

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Background: De novo cancer risk after solid organ transplantation is a known entity due to immunosuppressive regimens. While post-transplant leukemias and lymphomas can occur, primary brain tumors are remarkably rare.

Objectives: To describe a rare case of a five-year-old male who developed a high-grade anaplastic ependymoma 14 months after living related donor kidney transplantation.

Design/Method: Case report/literature review

Results: A 5-year-old male with a history of posterior urethral valves and renal failure requiring a living-related donor kidney on immunosuppressive therapies developed right foot drop approximately 8 months after transplantation. His symptoms progressed to weakness along with discoordination of his right upper extremity. He was referred for an outpatient magnetic resonance imaging (MRI) and eventually found to have a large left hemispheric mass, measuring 8.7cm antero-posteriorly, 5.6cm transversely, and 5.3cm cephalo-caudad involving the white matter of the left mid- and posterior-frontal and left parietal lobes with areas of cystic/necrotic changes along with left lateral ventricle compression and an 8mm midline shift. High choline levels indicated highly active cellular turnover suggestive of a high-grade primary brain tumor. He was admitted to the Pediatric Intensive Care Unit (PICU) and underwent gross total resection of the mass. The pathology was consistent with a WHO grade III anaplastic ependymoma. Immunohistochemistry showed focally positive Glial Fibrillary Acidic Protein B2 (GFAP B2), B2 focally positive with dotlike intracytoplasmic pattern Epithelial Membrane Antigen (E29), 25% focally positive (hotspot) Ki-67 QT, man (30-9) B2, and focally positive S100 Polyclonal B2. A 500 gene next-generation sequencing panel did not reveal pathogenic mutations, deletions, amplifications, or structural variants known to be altered in some ependymomas, including RELA, YAP1, NF2, MYCN, TERT promoter, CDKN2A, H3F3A, and HIST1B3B. Chromosomal copy analysis demonstrated loss of chromosome 8, with an otherwise balanced diploid genome. Post-operatively, the patient underwent intensive rehabilitation and eventually completed proton radiation at a cumulative dose of 5940 cGy. Given his history of renal transplantation and concern for risks of serious nephrotoxicity adverse effect, no maintenance chemotherapy was administered. He completed proton therapy approximately 7 months ago and has no evidence of recurrence.

Conclusion: This case illustrates the increased risk of malignancy in the post-transplant population. It is the first report in the pediatric literature of an anaplastic ependymoma after renal

transplantation.

Poster # 327

SUPERIOR RESPONSE OF PROGRESSIVE BRAFV600E-MUTATED PILOCYTIC ASTROCYTOMA TO DABRAFENIB/TRAMETINIB

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Background: Aberrations in RAS/BRAF/MAPK/MEK pathways, well-described across diverse malignancies including pediatric brain tumors, provide targeted theraputic options. Robust responses to BRAF-inhibitor monotherapy (BRAF-i) are reported in pediatric BRAF V600E-mutated pilocytic astrocytoma (PA). However, optimal treatment duration remains undefined, and progressive disease (PD) after discontinuing BRAF-i can occur. Comparative efficacy of BRAF-i alone or in combination with MEK-inhibitor (MEK-i) to treat PD after BRAF-i discontinuation is not well-characterized.

Objectives: To report a child with life-threatening medullary pilocytic PA who had rapid PD following cessation of prolonged vemurafenib and then experienced a robust response to combined BRAF-i/MEK-i therapy.

Design/Method: Review of patient medical records, radiographic imaging, pathology, and published literature.

Results: A former 34-week gestation girl was diagnosed at age 2 years with "atypical breath-holding spells" characterized by episodes of cyanosis, apnea, loss of consciousness without apparent antecedent symptoms. By age 5-years, these episodes had increased in severity, sometimes requiring cardiopulmonary resuscitation. Sleep study done in work-up of these episodes showed severe central sleep dysregulation. Brain magnetic resonance imaging (MRI) showed a large heterogeneously enhancing solid/cystic lesion in her medulla; biopsy confirmed PA WHO grade I. Despite initial improvement with 6-monthly carboplatin/vincristine courses, MRI showed PD. Transient improvement occurred following definitive focal irradiation, but within 3 months, PD was evident. Molecular analysis of banked biopsy specimen demonstrated BRAFV600E mutation. Compassionate vemurafenib therapy was initiated, and she improved clinically. However, soon thereafter, she developed severe pneumonia related to silent aspiration, requiring prolonged ECMO therapy followed by tracheostomy and ventilator support. As MRI showed a partial response, Vemurafenib was continued. She showed marked clinical and radiographic improvement over the subsequent 2.5 years. After 36 months, vemurafenib was discontinued. Within a month, she developed severe dysphagia and significant respiratory compromise. MRI showed marked PD. Treatment with trametinib and dabrafenib was initiated and her symptoms rapidly improved. Three months later, MRI showed marked tumor regression exceeding that which occurred with vemurafenib alone. Treatment will continue for an undetermined duration.

Conclusion: Brain MRI is important in evaluating children with long-standing atypical breath-holding spells. Panel-based genomic evaluation may provide efficacious targeted therapy options, particularly in children with PA with tumor PD despite conventional therapies. Superior clinical and radiographic responses were seen with combined BRAF-i/MEK-i therapy as compared to BRAF-i monotherapy. This case also highlights two current outstanding clinical dilemmas-1) Optimal BRAF-targeted therapy duration and 2) BRAF-i versus combined BRAF-i/MEK-i therapy for treating pediatric BRAF V600E-mutated PA.

Poster # 328

LYMPHADENITIS WITH KIKUCHI-FUJIMOTO-LIKE FEATURES POST SARS-COV-2 MASQUERADING AS LYMPHOMA

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Background: Kikuchi-Fujimoto disease (KFD; Kikuchi disease or histiocytic necrotizing lymphadenitis) is a rare, non-malignant condition of unknown etiology. KFD is usually characterized by cervical lymphadenopathy and fever, though a variety of symptoms and physical findings can occur. KFD frequently mimics other conditions, such as lymphoma, tuberculosis adenitis, and systemic lupus erythematosus. Lymph node biopsy reveals varying degrees of necrosis and a histiocytic cellular infiltrate. Although the complete spectrum of consequences associated with SARS-CoV-2 (coronavirus 2, COVID19) infection have not yet been elucidated, reports of persistent symptoms and other related illnesses post recovery are emerging. SARS-CoV-2 has been associated with various inflammatory conditions including multisystem inflammatory syndrome in children (MIS-C), and has been implicated in certain immunological complications, such as macrophage activation syndrome and cytokine storm.

Objectives: To describe the case of an adolescent with KFD-like necrotizing mesenteric lymphadenitis following SARS-CoV-2 infection.

Design/Method: Case Report

Results: A 15-year-old male with no significant past medical history presented with a 1-month history of fevers, abdominal pain, weight loss, anorexia, and fatigue. There was no recent history of any respiratory symptoms. Physical exam was significant for painless left anterior cervical chain lymphadenopathy. Initial laboratory work-up revealed leukopenia (WBC, 2500/µL; lymphocyte, 580/µL), while other blood indexes were normal. Erythrocyte sedimentation rate (ESR, 38 mm/h [0-15]), lactate dehydrogenase (LDH, 474 U/L [130-250]), and C-reactive protein (CRP, 2.36 mg/dL [0.0-0.50]), and ferritin (535.6 ng/mL [13.7-78.8]) were elevated. Abdominal CT scans revealed multiple enlarged mesenteric lymph nodes in the right lower quadrant and an extensive infiltrative mesenteric mass. Investigation for HIV, tuberculosis, Bartonella, EBV and CMV infection resulted negative. A COVID-19 RNA nasopharynx swab was negative. SARS-CoV-2 IgG antibody was positive, consistent with previous exposure to SARS-CoV-2. He underwent an open biopsy of the abdominal mass, that revealed predominantly

necrotic tissue with patchy vasculitis, consistent with necrotizing mesenteric lymphadenitis. Flow cytometric analysis performed on the abdominal mass showed no evidence of a monoclonal lymphoid population. Fevers resolved, and his clinical condition started to improve with supportive care only.

Conclusion: This case highlights an atypical presentation of SARS-CoV-2 infection in a patient with Kikuchi-Fujimoto disease.

Poster # 329

HEMATURIA AS THE PRESENTING SYMPTOM OF A PATIENT WITH UNDIAGNOSED NEUROFIBROMATOSIS TYPE I

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Background: Pediatric bladder masses are extremely rare, but must be considered in cases of unexplained urinary symptoms such as painless, gross hematuria. Unlike the urothelial carcinomas seen in adults, rhabdomyosarcoma is the most common bladder tumor in pediatrics. However, clinicians need to consider non-rhabdomyosarcoma etiologies such as: papillary urothelial neoplasm of low malignant potential, transitional cell papilloma, transitional cell carcinoma, inflammatory myofibroblastic tumors, eosinophilic cystitis, and neurofibromas. Neurofibromas rarely manifest in the genitourinary tract, with fewer than 100 cases described in the literature.

Objectives: Describe the initial presentation, unique diagnostic challenges, and medical management of an inoperable, bladder plexiform neurofibroma in a pediatric patient with previously undiagnosed neurofibromatosis type I.

Design/Method: Chart and literature review.

Results: A 12-year-old male with autism presented with 1 day of painless, gross hematuria. He had no history of trauma and was otherwise well. Urinalysis was remarkable for moderate blood, but was otherwise normal. On physical exam, the patient was found to have numerous café-au-lait macules and axillary freckling. Ultrasound of the bladder revealed a large bladder mass. CT scan of the abdomen/pelvis confirmed a prominent mass at the base of the bladder (5 x 7cm). A small nodule was also seen at the base of the right lung.

A CT of the head was performed and showed no metastatic disease, but rather remodeling with widening of the right orbital structures consistent with a neurofibroma. MRI of the brain and orbits showed scattered spongiform changes and orbital plexiform neurofibromas consistent with neurofibromatosis type I.

Biopsy performed via cystoscopy showed a marked eosiniophilic infiltrate, which suggested a preliminary diagnosis of eosinophilic cystitis for which he was discharged on cetirizine and a

short course of prednisone. Final pathologic diagnosis was a benign nerve sheath neoplasm consistent with a plexiform neurofibroma (PN).

The family history was negative for neurofibromatosis. NF1 gene testing revealed a heterozygous pathogenic mutation in the NF1 gene, confirming the diagnosis of neurofibromatosis type I. Resection of the mass was associated with a high risk of morbidity due to its location. After discussing treatment options with family the patient was started on the MEK inhibitor selumetinib. His hematuria has since resolved.

Conclusion: While rhabdomyosarcoma is the most common pediatric bladder mass, other etiologies such as eosinophilic cystitis and neurofibroma need to be considered. Surgical resection for symptomatic PNs is still standard of care if feasible, but effective medical treatment options are now available for inoperable, symptomatic PNs.

Poster # 330

DICER-1 MUTATION IN A VAGINAL MASS OF A PRE-PUBESCENT FEMALE

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Background: The DICER-1 mutation is a pathogenic germline mutation that predisposes a patient to uncommon malignancies such as pleuropulmonary blastoma, pineoblastoma, thyroid tumors and on rare occasion, embryonal rhabdomyosarcoma. Patients with DICER-1 mutation have an increased risk for these malignancies in the first two decades of life. Consideration for DICER-1 mutation in tumors with complex pathology and unique presentation is crucial as this diagnosis will change management and direct future comprehensive surveillance.

Objectives: Discuss the diagnostic dilemma of DICER-1 mutation, management, and surveillance

Design/Method: Case Report

Results: A six-month-old female presented with an acute vaginal bleed and protruding vaginal mass found during a diaper change. There was no report of foreign body, trauma, or sexual abuse; furthermore, no personal or family history of easy bruising or bleeding. The patient's aunt had been diagnosed with pineoblastoma at age twenty-six. Physical exam revealed a healthy appearing infant with a soft, hemorrhagic mass protruding from the vaginal introitus and light vaginal bleeding. The vulva, urethra, and patent anus were anatomically normal.
Abdominal magnetic resonance imaging revealed a complex pelvic mass arising from the uterus 9.5 x 3.7 x 5.0 cm with mass effect on surrounding organs. General laboratory evaluation was normal, including uric acid 2.6 mg/dl and alpha-fetoprotein of 37.6 ng/dl.
Initial pathology analyzed locally and by various consultants appeared consistent with germ cell tumor but necessitated additional tissue. Gynecology preformed a biopsy suggestive of germ cell tumor with yolk sac components. Treatment for germ cell tumor commenced. Given the rarity of

germ cell malignancy in this population, additional pathologists reviewed the tissue proposing alternative diagnosis of extra-renal Wilms tumor and rhabdomyosarcoma. The complex pathology and unique presentation of the tumor prompted consideration for DICER-1 mutation. Molecular genetic testing revealed a DICER-1 mutation with pathology consistent with embryonal rhabdomyosarcoma.

Conclusion: Although DICER-1 mutation inheritance is autosomal dominant, there can be variable penetrance; thus, the discovery of this mutation should prompt familial surveillance for malignancy. Molecular genetic testing uncovered the DICER -1 mutation in both the patient's aunt pineoblastoma and sister's germline tissue, who subsequently screened and found to have a Type 1r pleuropulmonary blastoma. This case highlights the diagnostic complexity of medical conundrums and the need to test for the DICER-1 mutation in distinguishing malignancies as well as familial surveillance.

Poster # 331

ENDOVASCULAR RECONSTRUCTION OF AN ATRETIC INFERIOR VENA CAVA IN AN ADOLESCENT PATIENT

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Background: Atresia of the inferior vena cava (IVC) is infrequent and is speculated to be either congenital or acquired through thrombosis early in life. While most IVC atresia cases remain asymptomatic for the first few decades of life, this anomaly can be discovered incidentally or upon symptomatic presentation. Deep venous thrombosis (DVT) associated with atretic IVC presents management challenges.

Objectives: Report successful management of DVT with atretic IVC in an adolescent patient by IVC reconstruction, thrombolysis, and anticoagulation.

Design/Method: Case report

Results: A 17 year-old healthy male presented with worsening left leg pain and swelling one month following jumping off a couch. No prior thrombosis and no family history of thrombosis were reported. His birth was uneventful without history of umbilical catheterization.
Venous ultrasound with Doppler showed extensive DVT from the left external iliac vein through the calf veins, out of proportion to the minimal trauma. Computed tomography revealed thrombosis in left external, left common, and right common iliac veins. The IVC appeared severely atretic, with iliacs draining into paravertebral lumbar veins, then into the azygos and hemiazygos veins. A hypercoagulopathy workup was negative.
As IV heparin proved ineffective, the patient underwent pharmacomechanical catheter-directed thrombolysis (PCDT) successfully. However, within 24 hours, the entire left lower extremity re-thrombosed. Definitive IVC reconstruction was performed by balloon angioplasty, placement of 2 overlapping Venovo stents in the IVC and kissing Vici stents in bilateral iliac veins, followed

by left lower extremity DVT thrombolysis. Brisk flow was established throughout the left lower extremity, iliac veins, and IVC. The patient was aggressively anticoagulated with warfarin, and DVT symptoms resolved. One month later, left leg swelling recurred. Doppler ultrasound suggested re-thrombosis, however, intravascular ultrasound demonstrated no thrombosis, but severe circumferential narrowing at the inguinal edge of the left external iliac stent, due to the Poisson effect, resulting from stent oversizing and subsequent elastic recoil in the adjacent vein segment. A second stent sized to the common femoral vein was placed. The patient continued warfarin and has regained normal left leg function for more than 2 months.

Conclusion: This report describes successful reconstruction of an atretic IVC simultaneously with PCDT of left lower extremity DVT. This case underscores the importance of screening for proximal vascular anomalies when DVT occurs without apparent etiology. This case also demonstrates that without IVC patency, lower extremity venous flow cannot be maintained and definitive repair of IVC atresia needs to be aggressively pursued.

Poster # 332

CLINICAL AND MOLECULAR CHARACTERISTICS OF IMERSLUND-GRASBECK SYNDROME: A NOVEL FRAMESHIFT VARIANT IN EXON 11 OF AMN GENE

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Background: Imerslund-Gräsbeck syndrome (IGS) is a rare autosomal recessive disorder characterized by selective vitamin B12 malabsorption, megaloblastic anemia and proteinuria. The precise incidence of this disorder is unknown in the Middle East and Arab countries. The disease is caused by a homozygous mutation in either AMN or CUBN genes.

Objectives: To describe the clinical and molecular features of a family with early-onset IGS.

Design/Method: Clinical and laboratory data of patients diagnosed with IGS in Oman were retrospectively collected. Mutation analysis for all genes involved in vitamin B12/folic acid metabolism and megaloblastic anemia (7 gene panel: AMN, CUBN, TCN1, TCN2, GIF, SLC19A2 and DHFR) was conducted using Next Generation Sequencing (NGS).

Results: Three siblings (2 girls and a boy) have been diagnosed with the condition. They exhibit a phenotypic variability with different age of presentation and different spectrum of disease. The index case presented at the age of 3 years with full-blown clinical phenotype and delayed milestones. The other two siblings have been diagnosed at the age of 12 and 18 months, with milder clinical phenotype. All patients harbor a novel bi-allelic frameshift mutation in exon 11 of AMN gene (p.Pro409Glyfs*), which was not reported previously in literature. Both parents are heterozygotes for the same variant. All patients responded well to vitamin B12 parenteral therapy, but proteinuria persisted.

Conclusion: In communities with high incidence of consanguinity, cases of early-onset vitamin B12 deficiency should be thoroughly investigated to explore the possibility of Imerslund-Gräsbeck syndrome and other vitamin B12-related hereditary disorders. Further local and regional studies are highly recommended.

Poster # 333

METHOTREXATE USE IN END-STAGE RENAL DISEASE: A CASE REPORT

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Background: Methotrexate is critical to many chemotherapy regimens, however it is eliminated renally and therefore in patients with renal failure there are concerns that it could lead to unacceptably high blood levels and consequently high toxicity.

Objectives: Present case report regarding patient in end stage renal disease and subsequently developed osteosarcoma that was successfully and safely treated with methotrexate.

Design/Method: Single case report.

Results: A 18 year old girl with history of hemodialysis dependent lupus nephritis was diagnosed with osteoblastic type osteosarcoma of the right femur WHO grade II. Treatment per protocol AOST0331 with adjusted doses for renal failure was begun.

On weeks 1 and 6 of therapy she two consecutive days of cisplatin and doxorubicin and patient was dialyzed 24 hours after medications. On week 4,5,9 and 10 of therapy she received methotrexate at 25% of protocol dose (3 gm/m^2 in place of 13 gm/m^2), with high dose leucovorin 50 mg/m2, with twice daily hemodialysis and cleared methotrexate at ~120 hours after each dose. The frequent hemodialysis put her at risk for disequilibrium syndrome which was mitigated with intradialytic mannitol. Course was complicated by severe mucositis, requiring intradialytic TPN. Limb salvage surgery was performed and she has remained in remission upon 4 year follow up.

