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Papers

Posters (includes case reports/case series within each section)

PTCTC Abstracts

Plenary Paper # 2001

IMPACT OF PRE-HSCT