Conclusion: Methotrexate can safely be used in renal failure with an interdisciplinary approach.

Poster # 334

EARLY DETECTION AND STEM CELL TRANSPLANTATION OF A RARE IMMUNODEFICIENCY

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Background: Phosphoglucomutase 3 (PGM3) deficiency is a primary immunodeficiency, characterized by T cell lymphopenia and neutropenia that presents with a variable clinical phenotype including neurocognitive and skeletal abnormalities, atopy, and progressive bone marrow failure. The introduction of the T cell receptor excision circles (TREC) assay on the newborn screen (NBS) has resulted in early detection and evaluation of rare immunodeficiency syndromes associated with T cell lymphopenia.

Objectives: Discuss the early diagnosis of a rare immunodeficiency syndrome by NBS and treatment with reduced-intensity hematopoietic stem cell transplant (SCT).

Design/Method: We present a 4-month-old female with combined immunodeficiency and congenital neutropenia due to a compound heterozygous PGM3 mutation, including a novel variant, who was treated with allogeneic umbilical cord blood (UCB) SCT.

Results: Patient presented at 2 weeks of age with an abnormal TREC assay on NBS. Flow cytometry was remarkable for decreased CD3+ T cells (305 cells/microL), CD19+ B cells (398 cells/microL), and naïve CD45RA+ T cells (18%, normal 64 -95%), and severe neutropenia (0.3x109cells/L) refractory to filgrastim. Responses to mitogens were decreased. Thymus was present on radiograph. IgM and IgA were below the limit of detection with normal IgE and IgG. Targeted sequencing of 25 genes associated with severe combined immunodeficiency was negative. Whole-genome sequencing identified two pathogenic variants in PGM3: a maternally inherited c.1049T>C (p.Ile350Thr) missense variant and a novel de novo c.1558C>T (p.Arg520Ter) nonsense variant. No skeletal, hepatic, or neurological abnormalities were identified. At age 3 months, the patient underwent 5/6-matched UCB SCT with alemtuzumab, fludarabine, and melphalan conditioning. SCT was complicated by sinusoidal obstructive syndrome, treated with defibrotide, and grade 2 acute graft-versus-host disease of her skin, steroid-responsive. She has had no infections. At 100 Days post-SCT, she has normal absolute neutrophil counts, full donor chimerism, ongoing B and T cell recovery, and increased naïve CD45RA+ lymphocytes.

Conclusion: Phenotypic variability in patients with PMG3 deficiency can include isolated neutropenia and immunodeficiency. TREC screening allows prompt identification of newborns with rare immunodeficiencies associated with T cell lymphopenia. Reduced-intensity UCB SCT can achieve an excellent outcome in PGM3 deficiency, with resolution of neutropenia and improvement in immune status.

Poster # 335

NOONAN SYNDROME WITH CHYLOUS ASCITES SECONDARY TO INTRA-ABDOMINAL LYMPHANGECTASIA

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Background: Approximately 20% of patients with Noonan Syndrome (NS) have associated lymphatic dysplasia. Manifestations include testicular, intestinal or pulmonary lymphangiectasias, hydrops, chylous pleural effusions, chylothorax, thoracic duct aplasia, thoracic cage anomalous lymphatic vessels and hypoplastic inguinal, iliac or leg lymphatic vessels.

Objectives: The most common lymphatic disorders associated with NS are peripheral lymphedema and chylous pleural effusions. Here we report a case of chylous ascites secondary to intra-abdominal lymphangectasia.

Design/Method: When unable to address the underlying pathology via lymphatic duct embolization upon extensive review the literature the medical management of chylous ascites is based on a few systematic reviews, case reports and small observational studies. Additionally, the majoprity of the limited data found is from cases of chylous ascites secondary to surgery or malignancy not lymphatic malformations.

Results: A 5-year-old male with NS presented with rapid onset abdominal distension over a three-day period. Patient had prior history of intermittent abdominal distension to a much lesser degree. Patient had accompanying discomfort but no other associated symptoms nor acute illness. His abdominal girth reached seventy-eight centimeters with his height being one-hundred and three centimeters. His workup was negative for malignancy, nephrotic syndrome as well as kidney, liver and heart failure. Computed tomography revealed a large amount of abdominal and pelvic ascites with intra-abdominal organ centralization. Ultrasound with doppler showed no vascular anomalies and a patent portal vein. Chest x-ray showed reduced lung volumes but no chylothorax. Patient was started on Octreotide, a low-fat diet and MCT supplementation to reduce chyle production and flow. He underwent abdominal paracentesis four times for fluid analysis and symptomatic relief. Abdominal girths returned back to prior each time within two days. The peritoneal fluid had elevated triglyceride levels and serum-to-ascites albumin gradient suggesting lymphatic obstruction. Patient developed partial bowel and bladder obstruction as well as progressively worsening atelectasis with increasing oxygen requirements. Due to failed medical management with risk for respiratory failure he was transferred to the Children's Hospital of Philadelphia. He underwent dynamic contrast MR lymphangiography followed by successful selective lymphatic duct embolization using N-butyl cyanoacrylate glue to stop the leak and seal the abnormal lymphatic vessels.

Conclusion: For patients with NS presenting with rapid onset chylous ascites secondary to lymphatic abnormalities not responsive to medical management who progress to having impaired oral intake, urinary retention and bowel obstruction followed by respiratory compromise; special consideration should be given early on to performing lymphangiography followed by selective lymphatic duct embolization.

Poster # 336

FANCONI ANEMIA AND MALIGNANCIES: A CALL FOR EARLY DETECTION

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Background: Fanconi anemia (FA) is an inherited disorder characterized by mutations impairing DNA interstrand crosslinks repair and resulting in genomic instability, sensitivity to cytotoxic agents, and cancer predisposition. Children harboring FANCD1/BRCA2 and FANCN/PALB2 biallelic mutations have an increased likelihood of developing a childhood malignancy. Chromosomal gains 1q, 3q, 13q, and monosomy 7 confer an increased leukemic risk. Classically described congenital abnormalities may be subtle and overlap with other genetic syndromes, such as VACTERL-association. We present a case of initially undiagnosed FA complicated by the development of neuroblastoma and acute myelogenous leukemia (AML).

Objectives: To review the need for early diagnosis of FA and the contribution of genetic and treatment-related factors in the development of malignancies.

Design/Method: Case report

Results: A one-day-old girl was referred for management of an imperforate anus and recto-vaginal fistula. She presented with microcephaly, microphthalmia, low set right ear, high-arched palate, choanal atresia, cutis aplasia, clinodactyly, and vertical talus. She had a left atretic kidney, right ectopic kidney, a patent foramen ovale, and a mid-muscular ventricular septal defect. A year later, surveillance abdominal ultrasonography detected a left upper quadrant mass. Computed tomography of the abdomen and pelvis defined a retroperitoneal mass and hepatic lesions with corresponding uptake on metaiodobenzylguanidine scan. Urine vanillylmandelic acid was 209 ug/mg creat (normal <27), homovanillic acid 116.1 ug/mg creat (normal <33), neuron-specific enolase 87.8 ng/ml (normal <10.8). Pathology confirmed poorly differentiated MYCN non-amplified neuroblastoma of unfavorable histology, DNA index 1, and loss of heterozygosity at 1p and 11q23. Following one cycle of chemotherapy per COG ANBL0531 with etoposide and carboplatin, the patient developed hypoxemic respiratory failure, mucositis, liver dysfunction, gastrointestinal bleeding, and persistent fevers. Prolonged pancytopenia prompted a bone marrow evaluation; megakaryocytes with dysplastic features were seen without meeting myelodysplastic syndrome criteria. In addition to a known 1p cytogenetic abnormality, 5q deletion, gain of chromosome 17, and additional material on 18q were detected. Subsequently, FA was diagnosed by skin fibroblast diepoxybutane analysis and identification of a pathogenic mutation in PALB2. A month later, a bone marrow aspirate confirmed AML with 5q and 7q deletions. The patient passed away shortly thereafter from multiorgan dysfunction.

Conclusion: FA is a phenotypically heterogeneous disease and can be confused with VACTERL. FA Screening should be considered in patients with VACTERL to establish an early diagnosis, mitigate potential therapy-related complications, and enable close surveillance. We also highlight the contribution of genetic factors and chemotherapy exposures in the development of neoplastic processes in FA.

Poster # 337

LEVOFLOXACIN PROPHYLAXIS FOR A PATIENT WITH INFANT ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Infant acute lymphoblastic leukemia (ALL) is a rare, biologically and clinically distinct form of ALL, associated with poor outcomes, especially in the presence of the KMT2A (MLL) gene rearrangement. These patients receive intensive chemotherapy and are at risk for numerous treatment related complications, especially infection and induction related mortality. Many of these patients are hospitalized for several months in order to provide close monitoring and receive intensive supportive care per institution guidelines with recommendation to use empiric antibiotics if patients develop febrile neutropenia. Levofloxacin prophylaxis has been shown to significantly reduce bacteremia in older children with ALL and acute myeloid leukemia (AML). However, patients with infant ALL were not included in these studies.

Objectives: Describe a patient with infant leukemia that received antimicrobial prophylaxis with levofloxacin throughout therapy.

Design/Method: Case report

Results: A 10 month old female was diagnosed with MLL rearranged infant ALL in October of 2018. She started induction therapy per AALL15P1, without azacitidine, and the rest of her therapy was based on the Interfant-06 protocol. On day 3 of induction she was transitioned from cefepime (for empiric treatment of febrile neutropenia) to levofloxacin, 10 mg/kg/dose BID, for antimicrobial prophylaxis. She did not experience any infection related complications during induction. After induction, levofloxacin prophylaxis was continued with each cycle of chemotherapy and until the beginning of maintenance therapy. She also received prophylaxis against invasive candidiasis (micafungin during induction, transitioned to fluconazole), *Pneumocystis jiroveci* pneumonia (sulfamethoxazole-trimethoprim) and respiratory syncytial virus (palivizumab). She completed maintenance therapy in October of 2020. She remained mostly inpatient during intensive chemotherapy phases when she was expected to be neutropenic. Throughout treatment, she had 2 episodes of febrile neutropenia requiring escalation from levofloxacin prophylaxis, resulting in 14 total days of therapy with cefepime and 1 day of vancomycin. Levofloxacin prophylaxis was resumed after infection was excluded and neutropenia had recovered. In total, the patient received approximately 8 months of levofloxacin prophylaxis, during which she experienced no levofloxacin-related toxicity and despite multiple risk factors for infection, no episodes of infection or bacteremia occurred.

Conclusion: Levofloxacin prophylaxis is recommended in supportive care guidelines for pediatric patients with cancer, primarily for patients with AML or relapsed ALL. Patients with infant ALL are also high risk of infection throughout therapy requiring aggressive supportive care. Levofloxacin prophylaxis could be a potential addition to the supportive care

armamentarium for these patients in an attempt to reduce bacteremia and infection related complications.

Poster # 338

ACUTE ACALCULOUS CRYPTOSPORIDIUM CHOLECYSTITIS: A CASE REPORT AND REVIEW OF THE LITERATURE

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Background: Acute acalculous cholecystitis due to *Cryptosporidium* is rare in children undergoing chemotherapy with only two reported cases successfully treated with antiprotozoal therapy.

Objectives: To describe the case of a toddler with very high risk (VHR) Pre-B acute lymphoblastic leukemia (ALL) with intestinal cryptosporidium infection who developed subacute acalculous *Cryptosporidium* cholecystitis.

Design/Method: Case Report and Literature Review.

Results: A 3-year-old male with VHR ALL treated per COG protocol AALL1131 who presented during the first cycle of maintenance therapy with progressively worsening, copious non-bloody diarrhea and abdominal pain in the setting of a 3-week history of intermittent abdominal pain without ascertainable aggravating or alleviating factors. Workup revealed elevated CRP of 14.6 mg/dL, neutropenia (ANC 220 mL), and lymphopenia (ALC 80 mL), transaminitis (ALT 275 U/L, AST 159 U/L) and normal amylase and lipase levels. Abdominal computed tomography demonstrated a contracted gallbladder with pericholecystic fluid and periportal edema. Ultrasound imaging was consistent with acute cholecystitis. He was treated with intravenous piperacillin-tazobactam and started on granulocyte colony stimulating factor to aid count recovery. Oral mercaptopurine and methotrexate were held. Due to unremitting abdominal pain, emergent laparoscopic cholecystectomy was done with findings of inflamed intrahepatic gallbladder. Stool rapid antigen test resulted positive for *Cryptosporidium* antigen and he was treated with a 3-day course of nitazoxanide. Histopathology on resected gallbladder was positive for subacute acalculous *Cryptosporidium* cholecystitis with identification of oocytes. Stool testing 5 days later was negative for *Cryptosporidium* but repeat testing 4 weeks later was positive. He was re-treated with nitazoxanide for 14 days. Three months post-cholecystectomy, abdominal pain recurred with grossly elevated alkaline phosphatase 1,118 unit/L and gamma-glutamyl transferase 887 unit/L. Magnetic resonance cholangiopancreatography demonstrated enlargement of common bile duct (CBD) with short segment stricture of distal segment.

Conclusion: This is the third case of *Cryptosporidium* cholecystitis in a pediatric patient with ALL on maintenance chemotherapy and the first with the complication of CBD stricture. *Cryptosporidium* hominis (infects humans) and parvum (infects humans, pre-weaned

bovine calves and mammals) are the most prevalent causative species. Our patient had a puppy which tested negative and had no recent history of recreational water activities or contact with livestock. We believe that CBD stricture was most likely from parasitic infectious sequalae from colonization manifesting as persistently positive stool samples rather than operative morbidity from a non-complicated surgery. Parasitic infections, especially *Cryptosporidium* infection, should be considered as a cause for diarrhea or cholecystitis in immunocompromised children receiving chemotherapy.

Poster # 339

UNUSUAL PRESENTATION OF TTP IN A NEWLY DIAGNOSED PATIENT WITH SLE IN THE SETTING OF COVID19

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Background: Coronavirus disease 2019 (COVID-19) can profoundly impact the immune system and our understanding of this immune dysregulation is evolving. The overall manifestations in children have been milder. In addition to the classic features of COVID 19, recent studies reveal that children may present with a multisystem inflammatory syndrome (MIS-C) with fever, mucocutaneous and cardiac changes. In pediatrics, COVID-19 infections has been associated with autoimmune hemolytic anemia but thrombotic thrombocytopenic purpura (TTP) was not reported as compared to adult.

Objectives: An 11 year-old patient with unusual presentation of TTP and new onset systemic lupus erythematous (SLE) in the setting of COVID19 infection.

Design/Method: Case Report

Results: A previously healthy 11-year-old male presented with fevers, dizziness and new onset petechial rash with prolonged epistaxis for one week duration. Initial laboratory tests revealed anemia, thrombocytopenia, marked hemolysis, proteinuria and hematuria. Peripheral blood smear showed numerous schistocytes with significant polychromasia and thrombocytopenia. Direct antiglobulin was positive. A nasopharyngeal swab showed COVID-19 positive by RT-PCR, with elevated SARS-COV-2 IgG antibodies. Inflammatory markers and cytokines showed normal ferritin, elevated CRP, ESR, IL-6, IL2 soluble receptor and TNF-alpha and low IL-1B. Both troponin I and brain natrutic peptide were highly elevated. Echocardiogram showed ectasia of left main coronary artery (LMCA) with a moderately decreased left ventricular function (LVF). We therefore suspected MIS-C with likely TTP or Evan's syndrome. Rheumatological tests revealed strong positive SLE serology including ANA, anti-DsDNA, and anti-Smith antibodies along very low C3 and C4 levels. Patient was given IVIG for the treatment of Evan's syndrome followed by pulse methylprednisolone. Patient showed minimal clinical and laboratory response. Low ADAMTS13 activity and high inhibitor confirmed the diagnosis of TTP. Plasma exchange (PE) was immediately started and promptly exhibited an impressive clinical

improvement within 24 hours. Following 7 sessions of PE, his platelets count normalized and anemia gradually improved. He was also started on mycophenoloate mofetil and hydroxychloroquine sulfate. He had complete resolution of hemolysis markers, proteinuria and hematuria. Echocardiogram showed normalization of LVF, resolution of LMCA dilation with dilation of the RCA for which he was started on aspirin.

Conclusion: TTP should be considered in juvenile SLE with or without COVID-19 infection when presenting with thrombocytopenia, Coombs positive anemia and schistocytosis on blood smear. This will allow early intervention with life saving plasma exchange and avoiding contraindicated platelets transfusion. We report unique case of TTP as a presenting manifestation on new onset juvenile SLE in the setting of COVID-19 infection.

Poster # 340

SPLENIC MASS IN PATIENT WITH PIK3CA-RELATED OVERGROWTH SPECTRUM TREATED WITH TARGETED THERAPY

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Background: Vascular anomalies patients with overgrowth syndromes due to mutations in PIK3CA are now classified under the diagnosis of PIK3CA-related overgrowth spectrum (PROS). Splenic masses in patients with PROS have not been previously described.

Objectives: We describe the diagnostic workup and treatment of splenic mass in a patient with PROS.

Design/Method: Case Report

Results: This is a 3 year old patient who was noted to have a vascular anomaly at birth. She had diffuse overgrowth of her left face, arm, and abdomen, as well as a capillary malformation extending over her neck and abdomen. Genetic testing from affected skin demonstrated a somatic mutation in PIK3CA (p.H1047Y, variant allele frequency 8%). Routine abdominal ultrasounds were performed as part of cancer screening. Prior evaluations of her spleen showed no abnormalities. At two years of age, as part of enrollment on a clinical trial, a Whole Body MRI was performed. She was found to have a new splenic mass not seen on prior imaging. Ultrasound demonstrated a solid-appearing splenic mass measuring 2.9 x 2.8 x 2.8 cm. She was asymptomatic. Given concern for possible malignancy, splenectomy was considered. After discussing her case at our institution’s interdisciplinary vascular anomalies conference, ultrasound-guided biopsy by Interventional Radiology was performed. Pathology demonstrated a lymphatic malformation with papillary endothelial proliferation. Genetic testing of the splenic lesion confirmed the same somatic variant in PIK3CA (p.H1047Y). The lymphatic malformation grew to 3.4 x 3.6 x 3.4 cm in size after a period of one month. The patient was then enrolled on a clinical trial of miransertib, an oral AKT inhibitor. Over the past six months, the lesion has

showed no interval growth while on this therapy.

Conclusion: Patients with PROS may be at risk for developing masses in diverse anatomic locations. Without definitive biopsy, it is difficult to determine if these masses are benign or malignant. As more PROS patients are screened for enrollment in clinical trials, providers may be faced with incidental findings of non-specific masses. Involvement of interdisciplinary teams is paramount for accurate diagnosis and treatment. Core needle biopsies in this patient demonstrated a benign etiology and confirmed the patient's known PIK3CA mutation within the splenic lesion. Our young patient was able to avoid splenectomy due to confirmation that the mass was a manifestation of her underlying PROS disorder.

Poster # 341

PATIENT WITH BOCKENHEIMER DISEASE DUE TO SOMATIC TIE2 MUTATION TREATED WITH PIK3CA INHIBITOR

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Background: Bockenheimer disease is a rare vascular anomaly manifested by diffuse venous malformations affecting all tissues of the upper extremity and chest wall. It is characterized by pain, disfigurement, ulceration, paresthesia, and often, localized intravascular coagulopathy (LIC). Patients with TIE2 mutations have been treated with sirolimus, an mTOR inhibitor, with some effect. Utility of novel targeted agents for patients with TIE2 mutations has not been described.

Objectives: We present a woman with Bockenheimer disease with confirmed TIE2 mutation who responded to use of the PIK3CA inhibitor alpelisib.

Design/Method: Case Report

Results: This is a 48-year-old female with extensive venous malformation of her chest and right extremity consistent with Bockenheimer's disease. As a child, she maintained normal function of her right extremity. Between the ages of 23 and 25 years, she underwent over 20 sclerotherapy procedures, but experienced minimal relief. She had significant LIC (fibrinogen 70 mg/dL, D-dimer >20 mcg/mL, and platelet count of 130 K cells/uL). At age 33, she experienced hemorrhagic shock and lost approximately 30% of her total blood volume due to a ruptured ovarian cyst. After her first pregnancy at age 39, she experienced bowing of her right radius. At age 46, she experienced a spiral fracture of her right wrist. She was no longer able to continue her job due to significant limitations in range of motion and function. Approximately four months after her wrist fracture, sirolimus medical therapy was initiated. She also began apixaban, which improved her coagulopathy (fibrinogen 150 mg/dL, platelets 190 K cells/uL). She initially experienced mild softening of her lesions, but after 7 months, saw no further improvement, and this therapy was discontinued. Biopsy of affected tissue from her chest confirmed a TIE2 mutation (TEK p.L914F). Peripheral blood testing was negative. Due to progressive disease,

approval for compassionate use of the oral PIK3CA inhibitor alpelisib via a single-patient IND was obtained. She has been treated with 50 mg alpelisib daily for 13 months without significant adverse effects. Her coagulopathy has improved further, with rise in fibrinogen to 255 mg/dL, D-dimer of 13 mcg/mL, and platelets 249 K cells/uL. She has had clinical improvement with softening of her arm lesions. She has not had any bleeding episodes. MRI performed after eight months of therapy showed decrease in the size of the malformation and venous channels.

Conclusion: Patients with extensive venous malformations due to TIE2 mutations may be effectively treated with PIK3CA inhibitors.

Poster # 342

UPFRONT USE OF RITUXIMAB FOR ACQUIRED PEDIATRIC THROMBOTIC THROMBOCYTOPENIC PURPURA

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Background: Acquired thrombotic thrombocytopenic purpura (TTP) is an emergency characterized by thrombocytopenia, microangiopathy, end-organ ischemia, and severe ADAMTS13 deficiency. Standard of care consists of immediate initiation of therapeutic plasma exchange (TPE) along with corticosteroids.

Objectives: To discuss the role of upfront use of Rituximab in acquired pediatric TTP.

Design/Method: Case Report

Results: A 15-year-old Caucasian female presented acutely with slurred speech, right-sided hemiparesis, and altered mental status. On examination, she was noted to have petechiae on her extremities. Brain imaging showed no evidence of ischemia or hemorrhage. Laboratory investigations showed a hemolytic anemia, thrombocytopenia, and the peripheral smear showed abundant schistocytes. Renal, hepatic function, and vitamin B12 were normal. Viral serologies (HIV, EBV, hepatitis) were all negative.
TTP was presumed with immediate institution of TPE and corticosteroids. ADAMTS13 testing confirmed severe TTP with undetectable activity (<10%) and inhibitor titer >90 U/mL. Neurological symptoms resolved and TPE was continued for 15 days until laboratory parameters normalized. Rituximab was administered starting on day 4 for a course of four doses and immunosuppression was gradually weaned after a month. The patient was followed in the clinic and at 6 months post-diagnosis remains free of relapses and infectious complications.
Rituximab, a monoclonal antibody directed against CD20, depletes B cells thereby suppressing ADAMTS13 antibodies. Typically, use has been reserved for pediatric patients with refractory disease and in those with relapses. However, recently published ISTH guidelines recommend conditional consideration to mitigate the risk of relapse if used upfront. Pediatric patients with acquired TTP have been shown to have a relapse rate of 20-30%, consistent with observations in

the adult population. Independent predictors of relapse in adults have been defined as younger age (< 25 years old) and non-O blood group but not the severity of ADAMTS13 deficiency. Due to the rarity of this entity in children, these predictors have not been clearly defined in the pediatric population. Clarification is needed on which pediatric patients would benefit from upfront Rituximab use. Analysis in an adult cohort of the use of Rituximab during an initial TTP episode showed a decrease in subsequent hospitalizations and TPE procedures by delaying relapses and resulted in significant hospital savings along with decreased morbidity and mortality. However, this requires further validation in the pediatric setting.

Conclusion: Considering the devastating effects of relapsed episodes of TTP, the benefits of upfront Rituximab use should be considered in the pediatric population.

Poster # 343

LI- FRAUMENI SYNDROME RELATED MALIGNANCIES IN A SINGLE TERTIARY CENTER

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Background: Patients with Li Fraumeni Syndrome (LFS) differ significantly in their path to diagnosis, age at diagnosis, complications and outcome. In the last decade tumor and germline genomic sequencing of children with cancer has led to an increase in diagnosing underlying LFS with the decision to investigate for LFS being informed in some cases by the molecular profile of the presenting tumor.

Objectives: To describe our experience managing 5 children who were diagnosed with LFS since 2016 at our institution. We outline their medical history, presentation, course, malignant complications, tumor molecular profiles, therapy and outcomes.

Design/Method: Retrospective review of clinical data from EMR

Results: Patient 1: Female, DOB 3/5/2016, mother/family members diagnosed with LFS after patient, congenital adrenocortical mass (resected only), disseminated choroid plexus carcinoma at 6 months age, completed Headstart 2 therapy in July 2017. Currently alive and well. **Patient 2:** Male, DOB 7/13/2001, no known family history of LFS, diagnosed with anaplastic medulloblastoma at 13 years, completed therapy as per ACNS 0332 in May 2015, diagnosed with a CDKN2a/2b, NF1, PTPN, TP53 mutated Glioblastoma Multiforme and with LFS in July 2018, treated as per study PNOC 005 (intra-tumoral modified measles vaccine), followed by radiation + Temozolomide, Bevacizumab, Trametinib, Everolimus and Nivolumab. Expired 7/8/2020. **Patient 3 :** Male, DOB 5/27/2002, strong family history of malignancy, diagnosed at 15 years with SUFU/P53 mutated SHH medulloblastoma and subsequently with LFS by germline genomic sequencing. Completed treatment as per ACNS 0332 in March 2018,

presented with 3 cranial lesions (vascular malformation, GBM, undifferentiated pleomorphic sarcoma) and one L1 vertebral lesion (undifferentiated pleomorphic sarcoma) in Aug 2020. Lesions resected and he has completed radiation therapy with plan to treat with combination Bevacizumab/Temozolomide/Checkpoint Inhibitor therapy. **Patient 4:** Male, DOB 6/14/14, diagnosed with LFS at 2 years, family history of LFS (mother), diagnosed with Burkitt Leukemia at age 6 and currently receiving therapy as per ANHL 1131. **Patient 5:** Female, DOB 12/22/2009, diagnosed with LFS at age 4, family history of LFS (mother) and of malignancy (several family members)

Conclusion: Three of our patients were diagnosed with LFS after being diagnosed with cancer. While our ability to consider and diagnose cancer predisposition syndromes has improved in the era of genomic sequencing, LFS is still probably underdiagnosed in children. Since making a diagnosis early in life and subsequent surveillance has clear benefits, we would recommend a low threshold to investigate a child with cancer for LFS regardless of family history.

Poster # 344

IMPORTANCE OF A SURVEILLANCE REGIMEN FOR PATIENTS WITH VON HIPPEL LINDAU DISEASE

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Background: Von Hippel Lindau disease (vHL) is an autosomal dominant cancer predisposition syndrome associated with the development of rare tumors including hemangioblastomas, retinal angiomas, endolymphatic sac tumors, renal cell carcinoma, pancreatic cysts, pheochromocytomas, and neuroendocrine tumors. The presence of these pathognomonic tumors, multiple tumors, young age at diagnosis, and/or the presence of other manifestations of vHL should prompt genetic testing for a germline mutation.

Objectives: To review the case of a patient with vHL disease and the importance of adhering to a recommended surveillance protocol.

Design/Method: Here we describe the case of a 10-year-old female who presented with persistent headaches, found to have a rare brain tumor, leading to the diagnosis of vHL. She later developed another unusual tumor associated with this cancer predisposition syndrome.

Results: Initial imaging revealed a posterior fossa mass and the patient underwent gross total resection. Pathology confirmed a hemangioblastoma, WHO grade I low-grade tumor. Due to the rarity of this tumor, the possibility of vHL was raised. Although the patient had no obvious physical stigmata associated with vHL, based on the pathology and young age at diagnosis, genetic testing was pursued. vHL was confirmed. The family met with the oncology genetics team to discuss vHL and they recommended a surveillance protocol. The family agreed with the plan and surveillance started as recommended by an expert panel, including ophthalmology exams, catecholamines, audiograms, and MRI brain/spine/abdomen.

On routine imaging of the abdomen, approximately 6 years after the diagnosis of vHL, the patient was found to have several pancreatic lesions. MRI confirmed a mass at the head of the pancreas. A dedicated Gallium-68 DOTATATE PET/CT, which is used to detect neuroendocrine tumors (NET), demonstrated increased activity in the pancreatic head, diagnostic of a pancreatic NET. The patient was referred to surgery. The family elected to follow with imaging since the tumor was <2cm. The patient continues to have surveillance imaging and the pancreatic lesions remain stable.

Conclusion: Rare tumors in a young patient should raise the question of a cancer predisposition syndrome. The diagnosis of hemangioblastoma in our patient prompted further genetic testing, revealing vHL disease. This case highlights how crucial it is to evaluate for cancer predisposition syndromes in patients with unusual tumors and initiate surveillance screening, potentially allowing for an early diagnosis of other rare and possibly lethal tumors associated with the underlying cancer predisposition syndrome.

Poster # 345

ALL THAT GROWS ISN'T MALIGNANT: THE HIBERNOMA

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Background: Pediatric chest masses are a concerning finding. The differential is wide and a broad index of suspicion must be maintained. In this report we present a case of chest mass that resulted with a benign course. They can be divided into congenital, infectious, neoplastic, inflammatory, and vascular causes. Neoplastic can be subdivided into benign vs malignant etiologies. Any mass, whether found incidentally or due to workup for symptoms deserves a closer evaluation. Hibernomas are rare, benign growths of neonatal fat tissue that can present in any period of life, but most frequently occur in the 3rd and 4th decades, about 5% of cases are seen in the pediatric population, in children they have most often been found in the neck. There have been no reported cases of recurrence after excision.

Objectives: Report a case of hibernoma and discuss the workup, differential, and outcome.

Design/Method: Single case report with discussion of differential and work up as based on literature review.

Results: A previously healthy 15 year old female presented to hospital due to acute onset right sided chest pain, shortness of breath that progressed to episode of syncope. She was found on chest x-ray to have right lung mass concerning for Ewing sarcoma. CT revealed a large pleural mass in the right chest measuring 8.3 cm with posterior right pleural effusion. COVID testing resulted positive. Ultrasound-guided biopsy was performed and resulted with coarsely granular to multivacuolated eosinophilic to pale cytoplasm and large mature univacuolated adipocytes,

without atypia or mitosis. Immunohistochemical analysis was immunoreactive for S100, negative for Desmin, with presence of CD34 and CD31, highlighting a vascular network. These findings were consistent with hibernoma. Excisional surgery was performed and she did well with no recurrence of symptoms upon 2 month follow up.

Conclusion: Hibernoma is a rare cause of benign chest mass, especially in children, with no reported recurrence after excision.

Poster # 346

ALLOGENIC BONE MARROW TRANSPLANT FOR REFRACTORY IMMUNE THROMBOCYTOPENIA

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Background: Immune thrombocytopenia (ITP) is a heterogeneous autoimmune bleeding disorder with a complex pathophysiology of humoral and cell-mediated immune destruction of peripheral platelets as well as alteration of megakaryopoiesis. Refractory ITP is difficult to treat, requiring multi-modal therapy often consisting of sequential trials of immune-modulating and/or thrombopoietin-receptor agonist therapies. Stem-cell transplant has rarely been employed for refractory ITP.

Objectives: Given that bone marrow transplant (BMT) is an uncommon treatment for refractory ITP, we set out to describe the decision-making leading to BMT, the BMT regimen and course, and the outcome for this case of refractory ITP.

Design/Method: Case report.

Results: A 17-year-old female with chronic, refractory ITP presented for consultation for BMT. She was diagnosed at age 10 when she presented with heavy menstrual bleeding and severe thrombocytopenia. Complications of ITP included significant heavy menstrual bleeding, gastrointestinal bleeding, hematuria, and epistaxis. She had two spontaneous intra-cranial hemorrhages. Her ITP treatments included: IVIG, prednisone, dexamethasone, rituximab, splenectomy, romiplostim, eltrombopag, mycophenolate, sirolimus, cyclophosphamide, vincristine, methotrexate, high dose vitamin C, and fostamatinib. Combination therapy with immune suppression and thrombopoietin-receptor agonists was employed. She had inconsistent and un-sustained or no response to therapies. No etiology for thrombocytopenia was identified despite multiple re-evaluations. Decision to undergo bone marrow transplant was based on risk for a third intracranial bleed as well as autoimmune cytopenias and lymphoma due to prolonged immunosuppression. Patient underwent matched sibling bone marrow transplant with conditioning of busulfan, cyclophosphamide, and ATG. GVHD prophylaxis was tacrolimus and mycophenolate mofetil. There were no significant complications, bleeding, or GVHD following transplant. Patient responded to platelet transfusions followed by IVIG. Neutrophil and platelet engraftment were achieved on Day +12 and Day +29, respectively.

Chimerism at Day +27 showed complete engraftment of myeloid lineage cells (CD33+) with T-cell lineage (CD3+) 65% Donor. Although chimerism was mixed, it remained stable with platelet counts above 100,000. At one-year post-BMT, the patient was able to achieve acceptable platelet levels without need for transfusions even with mixed chimerisms.

Conclusion: In the majority of children, ITP self-resolves and is associated with minor bleeding. Rarely, ITP can be severe, chronic, and refractory. Current literature supports trialing multiple therapies aimed at improving platelet counts and decreasing bleeding symptoms. While BMT is a high-risk therapy and rarely employed in the treatment of ITP, it should be considered for those with refractory disease who have failed other therapies.

Poster # 347/Early Career Award Recipient

HSCT RESCUES MARROW FAILURE IN A PATIENT WITH LEUKEMIA AND PREVIOUSLY UNDIAGNOSED LIGASE IV SYNDROME

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Background: Patients with DNA double-strand breakage repair disorders are at increased risk of immunodeficiency, bone marrow failure, and malignancy. Malignancy in this cohort of patients is particularly difficult to treat given the underlying sensitivity to chemotherapy and radiotherapy, lending an important role to hematopoietic stem cell transplantation (HSCT). The choice of conditioning regimen employed poses a challenge, however, as equipoise is crucial between reducing risk of rejection or poor stem cell engraftment with adequate cytoreduction and minimizing excessive toxicity from myeloablative chemotherapy or ionizing radiation in patients with DNA repair defects.

Objectives: This case report describes the successful use of a reduced intensity conditioning (RIC) HSCT in a patient with ligase IV syndrome and numerous pre-transplant complications including malignancy, cardiac failure, typhlitis, marrow aplasia, and secondary hemophagocytic lymphohistiocytosis (HLH).

Design/Method: Single subject case report

Results: A previously healthy microcephalic 5-year-old male presented with B/myeloid mixed phenotype acute leukemia with a *RUNX1-CBFA2T3* fusion. After only 12 days of lymphoid-directed induction therapy including a total of 50mg/m^2 of anthracycline, he developed protracted marrow aplasia, typhlitis, secondary HLH, and cardiac dysfunction with severely depressed left ventricular function, initiating evaluation by whole exome sequencing. The identification of biallelic variants in *LIG4* consistent with DNA ligase IV syndrome, with ongoing protracted marrow aplasia, prompted rescue with HSCT. Prior to transplantation, the patient's HLH was controlled with dexamethasone and emapalumab. His cardiac function

normalized and he was weaned off of epinephrine and milrinone. Bone marrow evaluation two months after induction chemotherapy demonstrated marked hypocellularity (<5%) with trilineage aplasia but no evidence of leukemia. He tolerated a RIC regimen of alemtuzumab, fludarabine (150mg/m^2), and cyclophosphamide (20mg/kg) followed by a 9/10 matched unrelated donor bone marrow HSCT. Transplant course was complicated by bacteremia and typhlitis leading to G-CSF initiation. He is now greater than 30 days post-transplantation and doing well with neutrophil engraftment, no evidence of graft-versus-host disease, and no current infections.

Conclusion: Case series have described successful HSCT with RIC preparative regimen for patients with ligase IV syndrome, though data are scant for the successful treatment of malignancy and recovery from organ dysfunction and HLH for this disease. Our case demonstrates successful rescue HSCT in a patient with cardiac failure, HLH, leukemia, and marrow aplasia, demonstrating that these patients may recover from significant co-morbid conditions that would otherwise preclude curative HSCT and tolerate a RIC regimen that facilitates engraftment.

Poster # 348

DEFIBROTIDE THERAPY FOR SOS/VOD IN PEDIATRIC CANCER FOLLOWING NONTRANSPLANT-ASSOCIATED CHEMOTHERAPY

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Background: Sinusoidal obstruction syndrome (SOS), formerly hepatic veno-occlusive disease (VOD), in pediatric cancer patients often presents as a complication of hematopoietic stem cell transplantation (HSCT), and less commonly as an adverse event from nontransplant-associated chemotherapy. The epidemiology and pathophysiology for the former is well-described in the literature. As such, defibrotide therapy has been established as the standard of care for transplant-associated SOS/VOD, however, treatment of nontransplant-associated SOS/VOD is less clear.

We present a case of a 3-year-old female with relapsed Wilms' tumor and recurrent SOS/VOD during therapy with use of defibrotide as treatment.

Objectives: This study aims to: 1) review a case of SOS/VOD in a patient with relapsed Wilms' tumor; 2) review prior case findings regarding prophylaxis and treatment of SOS/VOD with defibrotide.

Design/Method: A review of our case of SOS/VOD was performed followed by a literature review from the PubMed database, including studies published between 2009 and 2020. Study inclusion criteria consisted of: pediatric patients diagnosed with nontransplant-associated SOS/VOD and subsequent defibrotide therapy.

Results: A 3-year-old female with relapsed Wilms' tumor treated with cyclophosphamide, doxorubicin, vincristine, and etoposide, as well as abdominal radiation therapy developed SOS/VOD and was treated with defibrotide with resolution of the SOS/VOD. Upon resumption of chemotherapy with vincristine and irinotecan, she again developed SOS/VOD and was again treated with defibrotide. The subsequent chemotherapy courses, consisting of topotecan, were given with prophylactic defibrotide, and she experienced no further SOS/VOD.

The literature review revealed 78 pediatric cancer patients with nontransplant-associated SOS/VOD treated with defibrotide. The majority of patients were diagnosed with acute lymphoblastic leukemia (ALL) or acute myeloid leukemia (AML). As part of their chemotherapy regimen, most patients received cyclophosphamide and vincristine, and four patients received radiotherapy. Sixty-two (79.5%) patients were reported to be in remission for SOS/VOD after defibrotide therapy, 13 (16.7%) patients died with SOS/VOD, and three (0.04%) patients were lost to follow-up. Multi-organ dysfunction (MOD) was experienced in 31 (39.7%) patients, and 22 (71%) of these patients were reported to be in remission from SOS/VOD. In contrast, 40 of 47 (85.1%) patients without MOD were alive without SOS/VOD.

Conclusion: Most nontransplant-related SOS/VOD cases presented with underlying ALL or AML. Conventional chemotherapies, such as vincristine and cyclophosphamide, were associated with higher SOS/VOD risk. Treatment with defibrotide resulted in a high survival rate, with greater prognosis in patients without MOD. This review supports early treatment with defibrotide, before progression to MOD in patients with nontransplant-associated SOS/VOD.

Poster # 349

HEMATOPOIETIC STEM CELL TRANSPLANT AS A NOVEL APPROACH TO TRIOSEPHOSPHATE ISOMERASE DEFICIENCY

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Background: Our case patient was diagnosed with triosephosphate isomerase (TPI) deficiency at age 12 months. TPI deficiency is a rare, congenital red blood cell disorder associated with hemolytic anemia, susceptibility to infection, and neurodegeneration by toxic metabolites. Typical treatment is supportive, including splenectomy to reduce hemolysis and regular red blood cell transfusions to transiently increase enzyme levels in the blood. Neurodegeneration often impacts the diaphragm, leading to respiratory failure and death by age 6 years in most patients.

Objectives: In order to prevent the debilitating neurodegeneration associated with TPI deficiency, we pursued permanent replacement of the TPI enzyme by production within the bone marrow using hematopoietic stem cell transplant (HSCT).

Design/Method: Our case patient was followed from diagnosis until present day at age 7 years with regular labs and neurologic exams. He received first HSCT at age 17 months. Due to

waning chimerism and return of hemolytic anemia, our patient received a second HSCT at age 20 months. Shortly after the second HSCT, our patient acquired stenotrophomonas bacteremia and experienced respiratory failure requiring tracheostomy. Rescue unrelated cord blood HSCT was performed at age 23 months.

Results: At time of evaluation for first transplant, our patient had bilateral lower extremity weakness and reduced tone, vibration sensation, and deep tendon reflexes, thought to be secondary to lower motor neuron degeneration. After first transplant, serum TPI enzyme levels increased to within the normal reference range before declining with waning chimerism. Although initially increasing, serum TPI levels never achieved normal reference range after the second transplant, which likely contributed to the significant neurodevelopmental decline that occurred in association with our patient's critical illness. Following his third transplant, our patient has maintained serum TPI enzyme levels within the normal reference range. Now 7 years old, he has not experienced any further neurodegeneration, and with the assistance of intensive physical therapy he has regained many lost neurodevelopmental milestones.

Conclusion: This report describes the first documented case of HSCT used in the treatment of TPI deficiency in the United States. As anticipated, this case demonstrates that HSCT can provide a permanent source of TPI enzyme production for patients with congenital TPI deficiency. Further multi-center research is necessary to determine the degree to which enzyme replacement can salvage neurodevelopment, and to define the efficacy and safety associated with HSCT as a potentially curative treatment for TPI deficiency.

Poster # 350

A SPECTRUM OF MALIGNANT/NON-MALIGNANT PHENOTYPE WITH HOMOZYGOUS MUTATION OF PMS2 IN CMMRD AFTER BMT.

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Background: Constitutional Mismatch Repair Deficiency (CMMRD) is caused by a biallelic mutation on one of the four major mismatch repair (MMR) genes. It is a rare autosomal recessive syndrome that predisposes to childhood cancer. Constitutional Mismatch Repair Deficiency (CMMRD) is caused by a biallelic mutation on one of the four major MMR genes: PMS2, MLH1, MSH2, MSH6. It is a rare autosomal recessive syndrome that predisposes to childhood cancer. The malignant phenotype varies from lymphoma, leukemia, brain, and intestinal cancer. Nonmalignant features include adenomas, polyps, and café-au-lait spots. The PMS2 defect accounts for 50% of the cases.

Objectives: To discuss the presentation, workup, and management of CMMRD.

Design/Method: A single study case report.

Results: A 21-year-old male, past medical history of T-cell lymphoma diagnosed at age 7 who underwent a bone marrow transplant at 14 years old maintaining remission. He had been found to have nasal, colonic and duodenal polyps diagnosed 1 year before admission. He presented with one month of abdominal pain, intractable emesis, and severe weight loss. Pertinent physical exam findings included cachexia, diffuse abdominal tenderness, multiple birth marks of café-au-lait spots on chest and extremities, hypertrophic nails, and eroded teeth. CT abdomen revealed severe thickening of the wall of the second portion of the duodenum. Additionally, MRI showed retroperitoneal adenopathy and multiple liver lesions suggestive of metastasis. Nonmalignant lesions (hepatic and spinal hemangiomas) were also described. Upper endoscopy revealed a polyp with narrowing and ulceration in the second portion of the duodenum. Biopsy reported poorly differentiated adenocarcinoma with signet ring features. Immunohistochemistry for MMR genes showed loss of nuclear expression of PMS2 in both neoplastic and normal cells and MSI-low detected in 1 of the mononucleotide markers. This demonstrates homozygous PMS2 loss which is confirmatory for CMMRD presenting with metachronous lymphoma during childhood, and stage IV duodenal adenocarcinoma as a young adult. The decision to start neoadjuvant chemoimmunotherapy was made.

Conclusion: CMMRD is a relatively new condition that is now known as a distinct childhood cancer predisposition syndrome. Despite this, it is often underdiagnosed due to lack of awareness, variable phenotype, and similarity to other more known conditions like Neurofibromatosis type 1. Early diagnosis is warranted for the proper screening, optimal treatment, and follow-up of the patient and their family members.

Poster # 351

CONCURRENT SUBTYPES OF POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDERS AFTER SOLID ORGAN TRANSPLANT

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Background: Post-transplant lymphoproliferative disorder (PTLD) is a heterogenous group of premalignant and malignant conditions and remain a serious complication in children after organ transplantation. PTLD is classified into four main WHO histological categories including early lesions, polymorphic, monomorphic, and classic Hodgkin lymphoma-like. PTLD is often related to Epstein Barr Virus (EBV) infection but EBV negative PTLD also occurs. Incidence of PTLD is highest within one year after solid organ transplant, called early PTLD. A second peak 2-10 years after receiving transplant occurs called late PTLD. Recurrent PTLD is rare and not well-understood. There are currently no report of patients developing multiple subtypes of PTLD concurrently in the pediatric population following solid organ transplantation

Objectives: We report three cases of pediatric patients with multiple subtypes of late onset PTLD occurring concurrently.

Design/Method: Retrospective chart review was performed of all patients at our center with a PTLD diagnoses. IRB approval was obtained from the University of Florida.

Results: Case 1 is a 5-year-old male with EBV positive polymorphic PTLD or oral mucosa 4 years after orthotopic heart transplant treated with 6 weekly doses of Rituximab. Four months later, he developed oropharyngeal infiltrating lesion that was EBV negative polymorphic PTLD treated with 6 cycles of prednisone, rituximab and cyclophosphamide. Case 2 is a 6-year male with EBV positive Burkitts type monomorphic PTLD 3.5 years after orthotopic heart transplant with incomplete treatment with prednisone, rituximab, and cyclophosphamide due to acute heart rejection. One month later, he developed orbital monomorphic diffuse large B cell lymphoma. Despite starting treatment with cyclophosphamide, rituximab and dexamethasone, he succumbed to his disease. Case 3 is a 15-year-old female with EBV positive T/NK cell type PTLD involving mesenteric lymph nodes with multiple pulmonary nodules treated with prednisone. Two months later, worsening duodenal wall lesions and lung nodules were found to be EBV negative monomorphic diffuse large B cell lymphoma. Refractory to 6 cycles of rituximab, prednisone and cyclophosphamide, she was treated with intensive chemotherapy with rituximab, prednisone, cyclophosphamide, vincristine, doxorubicin, high dose methotrexate, cytarabine, mercaptopurine, and etoposide (Protocol 901) that was curative.

Conclusion: PTLD in pediatric patient refractory to standard treatment should raise suspicion for a concurrent different subtype of PTLD. Recurrent late onset PTLD is often EBV negative and continues to remain poorly understood. Further research is needed to develop optimal treatment strategies.

Poster # 352

OCCULT SPLENIC KAPOSIFORM HEMANGIOENDOTHELIOMA PRESENTING AS CONSUMPTIVE COAGULOPATHY

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Background: Kaposiform hemangioendothelioma (KHE) is a rare, locally aggressive vascular tumor. Platelet trapping within the vasculature of large, deep tissue KHEs can trigger Kasabach-Merritt Phenomenon (KMP), a life-threatening consumptive coagulopathy characterized by severe thrombocytopenia and hypofibrinogenemia. Deep
tissue KHE lesions that present without cutaneous clues are difficult to diagnose. Magnetic resonance imaging (MRI) with gadolinium is the current preferred non-invasive method to diagnose deep KHE; however, in our case, all imaging modalities failed to diagnose splenic KHE, and histological examination was required.

Objectives: Describe the presentation and management of a rare pediatric case of splenic KHE.

Design/Method: Case Report

Results: A 2-year-old previously healthy male presented with asymptomatic thrombocytopenia (PLT = 33 10^9/L), leukocytosis (WBC = 20.7 10^9/L), and anemia (RBC = 9.3 g/dL). Physical examination was negative for organomegaly or cutaneous lesions. Extensive work-up was performed to exclude malignancy, autoimmune disease, hemolytic processes, and infectious etiologies. While pursuing a diagnosis of immune thrombocytopenic purpura, he developed mucocutaneous bleeding and unsuccessfully trialed oral steroids, intravenous immunoglobulin, and platelet transfusions. Subsequently, new splenomegaly was developed on exam. A full-body computed tomography scan confirmed growing splenomegaly (14.6cm) without other detectable abnormalities. He soon manifested laboratory evidence of consumptive coagulopathy that did not respond to further immunosuppressive agents or transfusions. Contrast MRI with arteriography re-demonstrated heterogeneous splenomegaly (16cm) without discrete splenic lesions. Despite daily transfusions with PRBCs, platelets, FFP, and cryoprecipitate, plasma factor levels and fibrinogen levels remained dangerously low (<20 mg/dL). Ultimately, he underwent splenectomy supported by continuous FFP and platelet infusions and tolerated the procedure well. Within days, all measures of coagulopathy self-resolved. Pathology of the spleen revealed a diffuse KHE and three splenules. Two years later, the patient remains healthy with normal lab work.

Conclusion: We describe a 2-year-old male with progressively worsening thrombocytopenia who acutely developed consumptive coagulopathy and splenomegaly, eventually found to have splenic KHE that was unable to be diagnosed by imaging. The patient's coagulopathy and bleeding were unresponsive to all medical interventions and only resolved by removing the spleen. Reports of isolated splenic KHE are exceedingly rare, with only 3 pediatric cases and 1 adult case reported in the literature. This case highlights the diagnostic challenges of KHE and the limitations of MRI/MRA in identifying these tumors. When faced with unexplained aggressive coagulopathy in the setting of non-diagnostic imaging, clinicians should have a high index of suspicion for deep vascular tumors.

Poster # 353

COMBINATION MEDICAL THERAPY IN VASCULAR ANOMALIES - ALTERNATIVES TO MONOTHERAPY

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Background: Medical management of a variety of vascular anomalies is still at an empiric level, with few agents functioning as targeted therapy. If a patient fails the first line of treatment, he/she is offered either a different agent or a combination of medications anticipated to achieve synergy. We present a case series where combination medical therapies were used at two large Vascular Anomalies Centers.

Objectives: To present current experience with various treatment regimens for vascular anomalies involving a minimum of two medications. The published data collection will provide a descriptive study used as a baseline reference for combination medical therapies administered in various vascular anomalies with dosing, adverse events and long-term effects.

Design/Method: This study is a multi-institutional retrospective review of medical records.

Results: We are presenting 4 cases from 2 institutions as examples of combined regimens.
Case 1 – Generalized Lymphatic Anomaly (GLA) treated with vincristine and celecoxib for 3 years, followed by celecoxib alone for 6 years without complications. Sirolimus was added years 9-11 of treatment due to progressive formation of bone lytic lesions. The combination therapy resulted in symptoms improvement and stabilization of disease.
Cases 2 and 3 - GLA with multiple bony lesions, large lymphatic malformations causing external leaks from lymphatic vesicles, protein losing enteropathy and ascites. Sirolimus and zoledronic acid were initiated first with significant decrease in external lymphatic fluid but inadequate control of rest of the symptoms. Added interferon alpha-2b resulting in marked improvement. Interferon was discontinued 2 years later.
Case 4 - Pleural based multifocal infantile hemangiomas causing reactive pleural effusions and need for chest tube. Initiated propranolol with no improvement until sirolimus was added 1 month later. In 2 weeks, the effusions resolved and chest tubes were removed. Continued sirolimus until 1 year old and propranolol until 15 months with no further symptoms or recurrence.

Conclusion: Various combination regimens may be pursued as second-line treatment in patients with poorly controlled vascular anomalies when monotherapy is not achieving the needed clinical control of a symptomatic vascular anomaly. No standard of care or guidelines currently exist for second line therapy, however combination regimens may be effective and safe. We are presenting our experience as a case-series in a “How Do I Approach” format.

Poster # 354

KAPOSIFORM HEMANGIOENDOTHELIOMA (KHE) OF THE BONE IN CHILDREN

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Background: Kaposiform hemangioendothelioma (KHE) is a rare, locally aggressive vascular tumor that mainly occurs during infancy or early childhood. Approximately 70% of cases are complicated by Kasabach-Merritt phenomenon (KMP). Although osseous extension of the primary is relatively common, primary bone involvement by KHE is rare.

Objectives: We report a case series of KHE of the bone treated at our institution.

Design/Method: Retrospective medical record review of patients with primary KHE of the bone diagnosed and treated at our institution.

Results: We identified 6 patients with histologically confirmed KHE centered in the bone, with male predominance (4/6). Two patients had lesions in the extremity bones, two in the spine and sacrum, one in the scapula, and one in the sternum. The age at diagnosis ranged from 0.5 to 15 years (median 5 years). Time to diagnosis from symptom onset ranged from 4.4 to 108.4 months (median 24.1 months). Half had cutaneous findings and all patients had immunohistochemistry consistent with KHE. Median follow up was 47.5 months (range 31.9 to 151.7 months). Median time to progress or recur was 9.1 months (range 1 to 33.2 months).

Treatments received were varied. One patient had complete excision, one patient had a gross total excision followed by treatment with sirolimus at recurrence, one patient received vincristine and celecoxib followed by a gross total resection and was then initiated on sirolimus at the time of recurrence, and 3 patients were initiated on sirolimus as primary treatment. One of six patients exhibited KMP at diagnosis and was started on treatment with sirolimus. None of the patients had secondary lesions/metastases and all were alive at the time of last follow up. Treatment responses were variable, two had complete involution, one had near complete involution, two had no change, and one had further growth. Three patients remain on sirolimus following disease progression or for symptom control.

Conclusion: Despite treatment consensus recommendations published in 2013 recommending treatment with corticosteroids and/or vincristine, our patients primarily received sirolimus with both subjective improvement in symptoms and objective improvement in hematologic parameters and radiographic findings. Therefore, sirolimus is now the first line for medical therapy in our patients with KHE. Albeit rare, KHE should be included on the differential diagnosis for bone and musculoskeletal pain, especially for general pediatricians or orthopedists given that they may first present to them for evaluation. Prompt diagnosis and treatment could minimize long-term sequela and optimize quality of life.

Poster # 355

PATIENT WITH DIFFUSE VENOUS MALFORMATION RESPONDS TO TARGETED THERAPY WITH PIK3CA INHIBITOR

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Background: Patients with diffuse venous malformations are at risk for significant morbidity from widespread involvement and localized intravascular coagulopathy (LIC). These patients have limited therapeutic options.

Objectives: We present a 29 year old man with diffuse venous malformation who responded to the oral PIK3CA inhibitor alpelisib.

Design/Method: Case Report

Results: The patient is a 29-year-old male who was born with diffuse venous malformation affecting his paratracheal area, esophagus, chest, abdomen, pelvis, retroperitoneum, spine, left lower extremity and gluteal region. Shortly after birth, he was treated with daily interferon for approximately one year, with no improvement. He developed spastic diplegia and became wheelchair-bound in early childhood. At age 10, a tracheostomy was placed due to obstructive airway symptoms. Sclerotherapy was performed to targeted areas, which led to short-lived relief. He had significant LIC with fibrinogen of 60 mg/dL, D-dimer >20 mcg/mL, and platelets 80 K cells/uL. At age 25, he received treatment with sirolimus for six months without significant improvement. While on sirolimus, he had several episodes of life-threatening bleeding, including a spontaneous retroperitoneal bleed, significant hemorrhage due to laceration of an involved area of his tongue after eating a piece of pizza, and 5 g/dL drop in his hemoglobin after sitting in his wheelchair for a prolonged period. He was treated with rivaroxaban to treat his LIC, with some improvement. Over his lifetime, he has received a total of 87 units of blood products (16 packed red blood cells, 12 platelets, 20 Cryoprecipitate, 36 fresh frozen plasma). Biopsy of affected tissue could not be obtained due to risk of significant hemorrhage. Treatment with alpelisib (50 mg daily) was initiated in November 2019 via a single patient IND for compassionate use. After 3 months, his dose was increased 100 mg daily and he has remained at this dose for 12 months. He has had no significant adverse events. He has not required transfusion of blood products and his anticoagulation was discontinued due to normalization of his coagulation parameters. He has not required hospital admission. He has experienced softening of his venous malformations and fewer phleboliths. His weight has decreased by 15 kilograms, attributed to both decrease in lesion volume and increased physical activity due to improved quality of life.

Conclusion: Use of alpelisib led to transfusion independence without the use of concomitant anticoagulation for LIC, as well as significant weight loss, decrease in lesion size, and improved quality-of-life in this patient with diffuse venous malformation.

Poster # 356

PROPRANOLOL FOR TREATMENT OF INFANTILE HEMANGIOMA IN INFANTS <5 WEEKS CORRECTED GESTATIONAL AGE

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Background: Propranolol is the first-line therapy for problematic infantile hemangiomas (IH). However, propranolol has not been approved for use in infants with corrected gestational age (CGA) less than 5 weeks, an age when IH may be proliferating rapidly.

Objectives: Examine the safety and efficacy of propranolol for treatment of IH in infants less than 5 weeks corrected gestational age.

Design/Method: We retrospectively reviewed the records of patients prescribed propranolol prior to the age of 6 months between 2017 and 2021. We identified 24 patients who were started on propranolol for IH prior to the corrected gestational age of 5 weeks. Data on location of hemangioma, weight at initiation of treatment, dosing information, side effects, response, and duration of treatment was included.

Results: Of the 24 patients identified, the mean CGA at initiation of therapy was 2 weeks 5 days (range 0 weeks - 4 weeks 6 days). Mean weight at initiation of therapy was 3.98 kg (range 2.23 kg - 5.595 kg). Propranolol had clear benefit in 20/24 (83.3%) of infants treated prior to 5 weeks CGA when prescribed per guidelines (1 mg/kg/day to start, then 2-3 mg/kg/day as a goal dose). Rates of side effects were similar to that of propranolol in infants >5 weeks CGA, with sleep disturbances detected in 25%, coolness of the hands and/or feet in 12.5%, agitation/irritability in 8.3%, diarrhea in 8.3%, sleepiness in 4.2%, decreased appetite in 0%, and symptomatic low heart rate, blood pressure, or blood sugar in 0%.

Conclusion: In this cohort of patients with corrected gestational age less than 5 weeks, propranolol was safe and effective for treatment of infantile hemangiomas, with a similar side effect profile to older patients. Larger, prospective studies are indicated to investigate propranolol in this age group.

PTCTC Abstracts

1. Pulmonary toxicity after total body irradiation-based and busulfan-based myeloablative conditioning for allogeneic hematopoietic stem cell transplantation for pediatric and young adult patients

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Theme: Allogeneic HSCT

Background: Pulmonary toxicity (PT) is a known complication associated with allogeneic hematopoietic stem cell transplantation (allo-HSCT) and can be life threatening. Furthermore, PT after allo-HSCT using total body irradiation (TBI)-based myeloablative conditioning has been associated with worse overall survival (OS). In recent years, busulfan-based myeloablative conditioning has also been used for allo-HSCT in pediatric patients; however, a comparison of PT after TBI-based and busulfan-based myeloablative conditioning for allo-HSCT has not been performed.

Objective: The primary objective is to compare the incidence of PT between patients receiving TBI-based and busulfan-based myeloablative conditioning. Secondary objectives were to determine factors that correlate with PT and OS.

Design/Method: Retrospective single-center cohort study at Boston Children's Hospital for patients with leukemia or myelodysplastic syndrome who underwent allo-HSCT under the age of 26 years between 2008 and 2018. Medical records were reviewed to collect demographics, treatment modalities, transplant characteristics, including donor type and stem cell source, and patient outcomes, including relapse, survival, pulmonary toxicity, graft-versus-host disease (GVHD). Pulmonary toxicity was graded using Common Terminology Criteria for Adverse Events (CTCAE) v5.0. Incidence of PT was analyzed using Kaplan-Meier curves and log-rank test. Cox regression analyses were used for univariate and multivariable analyses.

Results: We identified 311 patients who received allo-HSCT with TBI-based (n=227) or busulfan-based (n=84) myeloablative conditioning at a median age of 11.0 years (range: 0.6-25.2) at time of HSCT. We found no difference in incidence of grade ≥3 PT (37.3% vs. 42.8% at 5 years, p=0.243) or grade 5 PT (12.3% vs. 7.6% at 5 years, p=0.238) between TBI and busulfan groups, respectively. Univariate analysis found that age, PT during prior treatment or pre-existing pulmonary conditions, acute GVHD (aGVHD), infection within 100 days of HSCT significantly correlated with grade ≥3 PT, while other factors, such as radiation dose, donor type, and HSCT source did not correlate with grade ≥3 PT. Age (HR=1.73, 95%CI 1.17-2.56; p=0.006), prior PT/pre-existing pulmonary conditions (HR=1.80, 95%CI 1.23-2.63; p=0.003), aGVHD (HR=1.57, 95%CI 1.08-2.30; p=0.019), and infection (1.49, 95% CI 1.01-2.20; p=0.043) remained significant on multivariable analysis. Developing grade ≥3 PT correlated with worse OS (47.1% vs. 77.7% at 5 years; p<0.0001).

Conclusion: TBI-based conditioning was not associated with increased incidence of PT compared to busulfan-based conditioning. Age, prior PT or pre-existing pulmonary conditions, any infection in the first 100 days after HSCT, and aGVHD were associated with grade ≥3 PT. Furthermore, grade 3 or 4 PT was associated with decreased OS.

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2. Haploidentical Hematopoietic Stem Cell Transplant in Sickle Cell Disease

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Theme: Allogeneic Hematopoietic Stem Cell Transplant

Background: Sickle cell disease (SCD) is a genetic disorder which affects approximately 1 in every 400 African American newborns and 70,000 persons in the U.S. Hematopoietic stem cell transplant (HSCT) is the only curative therapy currently approved by the FDA for the cure of SCD. However, only about 30% of patients have a matched sibling donor.
Low representation of volunteers from certain racial and ethnic groups in the global donor pool remains the greatest challenge for procuring a matched unrelated donor. For example, the likelihood of finding an 8/8 HLA matched unrelated donor through the National Marrow Donor Program (NMDP) registry is 75% for whites of European descent and 45% for whites of Middle

Eastern/North African descent, compared to only 16 to 19% for Black Americans of all backgrounds.
On the contrary, almost every patient will have a parent, sibling, or other first degree relative who meets criteria for a haploidentical donor; thus, greatly increasing the chances of obtaining cure. HLA haplo-identical HSCT (haplo-HSCT) using post-transplantation Cyclophosphamide (PT-Cy) is an alternative strategy that has been utilized to expand the donor pool for non-malignant hematologic disorders when a matched sibling donor is unavailable. We present pilot data from our institution for four patients who successfully underwent a haploidentical HSCT for SCD.

Objectives: To determine a.) donor engraftment, at 100 days post haploidentical HSCT b.) Cumulative incidence of acute and chronic GVHD, c.) hematologic and non-hematologic complications.

Design/Method: Four patients with severe SCD received haplo-HSCT after undergoing a reduced intensity conditioning regimen consisting of Fludarabine, Thiotepa and Melphalan with rabbit anti-thymocyte globulin, prograf and mycophenolate for and high dose cyclophosphamide on Day+3 and 4 for GVHD prophylaxis. Rituximab was given as chronic GVHD prophylaxis. Indications for HSCT were stroke, recurrent ACS, severe VOC, chronic transfusion therapy complicated by iron overload or alloimmunization.

Results: There was no treatment related mortality in the four patients. Neutrophil engraftment was achieved at an average of 16 days (range 12 to 24 days) post HSCT. Donor chimerism has been around 98 to 100%. Grade I-II acute graft versus host disease has occurred in two patients who responded to a short course of topical and system steroid. One patient developed Posterior Reversible Encephalopathy Syndrome with full recovery.

Conclusion: Haplo- HSCT is a safe and effective alternative therapy for patients with severe SCD, particularly African American patients, who historically have are less likely to find fully HLA-matched donors.

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3. Curing Two Diseases with One Transplant: The Case of a Male Infant with Both Wiskott-Aldrich Syndrome and Sickle Cell Disease Treated with an Ex-vivo T cell Depleted Haploidentical Stem Cell Transplant

Author: Sara Silbert, MD, Hannah Kinoshita, MD, Mariah Jensen-Wachspress, BS, Michael Keller, MD, Catherine M. Bollard, MD, David Jacobsohn, MD, Michael Pulsipher, MD, and Allistair Abraham, MD
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Theme: Allogeneic HSCT

Background: Wiskott-Aldrich syndrome (WAS) and sickle cell disease (SCD) are associated with significant morbidity and mortality. The presentation of an infant with both WAS and SCD

posed an even higher risk of poor outcomes, with hematopoietic stem cell transplant as the only option for cure.

Objective: The primary objective was to determine the efficacy of HSCT to cure both WAS and SCD. The secondary objective was to evaluate the impact of virus specific T-cell (VST) therapy on viral infections after HSCT.

Design/Method: Case report

Results: A 4-month-old male with SCD presented following 4 hospitalizations for recurrent infections, transfusion dependence (15 RBC and 18 platelet transfusions prior to HSCT), splenomegaly and eczema. WAS gene testing revealed a missense mutation in WAS: c. 397 G>A, p.Glu133Lys. No HLA matched sibling or unrelated donors were identified, so the patient proceeded to haploidentical transplant (NCT02646839) from his mother using an ATG, fludarabine, melphalan, thiotepa, rituximab preparative regimen, with alpha beta T-cell depletion for GVHD prophylaxis. Transplant course was complicated by grade 2 skin GVHD on day +34 requiring a maximum of 1mg/kg/day of prednisone and sirolimus, as well as polymicrobial bacteremia necessitating central line removal on day +114.
Transfusion independence occurred by day +11. Only 3 doses of IVIG were required following transplant for IgG<400, last given day +163.
Donor-derived VSTs targeting CMV, EBV, Adenovirus, BK, HHV6 and Parainfluenza-3 were infused on day +149 to optimize immune reconstitution (NCT03180216). There were no toxicities related to infusion and the patient remained virus free as of day +180.
Chimerism studies showed the patient was 100% donor for CD3 and CD33/66 by day +30 and 100% donor for CD3 and 88% donor for CD33/66 as of day +180. WASp testing at day +149 demonstrated near full expression in T and NK cells (96-97%). Maximum hemoglobin S percentage as of day +180 was 37%, reflecting carrier status of donor. At day +180 absolute T cells were 435/mcl (2100-6200), CD4 282/mcl (1300-3400), CD8 41/mcl (620-2000), B lymphocytes 33/mcl (720-2600), and NK 184/mcl (180-920). Flow cytometry demonstrated that the majority of T, B and NK cells were of donor origin (>90 %).

Conclusion: This patient with WAS and SCD successfully received a T-cell depleted haploidentical donor transplant with alpha beta depletion followed by VST therapy at 5 months. By 6 months post-transplant, the patient remained virus free, WASp expression had normalized, and HbS percentages aligned that of sickle cell trait.

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4. Dysregulation of Hypoxia Induced Factor 1 alpha (HIF1α), Caspase 8 Associated Protein 2 (CASP8AP2) and miR-210 in patients with graft versus host disease (GVHD)

Authors: Azada Ibrahimova MD, Nathan Luebbering MS, Sheyar Abdullah BS, Adam Lane PhD, Alexandra Duell BS, Kelly Lake MS, Stella M. Davies MBBS PhD, Kasiani C Myers MD
Institution: Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio, USA

Theme: Allogeneic HSCT

Background: Hypoxia induced factor 1 alpha (HIF1α) is a transcription factor that plays a role in hypoxia induced apoptotic pathway and is regulated by miR-210. Caspase 8 associated protein 2 (CASP8AP2) is a pro-apoptotic protein that is also negatively regulated by miR-210. The association between these molecules and their role in GVHD has not been studied.

Objective: To analyze CASP8AP2, HIF1α, and miR-210 protein level and gene expression in allogenic pediatric HSCT patients.
Methods: Blood samples collected from 102 consecutive allogeneic pediatric HSCT patients were analyzed (n=77 without GVHD, N=25 with GVHD). CASP8AP2, and HIF1α protein levels were measured from plasma obtained at days +14, 30, 60 and 100. Mononuclear cell samples for measurement of gene expression were obtained at day +100. T cells were isolated from other mononuclear cells using EasySep Human CD3 positive selection kit (StemCell). Total RNA was isolated with MirVana miRNA isolation kit (ThermoFisher) and High-capacity RNA to cDNA kit was used to reverse transcribe RNA to cDNA. TaqMan Gene Expression Assays (Applied Biosystems) were used for real-time PCR to quantify CASP8AP2, HIF1α and miR-210 expression. Relative expression values are reported as ΔCt (number of PCR cycles) which are normalized with Eukaryotic 18S rRNA Endogenous Control. CASP8AP2 (MyBioSource) and HIF1α (ThermoFisher) ELISA was used to measure protein levels.

Results: Patients with GVHD had significantly lower expression of CASP8AP2 (median 19.3 vs 18.9, p=0.03) and HIF1α transcripts in (median 16.5 vs 16, p=0.038) in T cells as compared to patients without GVHD. Expression of CASP8AP2 was also downregulated in CD3- mononuclear cells in patients with GVHD (median 19.4 vs 19, p=0.045), but HIF1α remained constant (median 16 vs 15.8, p=0.3). miR-210 expression was similar for both groups in T and CD3- cells (median 5.7 vs 6, p=0.6; 6.5 vs 6.3, p=0.66). We then examined longitudinal levels of CASP8AP2 and HIF1α protein after HSCT and found that levels were undetectable 14 days after HSCT, but then increased steadily through day 30 and 100. Higher day 100 levels for CASP8AP2 were strongly correlated with occurrence of GVHD.

Conclusion: HIF1α and CASP8AP2 gene expression is downregulated in patients with GVHD at 100 days post-HSCT, while HIF1α and CASP8AP2 protein level remains high. The potential negative regulatory effect of miR-210 on this pathway needs to be investigated more. A lag-time in pathway regulation would explain the observation of high correlative protein levels of CASP8AP2 while mRNA is being downregulated.

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5. Outcomes of unrelated donor (URD) HSCT with TCRαβ/CD19$^+$ depletion for children and young adults (YA) with acute leukemia

Author: Allison Barz Leahy, Yimei Li, Julie-An Talano, Alix Seif, Yongping Wang, Dimitri Monos, Nancy Bunin

Theme: Allogeneic HSCT

Background: TCRαβ/CD19$^+$ depletion may reduce the risk of severe GVHD while maintaining a graft-versus-leukemia effect for children/YA with high-risk leukemias receiving URD HSCT.

Most outcome data with TCRαβ/CD19+ depletion is with haploidentical donors; there is limited data evaluating this approach for URD HSCT.

Objective: To determine outcomes for pediatric/YA patients with high-risk leukemias receiving URD TCRαβ/CD19^{+}-depleted peripheral stem cells.

Design/Method: This study (NCT02323867) enrolled children/YA with MDS, ALL, and AML between 10/2014-09/2019 at Children's Hospital of Philadelphia (PA, USA) and Children's Hospital of Wisconsin (Milwaukee, USA). Two-field resolution HLA-genotyping was utilized. Conditioning was myeloablative, using either total body irradiation or busulfan with thiotepa and cyclophosphamide, +/- ATG. Clinical outcomes, leukemia free survival (LFS) and overall survival (OS) were described by disease type (ALL vs AML/MDS), and analyses were performed considering time to relapse and to non-relapse mortality (NRM) as competing risks.

Results: Sixty patients (ALL=27, AML=30, MDS=3), 47% female, with median age 12.6y (1.2-23.2), were enrolled. 37 (62%) were 10/10 HLA-matched, 22 (37%) were 9/10, and 1 (2%) was 8/10. DP typing was available for 77%. Trilinear engraftment occurred in 59; one participant with primary graft failure received successful second HSCT.
Acute GVHD developed in 22 (Grade 1/2 n=14 [23%], Grade 3/4 n=8 [13%]). In univariate analyses, non-permissive DP mismatch was associated with a higher likelihood of aGVHD (OR 16.50, 95%CI 1.67-163.42, p=0.0166), and ATG with lower likelihood (OR 0.11, 95%CI 0.02-0.52, p=0.0056). Of fifty-three patients surviving >100 days, 14 (26%) developed cGVHD (6 extensive, 11%). DP mismatch was not associated with cGVHD, and ATG approached significance for a protective effect (OR 0.24, 95%CI 0.05-1.21, p=0.0836).
With median follow-up of 3.1y (0.6-5.6), 11 patients (18%) relapsed (median 6.6m, 2-38). Forty-five patients (75%) were alive at last follow-up, 41 in continuous CR, 3 in long-term remission following salvage therapy, and 1 in post-transplantation relapse. 4-year LFS probability was 64% (95%CI 48-76) and OS was 69% (95%CI 52-81), with no difference between ALL and AML (p=0.5441 and p=0.6297, respectively). The cumulative incidence of relapse was 21% (95%CI 11-34%) and NRM was 15% (95%CI 6.7-26%), again with no difference between disease types (p=0.8628 and p=0.6218, respectively).

Conclusion: URD TCRαβ/CD19^{+}-depleted PSCT is a safe and effective approach to transplantation for children/YA with leukemia, with outcomes comparable to haploidentical TCRαβ/CD19^{+}-depleted PSCT and superior to partially CD3^{+}-depleted PSCT. Further investigation is needed to parse contribution of DP mismatch characteristics and ATG exposure to GVHD and relapse.

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6. Understanding The Mechanisms Of Eculizumab Refractoriness In Patients With Transplant Associated Thrombotic Microangiopathy

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Theme: Allogeneic HSCT

Background: Some patients with high risk transplant associated thrombotic microangiopathy (hrTA-TMA) fail to achieve adequate terminal complement (sC5b-9) suppression despite appropriate eculizumab drug level. The mechanism of refractoriness to eculizumab remains unclear. Recent reports suggest that elevated thrombin may promote sC5b-9 generation via a C5 cleavage pathway that is not blocked by eculizumab.

Objective: To compare thrombin-antithrombin (TAT) complex level in patients with TA-TMA who are refractory to eculizumab and those with good response to eculizumab who achieved sC5b-9 normalization.

Methods: All patients undergoing HSCT were prospectively screened for TA-TMA. Patients with hrTA-TMA receiving therapy had sC5b-9, eculizumab drug level and CH50 monitored during eculizumab therapy. Refractoriness to eculizumab was defined as increase in sC5b-9 levels after a period of normalization with treatment despite therapeutic eculizumab levels and adequate suppression of total complement activity (CH50) in the blood. We analyzed thrombin-antithrombin complex (TAT) levels in the serum collected prospectively at hrTA-TMA diagnosis and compared TAT levels in TA-TMA patients who were refractory to eculizumab therapy with those who had good therapy response and normalization of sC5b-9. TAT complex measurements were performed using ELISA, according to manufacturer's instructions (Abcam).

Results: We identified 12 therapy refractory patients who failed to maintain sC5b-9 suppression despite therapeutic eculizumab levels and selected 10 consecutive patients with good response to eculizumab. Eculizumab refractory patients were more likely to have elevated TAT levels (>4 ng/mL) at the time of TA-TMA diagnosis (median = 4.470 ng/dL vs. 3.650 ng/dL, p=0.26). Patients refractory to eculizumab were more likely to have a history of gastrointestinal (GI) bleed and GI-TMA compared to eculizumab responsive patients (n=7 (58%) vs. n=2 (20%)). Median TAT level for patients with GI bleed was higher than those without bleeding (4.688 ng/dL vs. 3.683 ng/dL, p=0.042). Patients with refractory hrTA-TMA had higher prevalence of viremia (Adenovirus: n=5 (41%), CMV: n=2 (16%), EBV: n=4 (33%), BK virus: n=4 (33%) vs Adenovirus 1 (10%), BK virus: 1 (10%)).

Conclusion: Our data suggest that elevated thrombin generation, especially in patients with intestinal bleeding likely contribute to eculizumab refractoriness in HSCT recipients with TA-TMA. Further studies are required to better understand coagulation and complement pathway interactions in TA-TMA patients in order to determine if eculizumab refractory patients with elevated thrombin levels.

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7. Race as a Factor in Outcomes of Hematopoietic Stem Cell Transplant (HCT) for Children with Hematologic Malignancies (HM) in Florida

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Theme: Allogeneic HSCT

Background: Previous studies have investigated post-HCT outcomes by race in adults; however, pediatric data addressing this topic are scarce.

Objective: We studied race as a factor in outcomes of children with HM receiving HCT in Florida during 2010-2019 period.

Methods: Data from 5 Florida pediatric BMT programs were gathered through the Florida Pediatric HCT Consortium (FPBCC). A total of 316 children received transplants for HM (2010 to 2019). Race was reported as White (W), Black (B), Asian and unknown in 75%, 18%, 3% and 4% of cases, respectively. This correlates well with Florida population (2018) comprising 75% W, 16% B and 2.8 % Asians. Subsequent analyses focused on the two most numerous racial groups and included 295 children (238 W, 57 B). We used two-tailed Fisher's exact (FE), Chi square test, Kaplan-Meier estimates and log-rank test to study differences between the two groups related to transplant characteristics and outcomes (survival, cause of death, GVHD).

Results: We found no differences between W and B in: gender (male: 59% W, 60% B); performance score (≥90: 73% W, 79% B); comorbidity number (0-1: 78% W, 79% B); disease status (CR1/CR2: 79% W, 75% B), use of bone marrow, peripheral blood or cord blood (57%, 17%, 26% W and 49%, 23%, 26% B, respectively), donor-recipient gender match (matched: 51% W, 50% B), and donor-recipient CMV serology match (matched: 58% W, 63% B), use of myeloablative regimens (96% W, 91% B) and serotherapy (53% W, 61% B). There was a significant difference in the use of HLA-mismatched donors (HLA-MMD) (53% W, 71% B, FE p=0.02). While the proportion of mismatched unrelated donors (MMUD) was identical (16% W, 16% B), there was a trend of increased use of mismatched related donors (MMRD) and mismatched cord blood donors (MMCBD) among B (13%,19% W and 25%, 26% B). Despite higher frequency of HLA-MMD, there was no difference in GVHD (no acute-GVHD: 51%W, 65% B; no chronic-GVHD: 81% W,72% B). Causes of death comprising recurrent disease (16%W;14% B) and treatment-related toxicity (22% W;25% B) were similar.
KM 24-month survival was identical (61% [95% CI 54-68%] W, 60% [95% CI 38-68%] B).

Conclusion: Our study found that outcome measures were similar across W and B children receiving HCT for HM in Florida. Matched unrelated donors, known to be lacking for B patients[1], were replaced by MMRD and MMCBD without compromising outcomes.

1. Gragert Let al.,N Engl J Med, 2014.

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8. Outcomes of Conditioning with Alemtuzumab in Unrelated Donor Transplant for Hematologic Malignancies in Children and Young Adults

Authors: Shreeya Patel[1], Premal Lulla[1], Albert Jang[2], Shaun Bulsara[1], John Craddock[1], Khaled Yassine[1], Ghadir Sasa[1], Baheyeldin Salem[1], Erin Doherty[1], Caridad Martinez[1], Robert Krance[1], Tami John*[1], Brian Friend*[1]

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Theme: Allogeneic HSCT

Background: Allogeneic hematopoietic stem cell transplant (allo-HSCT) is curative for children and young adults with hematologic malignancies. Serotherapy, often anti-thymoglobulin, is commonly used to mitigate risk of graft-versus-host disease (GVHD), particularly in unrelated donor (UD) transplant. Alemtuzumab, a monoclonal antibody targeting CD52, depletes donor lymphocytes that play a major role in GVHD, resulting in a profound immunosuppressive effect that may increase risk for opportunistic infections.

Objective: We reviewed transplanted-related outcomes of patients at Texas Children's Hospital (Houston, TX, U.S.) that received allo-HSCT from an UD with a conditioning regimen including alemtuzumab. Outcomes of interest included overall survival (OS), GVHD/relapse-free survival (GRFS), incidence of GVHD, and infectious complications.

Design/Method: We retrospectively reviewed all patients that received UD HSCT (matched UD = 10/10 HLA match), mismatched UD = 9/10 HLA match) with weight-based dosed i.v. alemtuzumab (<15kg = 3mg/day, 15-30kg = 5mg/day, >30kg = 10mg/day for 4 days) from August 2012 through December 2017. Kaplan-Meier method was used to calculate OS and GRFS. Cumulative incidence curves were used to estimate incidence of relapse and treatment-related mortality (TRM).

Results:
Demographics:
84 patients (55 male) were included with median age of 12 years (range: 1-22 years). Malignant diagnoses included acute lymphoblastic leukemia (52.4%), acute myeloid leukemia/myelodysplastic syndrome (MDS) (28.6%), other leukemia (1.2%), Hodgkin lymphoma (8.3%), and non-Hodgkin lymphoma (9.5%). Disease status included complete remission 1/MDS (38.1%), complete remission 2 or greater (47.6%), and induction failure (14.3%). Donor type included 59.5% matched UD and 40.5% mismatched UD. Conditioning intensity was myeloablative for 75% of patients.

Outcomes:
OS at 1 and 3 years was 72.4% (95% CI 61.5%, 80.7%) and 61.4% (95% CI 50.0%, 70.9%), respectively. GRFS at 1 and 3 years was 61.9% (95% CI 50.4%, 71.5%) and 51.7% (95% CI

40.3%, 62.0%), respectively. Incidence of acute GVHD II-IV and III-IV was 22.6% and 9.5%, respectively. Incidence of chronic GVHD was 11.9% and extensive chronic GVHD was 3.6%. Relapse rates at 1 and 3 year were 21.3 and 31.7%, respectively. TRM at 1 year was 16.1%. 71% of patients had £1 infectious-related hospitalizations post-HSCT and 35% of deaths were infectious related.

Conclusion:
Our data suggests that UD HSCT with conditioning chemotherapy that includes alemtuzumab successfully mitigates severe GVHD in children and young adults with minimal impact on relapse resulting in respectable GRFS and TRM. Additional studies are needed to further optimize infection prevention and immune reconstitution in the setting of alemtuzumab.

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1. Effect of graft cell doses on severity of endothelial toxicity in pediatric autologous transplant in solid tumors

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Theme: Autologous HSCT

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Background: Autologous hematopoietic stem cell transplantation (aHSCT) is a key treatment modality in pediatric solid tumors. Endothelial toxicities (ETs) post-aHSCT may be seen in over half of patients depending on diagnostic criteria, resulting in morbidity/mortality and compromising subsequent therapy. ETs are mediated by interactions between damaged endothelium, immunologically active cells, and soluble inflammatory mediators. Given that autologous grafts contain variable numbers of immunologically active cells, we hypothesized that $CD34^+$ and total nucleated cell (TNC) graft content would be associated with ETs following aHSCT.

Objective: To assess ET occurrence and outcomes among patients receiving aHSCT for central nervous system tumors (CNST) or high-risk neuroblastoma (HRNBL), and evaluate whether $CD34^+$ or TNC content were associated with ETs post-aHSCT.

Method: Retrospective analysis of all patients undergoing aHSCT for CNST or HRNBL from 01/01/2009-30/06/2019. Patients underwent peripheral blood stem cell collection following chemo-mobilization with granulocyte colony stimulating factor (G-CSF) and antecedent chemotherapy. Infused $CD34^+$ and TNC were correlated with ETs (clinical diagnosis of transplant-associated thrombotic microangiopathy (TA-TMA), sinusoidal obstruction syndrome (SOS), engraftment syndrome, or idiopathic pneumonia syndrome including diffuse alveolar hemorrhage).

Results: 121 NBL and 61 CNST patients underwent 146 and 169 aHSCTs, respectively. ET was diagnosed following 18% and 6% of aHSCTs, respectively. SOS accounted for 81% and 20% of ETs following aHSCT for NBL and CNST, respectively. Among aHSCTs for NBL, 69% of all ETs occurred following busulfan conditioning – despite only 40% of NBL aHSCTs using this regimen. Overall day 100 treatment related mortality (TRM) was 3% for both NBL and CNST, with 83% of those secondary to ET. Median infused $CD34^+$ cell dose was $7.5x10^6$/kg (range 0.8–25.3) and $6.3x10^6$/kg (1.9–34.6) for NBL and CNST, respectively; median infused TNC dose was $1.8x10^8$kg (0.4 – 14.6) and $2.3x10^8$kg (0.5–15.2), respectively. No correlation was identified between $CD34^+$ or TNC content and ET. Patients with ETs received significantly more red cell and platelet transfusions, OR=1.31 (95%CI 1.07-1.64, p=0.01) and OR=1.08 (95%CI 1.01-1.15, p=0.01) respectively. No difference in disease-free survival was observed based on presence/absence of ETs.

Conclusion: We identified fewer ETs than prior reports, likely secondary to defining ETs by clinical diagnosis with supportive laboratory criteria, rather than laboratory criteria alone – a definition identifying more severe ET. ETs were still relatively common and contributed to TRM prior to day 100. There was no association seen between ET and $CD34^+$ or TNC graft content. A more granular analysis of graft content may be informative.

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2. Single Center Results to Improve Peripheral Blood Stem Cell Mobilization Success in Pediatric and Young Adult Patients

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Theme: Autologous HSCT

Background: Granulocyte-colony stimulating factor (G-CSF) is used for hematopoietic stem cell (HSC) mobilization for autologous hematopoietic stem cell transplant (auto-HSCT). Approximately 10-25% of patients fail to obtain an adequate CD34+ cell count with standard G-CSF dosing. Plerixafor, a CXCR4 antagonist, has been combined with G-CSF to boost CD34+ cell numbers for lymphoma and solid tumor patients who are poor mobilizers.

Objective: To report our institution's success of HSC mobilization using an algorithm among pediatric solid tumor and lymphoma patients considered to be poor mobilizers.

Methods: We performed a retrospective analysis including 170 pediatric solid tumor and lymphoma from 2016-2020 at Cincinnati Children's Hospital Medical Center whose peripheral blood HSCs were mobilized using G-CSF or plerixafor for auto-HSCT. Data on total harvest days, dosing frequency/duration of G-CSF or plerixafor and final CD34+ cell count/kg were collected. Heavily pretreated patients were defined as those who had received at least four cycles of chemotherapy.

Results: There were 41 patients (24.1%) classified as heavily pretreated at the time of stem cell mobilization. The most common primary diagnosis among heavily pretreated patients was lymphoma (n=12, 29.2%) compared to neuroblastoma (n=58, 44.9%) in the comparison cohort. Thirteen heavily pretreated patients (31.7%) required twice daily dosing of G-CSF compared to five patients (3.9%) in the not heavily pretreated group. Fourteen heavily pretreated patients (34.1%) required plerixafor for poor mobilization compared to four patients (3.1%) in the not heavily pretreated cohort. The mean final CD34+ count was similar between both groups, with 38.66 $x10^6$/kg cells in the heavily pretreated cohort compared to 39.46 $x10^6$/kg cells in the comparison group. Three patients failed HSC mobilization, despite following our harvest protocol. The first was a 26-year-old male with relapsed Wilms tumor who had received upfront therapy and radiation, followed by two cycles of salvage chemotherapy after relapse. The second was a 17-year-old female with history of small cell ovarian carcinoma hypercalcemic type (SCCOHT), who had previously received six cycles of chemotherapy as well as abdominal radiation. The third patient was a 20-year-old female with SCCOHT who had previously received five cycles of chemotherapy prior to stem cell harvest.

Conclusions: Identification of patients at highest risk for poor stem cell mobilization will detect a population who would most benefit from rescue with more frequent G-CSF dosing or plerixafor. In this single-center study, we report our success of stem cell mobilization among pediatric lymphoma and solid tumor patients utilizing our institution's algorithm.

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1. Characterization of Extramedullary Disease in ALL and Response to CAR T-cell Therapy

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Theme: Cellular Therapies

Background: Chimeric antigen receptor (CAR) T-cell therapy is effective in children and young adults with multiply relapsed/refractory B-ALL. There is limited information on efficacy and CAR T-cell kinetics in patients with non-central nervous system (CNS) extramedullary disease (EMD).

Objective: The primary objective was to systematically evaluate the response of non-CNS EMD to CAR T-cells, in relationship to bone marrow response to therapy. Secondary objectives included identifying time to best EMD response and characterizing CAR T-cell expansion in patients with EMD.

Design/Methods: We conducted a retrospective, centralized review of patients with serial PET/CT scans who had isolated EMD or combined medullary/EMD identifiable by imaging at presentation. Patients were enrolled on one of 3 CAR T-cell trials at our institution targeting CD19 and/or CD22 (NCT01593696, NCT02315612, NCT03448393). Non-CNS EMD was defined as disease involvement (with histologic or radiographic confirmation) at a site outside the bone marrow, excluding cerebrospinal fluid or parenchymal CNS involvement.

Results: Of 130 patients with ALL treated between 7/2012 and 5/2020, 17 (13.1%) patients had confirmed baseline EMD and had serial PET/CT scans pre- and post-cell infusion. Two patients received anti-CD19 CAR, 8 received anti-CD22 CAR, and 7 received anti-CD19/22 CAR. One CD22 CAR patient was analyzed for 2 separate infusions of CD22 CAR administered one year apart at initial therapy and disease recurrence. Sites of EM involvement included lymph nodes (cervical, supraclavicular, mesenteric, retroperitoneal, axillary, popliteal, and inguinal), maxillary sinus, breast, kidney, spleen, pancreas, liver, and testes. Fourteen of 18 (77.8%) patients attained a bone marrow complete remission (CR) at best response. Of these, 8 patients (57.1%) demonstrated EMD CR and 5 patients (35.7%) showed partial response; 1 had progressive EMD despite marrow CR. Fifteen of 18 achieved their best EMD response by day 28. Peak CAR expansion in patients with EMD versus those without differed by CAR construct. There was substantially higher peak CAR T-cell expansion with CD22 CAR in those with EMD (versus those without, median, 2174; range, 105.3-13653, vs. median, 562.2; range, 0.6500-11345, p=0.02) than with alternative constructs, where peak expansion did not differ between those with and without EMD.

Conclusion
Evaluation of non-CNS EMD is an important component of disease assessment in B-ALL; serial PET/CT scans aid the assessment of lymphomatous activity and response to CAR T-cells. Simultaneous eradication of medullary and EMD was seen in the majority of patients. However, residual EMD was substantial, despite marrow CR, warranting ongoing optimization strategies for therapy.

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2. First-in-human HA-1 targeting TCR memory T cell immunotherapy for pediatric patients with relapsed hematologic malignancies post allogeneic hematopoietic cell transplantation

Authors: Corinne Summers, Elizabeth F Krakow, Ann Dahlberg, Merav Bar, Melinda A Biernacki, Tanya Cunningham, Nicole Vartanian, Megan Hickner, Colette Chaney, Tsadik Habtetsion, Kyle Woodward, Robson Dossa, Michelle Brault and Marie Bleakley

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Theme: Cellular Therapies

Background: Recurrent cancer after hematopoietic cell transplantation (HCT) portends a poor prognosis. Targeted immunotherapies, such as CD19 CAR-T cells, are limited to lineage-specific antigen targets whereas T cell therapies targeting certain minor histocompatibility (H) antigens can be applied to a range of myeloid and lymphoid blood cancers. A novel, high-affinity T cell receptor (TCR) targeting the minor H antigen HA-1, which is expressed exclusively on hematopoietic cells and presented by HLA-A*02:01, was identified and validated in vitro. 1 The HA-1 TCR was incorporated into a transgene along with a CD8 coreceptor to enable HA-1-specific CD4 T cell activity, an inducible caspase-9 safety switch, and a CD34- CD20 epitope for cell selection and in vivo tracking. As a precaution for the donor-derived product, CD45RA-depleted T cells are used to reduce the risk of alloreactivity. CD4 and CD8 T cells are manufactured over 21 days and administered fresh at a 1:1 ratio for inter-subject product uniformity.

Objective: The primary objectives are to assess HA-1 TCR T cell product manufacturing feasibility and safety.

Design/Method: This single-center study (NCT03326921) utilizes a 3+3 phase I design. Subjects must be HLA A*02:01 and HA-1 positive and have undergone HCT for lymphoid or myeloid malignancy with a HA1 negative donor or HLA A*02:01-negative mismatched donor and developed recurrent or persistent disease. Patients may continue some immunosuppression but those with prior grade IV acute/severe chronic GVHD are excluded. Patients <16 years are treated on the pediatric arm with 3x106-30x106 HA-1TCR T cells/kg following fludarabine lymphodepletion. HA-1 TCR T cell engraftment, expansion, migration and persistence is monitored.

Results: One pediatric patient has been treated at the initial dose level of 3x106 cells/kg. This 2-year-old male with high-risk T cell ALL relapsed day +71 after matched unrelated donor HCT. He received fludarabine and HA-1 TCR T cells without infusion toxicities, cytokine release syndrome or GVHD. Following this a 1-2 log reduction in leukemia was observed. A second infusion at 1x107 cells/kg was subsequently administered, resulting in measurable residual disease (MRD)-negative complete response, durable at 6 months. HA-1 TCR T cells retrieved from the subject show HA-1 targeted T cell activity and leukemia cell lysis and have persisted for at least 6 months.

Conclusion: HA-1 TCR CD4+ and CD8+ memory T cells appear safe and may offer an effective therapeutic option for patients with hematological malignancies who develop post-HCT relapse.
1Dossa, Blood, 2018

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3. High-dose Donor CD45RO+ Memory T-cells Infusion after Allogeneic Transplantation: Safety and Outcome

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Theme: Cellular Therapies

Background: Immune Reconstitution (IR) is essential to control severe infections after Hematopoietic Stem Cell Transplantation (HSCT). Delay in T-cell recovery increases the risk of relapse, viral infections and transplant related mortality. Adoptive transfer of selected T cell subset with low alloreactivity potential is emerging as a strategy to improve IR.

Objective: CD45RA+ naive T-cells Depletion preserving CD45RO+ memory T cells could provide functional lymphocytes to protect against infection and leukemia relapse with low risk of graft versus host disease (GvHD). We present our experience with Donor Lymphocyte Infusions (DLI) of high-dose donor CD45RO+ memory T cell to assess safety and outcome.

Methods: A total of 172 DLIs of CD45RO+ T-cells after HSCT was performed in 44 patients. Indications for DLI were CMV reactivation (12,2%), mixed chimerism (21%), other infections (15%), persistent lymphopenia or delayed IR (12,2%), graft rejection (0,6%), relapse (3%) and Post-transplant lymphoproliferative disorder (PTLD) (1,8%). The rest of DLIs (34%) were infused on a prophylactic regimen on days +30, +60 and +90. DLI product was obtained performing a CD45RA+ depletion on donor leukapheresis product using the CliniMACS® device.

Results: Forty-four pediatric patients, median age 10 years (range 1-20), with malignant (n=35) and non-malignant diseases (n=9), received CD45RA+ (68,6%), TCR alpha/beta (17,4%) depleted and non-manipulated (14%) grafts from haploidentical (n=25) or allogeneic (n=19) donors. At a median of 104 days (range 15-996) after transplantation, patients received a median of 3 DLI of CD45RO+ cells (range 1-11), containing a median of $2.11x10^7$/Kg (range $4.8x10^4$-$2x10^8$/Kg) **CD45RO+**, $1x10^7$/Kg (range $6..5x10^5$-$1.07x10^8$/Kg) **CD3+CD45RO+** and **CD3+CD45RA+** cells $1x10^4$/Kg (range 0-$2.6x10^5$/Kg). All infusions were well-tolerated. De novo skin GvHD was developed in 3,48% cases (n=6: 5 grade I and 1 grade II). Cases with GvHD previous to DLI got worse in 6,9% (n=2).
After DLI due to CMV reactivation a decrease in the viral load was seen in 66,67% of patients (p=0,019). DLIs due to other infectious complications showed clinical improvement in 15,4% and decrease in viral load (EBV, Adenovirus, BK) in 26,9%. DLI indicated for delayed IR showed improvement in lymphocyte count (p=0,063). DLIs due to mixed chimerism, graft failure, PTLD or relapse weren´t significantly effective in reverting those situations.

Conclusion: Our preliminary data suggest infusions of **high dose CD45RO+ memory T cells** are a safe adoptive immunotherapy strategy. Efficacy has been observed in patients with CMV reactivation, infectious complications and lymphopenia, with no positive results in mixed chimerism, graft failure and relapse.

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4. Hematopoietic Toxicities and Coagulopathy Following CD22 CAR T-cells

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Theme: Cellular Therapies

This work was supported in part by the Intramural Research Program of the National Institutes of Health, National Cancer Institute, Center for Cancer Research and the Warren Grant Magnuson Clinical Center

Background: Hematopoietic toxicities, including cytopenias, bleeding and coagulopathy are associated with CAR T-cell therapy for hematologic malignancies, but comprehensive study has been limited, particularly for constructs targeting alternative antigens beyond CD19.

Objectives: We investigated the CD22 CAR T-cell associated hematologic toxicity profile that occurred among our patients who experienced CRS to better characterize the manifestations of coagulopathy and other hematopoietic toxicities.

Design/Method: This was a Phase 1 dose-escalation study of anti-CD22 CAR-T for children and young adults, registered at ClinicalTrials.gov (NCT02315612). The specific focus of this analysis was to look at hematologic toxicities associated with CAR T-cell therapy. Coagulopathy was defined by clinical bleeding, elevated d-dimer and prothrombin time and hypofibrinogenemia.

Results: Amongst the 65 treated subjects, 54 had CRS of whom 48 patients had full data available for analysis of hematologic toxicities and comprised the study population. Coagulopathy and endothelial activation were seen in 21 (44%) of CD22 CAR T-cell patients. 19 patients experienced bleeding symptoms and two patients had laboratory-based coagulopathy without bleeding. Bleeding complications were primarily mucosal and included bruising, petechiae or purpura (n=6), epistaxis (n=11), bleeding at IV or bone marrow biopsy sites (n=5), gingival/oral bleeding (n=4), hematuria (n=4), subconjunctival hemorrhage (n=2), gastrointestinal bleeding (n=1), presumptive diffuse alveolar hemorrhage (n=1) and intracranial hemorrhage (n=1). Three patients were further categorized as having complement activation and hemolysis, leading to utilization of eculizumab. The coagulopathy cohort had higher peak ferritin, D-dimer, CRP, PT, INR, LDH and a higher incidence of platelet degranulation as compared to those without coagulopathy. There were no significant differences in clotting factors. Notably, HLH-like toxicities (e.g. hyperferritinemia, transaminitis) were seen at a relatively high frequency on this study in 21/48 (44%) patients.[1] 16/21 (76%) patients with HLH and 11/19 (58%) patients with neurotoxicity had signs of hematopoietic toxicities (e.g. bleeding, coagulopathy). For those in remission, day 28 bone marrow cellularity ranged between 5 and 90% (median 30%) and did not differ by CAR expansion. Corresponding absolute neutrophil

counts were <0.2-2.98 K/uL (median 0.505 K/uL) and platelet counts ranged from 9-283K/uL (median 33K/uL).

Conclusion: Coagulopathy was seen at a relatively high frequency in patients receiving CD22 CAR T-cells, with an association of coagulopathy with HLH-like toxicities. Further investigations into the hematopoietic toxicity profile are underway.
Shah, et al., Journal of Clinical Oncology, 2020.

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5. Tumor-associated antigen-specific T cells targeting Peripheral T Cell Lymphoma

Authors: Keri Toner MD, Hema Dave MD MPH, Catherine M. Bollard MD

Theme: Cellular Therapies

Background: Peripheral T Cell Lymphoma (PTCL) comprises 15% of Non-Hodgkin Lymphomas (NHL) and respond poorly to conventional chemotherapy. Therefore, development of novel therapies is warranted. We have previously shown that tumor associated antigen (TAA) specific T cells can be generated from patients with acute leukemias, B cell lymphomas and solid malignancies. Because antigen presence is heterogeneous in PTCL, targeting multiple antigens may increase efficacy of adoptive cellular therapy for PTCL

Objective: To determine whether antigen-specific T cells targeting 5 tumor-associated antigens(TAAs) can be developed as a potential therapy for patients with PTCL.

Design/Method: TAAs WT1, PRAME, Survivin, SSX2, and MAGE-A1 were selected based on expression and prognostic significance in lymphomas including PTCL. Peripheral blood mononuclear cellsisolated from PTCL patients and healthy donors were stimulated with autologous dendritic cells pulsed with TAA pepmixes in the presence of exogenous cytokines to generate TAA-specific T cell products (TAAT). Antigen specificity was tested using Interferon-ɣ(IFN-γ) ELISpot assay (measured in spot forming cells/105 T cells). Immunophenotyping was performed by flow cytometry.

Results: TAA-T were generated from 10 healthy donors and 6 patient samples. The TAA-T were polyclonal with both CD4+ (median 3.5%; range 0.4-19%) and CD8+ T cells (median 55%; range 18- 80%). The majority were CD8+ T effector memory cells (median 61%; range 27-78%). 7/10 healthy donors and 4/6 PTCL patient derived TAA-T products showed specificity against multiple PTCL antigens (median 1.2 and 2 antigens respectively). TAA-T were polyfunctional as evident by release of IFN-ɣ and TNFα upon re-stimulation with TAA pepmixes (n=11). Additional Investigational New Drug (IND) enabling studies including demonstrating cytolytic activity against PTCL cell lines are ongoing but once complete will allow rapid filing of the IND to the Food and Drug Administration (FDA) to enable this novel therapeutic agent to be evaluated in a phase I clinical trial for patients with relapsed/refractory PTCL.

Conclusion: Healthy donor and patient-derived TAA-T cells targeting 5 antigens are polyclonal, polyfunctional and could meet an unmet need as a novel treatment for patients with relapsed/refractory PTCL.

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1. Tagraxofusp treatment of pediatric blastic plasmacytoid dendritic cell neoplasm

Quan Zhao MD, Albert Kheradpour MD. Loma Linda University Children's Hospital, Loma Linda, CA

Theme: Disease Specific, Transplant-Related

Background: Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a very aggressive hematological malignancy. BPDCN is extremely rare in children and has a poor prognosis. There is no optional treatment has been established in children.

Objective: We report one case of pediatric BPDCN. Patient achieved remission with Tagraxofusp treatment only, followed by HSCT.

Case presentation and result: 16-year-old female presented with one month history of cervical lymphadenopathy and multiple yellow-brown skin lesions. Incisional biopsy of cervical lymph node revealed diffuse infiltrate of neoplastic cells. Immunohistochemical stains were positive for CD123, TCL-1, CD4, CD7, CD45, CD56 and HLA-DR; negative for EBER, CD3, CD34, CD19, CD20, CD10, CD117, CD13, CD14, CD57, MPO and TdT. FISH studies detected a MYB rearrangement. Flow cytometric analysis of bone marrow showed 92% of blast population, CSF showed positive for neoplastic cells. The biopsy of skin lesion showed neoplastic cells infiltration. The PET CT showed lymphadenopathy throughout the cervical, supraclavicular, axillary, mediastinal, hilar, and inguinal regions with increased FDG activity; diffuse increased activity throughout the bone marrow; increased FDG activity in the left lower lobe and right lung base. She received total 4 courses of Tagraxofusp treatment. Tagraxofusp was given 12 µg/kg/day x 5 days, every 3 weeks. She had intermittent fever, headache, nausea, and increased weight in the first course. She received additional 3 courses of Tagraxofusp in clinic and tolerated well without complication. All the lymphadenopathy and skin lesions resolved after the first course of treatment. Bone marrow was remission and MRD was negative after the second course of treatment. She was given IT cytarabine every 3 days. CNS was negative after 4 doses of IT. Continue IT weekly until she received HSCT. She received matched sibling donor HSCT. Conditioning was performed with TBI/cranial and spinal boost, Etoposide, and cyclophosphamide. GVHD prophylaxis consisted of tacrolimus starting on day -1, as well as MTX on day +1, +3 and +6. Neutrophil engrafted on day +14. Platelet engrafted on day +12. She developed grade 1 acute skin GVHD. She was off all immune suppression on day +100. Currently, she is in remission 14 months post HSCT, not have GVHD and is doing well. The chimerism is 100% donor.

Conclusion: Tagraxofusp is a new targeted therapy for BPDCN. Tagraxofusp is recommended the frontline treatment for the new diagnosed pediatric BPDCN. HSCT is the recommended consolidative treatment for patients who achieve CR1, especially for patient who has matched sibling donor.

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2. Pulmonary Outcomes After Autologous Stem Cell Transplant for Hodgkin Lymphoma

Kimberly Davidow, MD; Nancy Bunin, MD; Samuel Goldfarb, MD; Jason Freedman, MD, MSCE

Theme: Disease Specific, Transplant-Related

Background: Autologous hematopoietic stem cell transplant (ASCT) may be curative therapy for pediatric patients with refractory or relapsed Hodgkin Lymphoma (HL). Both pre and post ASCT therapy may include pulmonary toxic chemotherapy, such as bleomycin and brentuximab, and radiation. There is little information regarding pulmonary function outcomes of HL patients post ASCT.

Objectives: The aim of this study was evaluation of pulmonary function in patients who underwent ASCT for HL at the Children's Hospital of Philadelphia.

Method: A retrospective chart review was performed for all patients who underwent ASCT between November 2015 and December 2019. Collected information included demographic and clinical characteristics, treatment regimens, radiation, pulmonary function testing (PFTs), comorbidities including atopy, and overall outcomes. All patients underwent BEAM conditioning (BCNU 300mg/m^2/dose, etoposide 200mg/m^2/dose x 4, cytarabine 400mg/m2/dose x 4, melphalan 140mg/m^2/dose). Lung disease was defined as a z-score $\leq$ -1.7 in the following: FEV1, FVC, TLC, or DLCO. There was variability in timing of obtaining post-transplant PFTs. Small sample size excluded detailed statistical analysis; data was graphed using Microsoft Excel to look for trends.

Results: Fourteen patients were included in the analysis. Median age at diagnosis was 14.5 years (12-19) and median age at ASCT was 16 years (13-21). 71% of patients were male and 57% identified as white. Initial staging: 36% stage 2, 14% stage 3, and 58% stage 4. Two patients had primary refractory disease and 57% relapsed within a year of discontinuation of therapy. Initial therapy included ABVE-PC (86%) and AVE-PC-Bv (14%). Salvage regimens varied, but included brentuximab in 64%. Radiation therapy was used in 86% prior to ASCT. Post-transplant therapy included brentuximab in 64% and radiation in 71%. Sixty-four-percent had lung disease post-ASCT, However, 6 of these 9 also had lung disease prior to transplant. Five of these six had further worsening in at least one PFT category following transplant. The majority of patients that developed worsening lung function did have measured improvement within 1 year. Interestingly, 3 patients with pre-transplant pulmonary dysfunction had improvement in their DLCO post-transplant.

Conclusion: Relapsed and refractory patients with Hodgkin Lymphoma undergo a variety of therapies with potential for pulmonary toxicity. There has been no pediatric data published looking at the outcomes and risk factors for this population. This data reinforces the importance of close follow up for these patients. Further large cohort studies would be helpful in identifying risk factors, such that possible mitigative strategies or alternate regimens could be used.
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3. HSCT RESCUES MARROW FAILURE IN A PATIENT WITH LEUKEMIA AND PREVIOUSLY UNDIAGNOSED LIGASE IV SYNDROME

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Theme: Disease Specific, Transplant-Related

Background: Patients with DNA double-strand breakage repair disorders are at increased risk of immunodeficiency, bone marrow failure, and malignancy. Malignancy in this cohort of patients is particularly difficult to treat given the underlying sensitivity to chemotherapy and radiotherapy, lending an important role to hematopoietic stem cell transplantation (HSCT). The choice of conditioning regimen employed poses a challenge, however, as equipoise is crucial between reducing risk of rejection or poor stem cell engraftment with adequate cytoreduction and minimizing excessive toxicity from myeloablative chemotherapy or ionizing radiation in patients with DNA repair defects.

Objectives: This case report describes the successful use of a reduced intensity conditioning (RIC) HSCT in a patient with ligase IV syndrome and numerous pre-transplant complications including malignancy, cardiac failure, typhlitis, marrow aplasia, and secondary hemophagocytic lymphohistiocytosis (HLH).

Design/Method: Single subject case report

Results: A previously healthy microcephalic 5-year-old male presented with B/myeloid mixed phenotype acute leukemia with a *RUNX1-CBFA2T3* fusion. After only 12 days of lymphoid-directed induction therapy including a total of 50mg/m^2 of anthracycline, he developed protracted marrow aplasia, typhlitis, secondary HLH, and cardiac dysfunction with severely depressed left ventricular function, initiating evaluation by whole exome sequencing. The identification of biallelic variants in *LIG4* consistent with DNA ligase IV syndrome, with ongoing protracted marrow aplasia, prompted rescue with HSCT. Prior to transplantation, the patient's HLH was controlled with dexamethasone and emapalumab. His cardiac function normalized and he was weaned off of epinephrine and milrinone. Bone marrow evaluation two months after induction chemotherapy demonstrated marked hypocellularity (<5%) with trilineage aplasia but no evidence of leukemia. He tolerated a RIC regimen of alemtuzumab, fludarabine (150mg/m^2), and cyclophosphamide (20mg/kg) followed by a 9/10 matched unrelated donor bone marrow HSCT. Transplant course was complicated by bacteremia and typhlitis leading to G-CSF initiation. He is now greater than 30 days post-transplantation and

doing well with neutrophil engraftment, no evidence of graft-versus-host disease, and no current infections.

Conclusion: Case series have described successful HSCT with RIC preparative regimen for patients with ligase IV syndrome, though data are scant for the successful treatment of malignancy and recovery from organ dysfunction and HLH for this disease. Our case demonstrates successful rescue HSCT in a patient with cardiac failure, HLH, leukemia, and marrow aplasia, demonstrating that these patients may recover from significant co-morbid conditions that would otherwise preclude curative HSCT and tolerate a RIC regimen that facilitates engraftment.

This research was performed at the Aflac Cancer and Blood Disorders Center, Children's Healthcare of Atlanta, Department of Pediatrics, Emory University, Atlanta, GA, USA

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1. Concurrent posaconazole and tacrolimus use in pediatric patients: a retrospective review to determine time to therapeutic tacrolimus concentrations in pediatric bone marrow transplant patients.

Authors: Jane Chu, PharmD Candidate 2021; Arpita Patel RN, MSN, CPNP- AC, CPHON; Carmen Echols, PharmD, BCPPS; University of North Carolina Children's Hospital, Chapel Hill, North Carolina, USA

Theme: Nursing/Allied Health

Background: Studies have reported dosing recommendations for concurrent use of intravenous (IV) tacrolimus and posaconazole in adult bone marrow transplant (BMT) patients; however, there is a lack of research in pediatric patients. Posaconazole strongly inhibits Cytochrome P450 3A4 which is the enzyme responsible for the metabolism of tacrolimus. To account for this interaction, our institution recommends patients who are initiated on posaconazole have a 50% empiric dose reduction of tacrolimus. Levels are monitored closely to ensure compliance with therapeutic goals. Ganetsky, et al demonstrated that higher tacrolimus concentrations during the first week after transplant with a reduced-intensity conditioning regimen were associated with significantly reduced risk of acute grade 2-4 Graft-versus-Host Disease (GvHD) without increasing risk of relapse.

Objective: To evaluate the time to therapeutic tacrolimus concentration in pediatric BMT patients receiving IV tacrolimus concurrently with posaconazole

Design/Method: Retrospective, single center analysis including patients between the ages of 0 to 21 years old who were admitted to the University of North Carolina Children's Hospital for a BMT between October 1, 2016 to December 31, 2018 with concurrent administration of IV tacrolimus and posaconazole

Results: With a total of nine patients, it took an average of 10 days to reach therapeutic tacrolimus serum concentrations. Patients who were started on the 50% reduced tacrolimus dose (0.01 mg/kg/day) took an average of 14 days to get to tacrolimus goal, while patients who were

started on 0.02 mg/kg/day took on average seven days to achieve therapeutic concentration. Patients on the reduced tacrolimus dose required an average of four tacrolimus dose adjustments and patients on the non-reduced tacrolimus dose required an average of two tacrolimus dose adjustments to reach therapeutic goal serum concentrations.

Conclusion: This case series suggests a delay in reaching therapeutic tacrolimus serum concentrations when using current recommendations gathered from adult data and warrants further research into concurrent dosing recommendations in the pediatric population. This delay in reaching therapeutic tacrolimus troughs mays lead to increased risk of GvHD.

References:
Ganetsky, Bone Marrow Transplant, 2016

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2. A Simulation Program for New Certified Nursing Assistants. Does incorporating simulation for Nursing Assistants improve skills mastery and role expectations?

Author(s) Caroline Costello, MBA, BSN, RN, CPON®, BMTCN®, Katherine Fournier, BSN, RN, CPHON®, & Brittany Root, BSN, RN, CPHON®

Theme: Nursing/Allied Health

Background: Hematopoietic Stem Cell Transplant (HSCT) is a complex treatment option available to children with various life-threatening illnesses, some of which include: hematologic malignancies, immunological diseases, bone marrow failure syndromes, and other genetic disorders. Complex patient care starts with basic activities of daily living (ADLs), which are important for Certified Nursing Assistants (CNAs) to master. Historically, CNAs attended Human Resources Orientation and Central CNA Orientation, followed by a brief HSCT overview by the HSCT Nurse Educator. A learning gap was identified between tasks CNAs perform and their impact on the nursing role. To close this gap an education day was created, involving didactic and simulation portions. There is literature to support the effectiveness of using simulations in nursing education, but none involving CNAs.

Objective: CNAs play a key role in overall function of the HSCT Unit at Boston Children's Hospital (BCH). Many new CNAs on the HSCT Unit have not worked in the role before. During this simulation day the basics of CNA role expectations are reviewed and expanded upon to show the importance of each task while working on skills mastery.

Design/Method: Effectiveness of the CNA (n=26) education initiative was evaluated via anonymous surveys, pre and post education. These 10-question surveys measured perceived knowledge and comfort with skills needed in their roles.
Surveys were also distributed to nurses (n=23) who were familiar with the orientation process prior to implementation of the class. This assessed the nurses' perception of the CNAs' performance after the education.

Results: Findings included the new CNAs' stated improvement in comfort level for necessary skills and a more general understanding of HSCT indications after attending the class. When

asked to grade level of comfort on a scale from 1-10 (1=uncomfortable, 10=very comfortable) prior to class, CNAs averaged 6.5 in regards to providing ADLs independently to a HSCT patient, which increased to an average of 9.5 post-class. Another question asked about the CNAs' understanding of HSCT indication; prior to class they averaged 6.25 and after the average increased to 9.75.
Nurses' perceptions showed improvement with approximately 91% of nurses reporting somewhat to definite improvement in CNA role expectations after the education and 87% reported somewhat to definite improvement in skills mastery.

Conclusion: HSCT patients require a high level of specialized care to be provided by all members of the healthcare team. Educating new CNAs on the proper way to provide this care through simulation has improved their role expectations and skills mastery.

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1. Increased body mass index is associated with increased risk of thrombotic microangiopathy in pediatric transplant patients

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Theme: Supportive Care

Background: Reports of the impact of body mass index (BMI) on clinical outcomes following allogeneic hematopoietic stem cell transplant (allo-HSCT) describe reduced outcomes in those with increased BMI. Elevated BMI has been linked to an increase in pro-inflammatory cytokines leading to endothelial dysfunction, which we hypothesized may increase the risk of transplant-associated complications connected with endothelial injury such as transplant-associated thrombotic microangiopathy (TA-TMA). Elevated BMI has been linked to an increase in pro-inflammatory cytokines leading to endothelial dysfunction. Endothelial activation and TA-TMA are associated with increase in biomarkers such as complement component 3 (C3), soluble suppression of tumorigenicity-2 (ST2) and soluble terminal complement complex (sC5b-9).

Objective: To determine the risk of TA-TMA in pediatric allo-HSCT recipients with elevated BMI.

Methods: We performed a study including 137 consecutive allo-HSCT pediatric patients between the ages of 0-20 years. Retrospective data on BMI (kg/m^2) were expressed in standard deviations from the mean (Z-score) for age, height and gender. C3 and soluble ST2 were prospectively quantified using enzyme-linked immunosorbent assays and sC5b-9 was measured by enzyme immunoassay in HSCT patient plasma samples. Study endpoints included moderate/severe TA-TMA, OS and NRM.

Results: Elevated BMI Z-score (median 1.0, range 0.2-1.6) was associated with increased incidence of severe TA-TMA ($p<0.001$). Higher BMI Z-score (median 1.0, range 0.5 to 1.4) was

also associated with receiving eculizumab therapy for treatment of TA-TMA (p = 0.012). Multivariate analysis showed a higher likelihood of TA-TMA in patients with higher BMI Z-scores (OR 1.7, p=0.004), higher body surface area (OR 2.58, p=0.041) and patients receiving umbilical cord blood grafts (OR 7.51, p=0.022). Higher BMI Z-score was significantly associated with higher baseline level of soluble ST2 (r^2=0.19, p=0.031), but not sC5b-9 (r^2=0.08, p=0.329). There was no correlation between BMI Z-score and baseline levels of C3 (r^2= 0.00021, p=0.89). However, elevated BMI Z-score and sC5b-9 on day +7 were correlated (r^2=0.23, p=0.008). Higher BMI Z-score was associated with worse OS and NRM at 1-year (p=0.08 and p=0.09 respectively).

Conclusions: Identification of demographic features for patients at highest risk for TA-TMA will identify a population in whom to study prophylaxis for TA-TMA. BMI Z-score was strongly correlated with incidence of severe TMA. Baseline elevations of C3 and sC5b-9 were not observed. Although, sC5b-9 levels correlated with BMI at day 7, suggesting further endothelial injury, likely from the preparative regimen is required for terminal complement activation to occur in patients with higher BMI.

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2. Pericardial Effusions Requiring Invasive Interventions in Pediatric Patients who underwent Allogeneic Stem Cell Transplant

Authors: Kelly Lyons CPNP-AC/PC, Niti Dham MD, Bryanna Schwartz MD, Blachy Davila Saldana MD

Institution: Children's National Hospital; Washington D.C, US

Theme: Supportive Care

Background: Hematopoietic Stem Cell Transplant (HSCT) is a curative treatment for many malignant and non-malignant conditions. Pericardial Effusions (PEF) are not infrequently reported condition in the peri-transplant period in pediatric patients undergoing HSCT. The inciting factors associated with PEF development in HSCT patients are not well described. In addition, to our knowledge there is no literature describing echocardiogram findings that predict development and severity of a PEF after HSCT.

Objective: The objective of this retrospective cohort study was to assess the risk for development of a pericardial effusion requiring pericardiocentesis in patients undergoing allogeneic stem cell transplant, requiring invasive interventions

Design/Method: We performed a retrospective chart review of all patients who received an allogeneic HSCT at our institution during the study period of January 2013 to December 2019. A control group of patients who underwent BMT but did not develop a PEF during the study period were also included in data collection. For all patients who were identified as having an effusion that required pericardiocentesis, pertinent clinical documentation and echocardiogram measurements were collected for data analysis. Interval differences between categorical variables were analyzed using chi-square analysis.

Results: A total of 50 patients out of 201 transplanted during the study period developed a Pericardial Effusions (PEF), with 15 symptomatic (7.5%) that required invasive intervention including pericardiocentesis (n=15) or pericardial window (n =1). All effusions were graded as moderate or large. It was found that myeloablative preps likely have a higher risk of the effusion, though this was not statistically significant (p=0.08). There was no difference between the rated of GvHD in the control and PEF group (p=1). Ta-TMA was significant for high risk of invasive intervention (p=0.01). 66% of the cases that required a second invasive intervention had an infection isolated from the pericardial fluid. Even though all the left ventricle end diastolic diameter (LVIDd) z-scores were within normal on pre-transplant echocardiogram, they were statistically larger (p 0.02) in the PEF group.

Conclusion: Pericardial effusions are a common complication post BMT. Active GVHD does not seem to be associated with a risk of pericardial effusions in this cohort. An active viral infection or diagnosis of ta-tma may be associated with a more complex course of a PEF and a second pericardial drainage procedure. There may be predictive value in the assessment of LV size and strain pre-BMT in risk stratification for development of PEF.

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3. Identifying predictive factors for loss to follow up in pediatric bone marrow transplantation patients using supervised machine learning

Authors: Matthew Nagy, Seth Rotz (Cleveland Clinic Children's)

Theme: Supportive Care

Background: Patients who survive Bone Marrow Transplantation (BMT) often face a litany of long-term complications. Consistent outpatient follow-up with an oncologist is necessary to screen and address possible sequelae of the BMT.

Objective: The goal of this study was to use explainable supervised machine learning to identify pediatric BMT patients are at high risk of becoming lost to follow-up, and determine the most important predictive factors.

Design/Method: Data regarding BMT patients <18 years old were acquired through previously published data from the Center for International Blood and Bone Marrow Transplant Research (CIBMTR)[1]. The main outcome, loss to follow up, was defined as missing two consecutive follow-up reporting periods. A supervised gradient boosted machine learning model, LightGBM, was trained with 80% of the available data to predict loss to follow-up, with the remaining 20% used to evaluate model metrics using 5-fold cross validation. The features included in the model consisted of demographic, treatment, and comorbidity data. Participants were split into risk groups via tertile split of predicted probability of lost to follow up (low-, medium-, and high-risk), and frequency of outcome between each group was compared via chi-square. Feature importance was determined using SHapley Additive exPlanations (SHAP) values.

Results: 3869 children (7.4±5.3 years old at time of BMT, 59% female, 21.5% non-white, 52% privately insured, 52% treated for malignancy) were included in this analysis. The area under the receiver operating curve (AUC) after 5-fold cross validation was 0.59 (0.56, 0.61) for loss to

follow-up (specificity: 0.65, sensitivity: 0.65, positive prediction value: 0.32, negative predictive value: 0.88). Using risk probabilities determined by the LightGBM model, participants classified as high-risk were significantly more likely to be lost to follow up (32%, $p<0.0001$) compared to those classified as medium (17%) or low (12%) risk. The top three predictors of lost to follow up determined by SHAP, in descending order, were further distance to treatment center, older age at BMT, and not having acute graft versus host disease.

Conclusion: Determining the greatest risk factors for lost to follow up from BMT may be useful for identifying patients in need of extra support or attention. Explainable supervised machine learning offers a novel opportunity to identify high risk groups and develop interventions catered toward the unique needs of each patient.

References

1. Buchbinder et al. BBMT. 2020

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4. Candidacy for extracorporeal life support in children after hematopoietic cell transplantation: a position paper from the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network's Hematopoietic Cell Transplant (HCT) and Cancer Immunotherapy subgroup.

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Theme: Supportive Care

Background: The field of pediatric Hematopoietic Cell Transplantation (HCT) is evolving rapidly with increasing application in a growing number of diseases. Historical data on a limited number of pediatric HCT patients receiving Extracorporeal Life Support (ECLS) report dismal survival resulting in frequent exclusion of HCT patients as ECLS candidates.

Objective: Due to advances in the field, ECLS is currently offered in populations previously considered ineligible. Improved outcomes in HCT and ECLS prompted the Hematopoietic Cell Transplant and Cancer Immunotherapy Therapy (HCT-CI) subgroup of the Pediatric Acute Lung Injury and Sepsis Investigator's (PALISI) Network to delineate factors important to consider in discussions of ECLS candidacy in HCT patients.

Methods: A literature review was performed searching for ECLS use in HCT patients. Consensus expert opinion was developed regarding factors to consider when evaluating candidacy of HCT patients for ECLS via discussions at the PALISI HCT-CI subgroup meetings and similar interactive discussions.

Results: Literature review revealed a paucity of evidence for factors predicting ECLS outcomes in HSCT patients, therefore factors considered important in determining candidacy were agreed upon through an iterative consensus process. First, the indication for HCT must be considered, as HCT for malignant and non-malignant disorders can present different challenges. Second, current graft function and the expected timing of immune reconstitution must be evaluated.

Third, the presence and severity of ongoing HCT-specific toxicities or complications needs to be evaluated, including graft versus host disease, endothelial injury syndromes, idiopathic pneumonia syndromes, and other HCT-specific complications. Fourth, current infections and multi-organ dysfunction must be thoroughly investigated and staged with special emphasis on bleeding and hemostasis. Fifth, family and patient (if applicable) desires and expectations regarding the provision of maximally intensive care with unpredictable outcome in the setting of severe critical illness must be assessed. Input from those who have provided longitudinal care for the patient and the psychosocial and palliative care teams is essential.

Conclusion: Definitive indications and contraindications regarding ECLS use in the HCT population are lacking. We present factors identified by the PALISI Network's HCT-CI subgroup to frame discussions regarding ECLS candidacy in pediatric HCT patients. Urgent prospective study of detailed factors such as above in these complex patients and associated outcomes is imperative to refine predictors of morbidity and mortality risk

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1. Single pediatric center experience of using abatacept for graft-versus-host-disease prophylaxis in haplo-identical hematopoietic cell transplant.

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Theme: Transplantation Biology

Background: Haplo-identical (Haplo) donors are becoming more commonly used in allogeneic hematopoietic cell transplants (HCT) for both malignant and non-malignant indications. Graft manipulation, post-transplant cyclophosphamide (PTCy) and/or antithymocyte globulin (ATG) are options for graft-versus-host-disease (GVHD) prophylaxis. However, in certain conditions, use of PTCy may not be optimal. Abatacept (Aba), a T cell co-stimulation blockade, has been shown to prevent severe acute GVHD with minimal toxicity in matched unrelated donor transplants. Aba was selected as an alternative to replace PTCy when its use is not the preferred option.

Objective: To explore the efficacy of a non PTCy regimen in preventing GVHD while supporting durable engraftment and disease control in patients undergoing Haplo-HCT.

Design/Method: We retrospectively reviewed our Pediatric Bone Marrow Transplant/Cellular Therapy database between January 2015 and July 2020 at The Hospital for Sick Children. Patients who underwent haplo-HCT without PTCy were included. Their clinical outcome including incidence of GVHD, transplant-related toxicities, and survival were described.

Results: A total of four patients (2-12 years) received a haploidentical PBSC graft and the Ababased GVHD prophylaxis. Our cohort included one patient with a prior liver transplant and 2 patients who had had a previous HCT complicated by secondary graft failure. All had a contraindication for PTCy (recent prior high dose cyclophosphamide or concern of alkylating therapy exposure). The regimen included Aba (10mg/kg) on day -1 & +5 in 4; ATG (day -3 to -

1, in 3), methotrexate (5mg/m2 on day +1, 3 & 6 in 3), tacrolimus (day +1, in 4) and mycophenolate (day +1, in 4). Rituximab (375mg/m2) was given on day +1 in 2 patients as EBV prophylaxis.
No infusion reaction with Aba was noted. Viral reactivations (CMV in 2, adenovirus in 1) responded well to anti-viral therapy. One patient had acute GVHD of skin stage 3 and one patient had both stage 3 skin and stage 1 GI acute GVHD. Two patients had limited chronic skin GVHD. All 4 patients are alive with full donor chimerism and without diseases at 5-23 months follow up, weaning or off immunosuppressive agents with no complications.

Conclusion: Successful Haplo HCT utilizing an Aba- based regimen results in reliable engraftment and acceptable GVHD. Similar to other studies, this supports the concept of Abainduced immune tolerance with minimal treatment-related morbidity. However, our small sample size limits generalizability and encourages the consideration of a larger randomized prospective trial to validate these results in the Haplo-HCT setting.

Late extramedullary relapses following tisagenlecleucel treatment

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Background: Outcomes in children with relapsed/refractory (r/r) acute lymphoblastic leukemia (ALL) have improved significantly over the last 5-10 years, especially with advancement of B-cell specific immunotherapies having revolutionized the approach to these patients. Tisagenlecleucel was the first CAR T-cell product targeting CD19 to be approved by the Food and Drug Administration after achieving a remission rate of 81% in a phase II trial for r/r pediatric ALL patients. Longer-term follow-up showed durable remission with a plateau of the event-free survival curve at 50% at 12 months after tisagenlecleucel. However, the clinical patterns of late relapses following tisagenlecleucel infusion are not well characterized.

Objectives: Describe two cases of extramedullary relapse from ALL in uncommon sites after tisagenlecleucel infusion.

Design/Method: Two case reports.

Results: We report two pediatric cases, both with a history of multiply-relapsed precursor B-cell ALL in CNS and bone marrow, who presented with biopsy-proven extramedullary relapses after treatment with tisagenlecleucel. The first patient is a 5-year-old girl, with KMT2A-rearranged, CD19+ isolated extramedullary relapse of the maxillary sinus, sphenoid bone, mediastinum, and lumbar spine at 2.5 years after tisagenlecleucel. She had B-cell recovery at 6 months post tisagenlecleucel infusion. The second patient is a 16-year-old boy with Ph-like ALL (consisting of IKZF1 deletion and CRFL2-IGH fusion) and CD19+ extramedullary relapse of the chest wall, mediastinal and axillary adenopathy, stomach and muscles of the pelvis, inguinal region and thigh, in addition to MRD 0.081% in the bone marrow, at 16 months after tisagenlecleucel. He

still had B-cell aplasia at the time of relapse. Both patients achieved a complete metabolic response on PET/CT after 1 to 3 cycles of conventional chemotherapy, with a plan to proceed to bone marrow transplant in MRD-negative remission.

Conclusion: We describe two cases of CD19+ primarily extramedullary relapse from ALL after treatment with tisagenlecleucel in multiple sites atypical for leukemia infiltration. Both cases share features of unfavorable genetic variants, histories of extramedullary CNS relapses, and late relapses more than 15 months after tisagenlecleucel infusion. While the early recovery of B-cells in the first patient may have contributed to relapsed disease, the mechanism of extramedullary relapse in the second patient is poorly understood. One hypothesis is that extramedullary sites provide opportunities for CAR T cell evasion by ALL blasts, contributing to treatment resistance and relapse. These cases warrant further studies to elucidate the mechanism behind tisagenlecleucel associated extramedullary relapse.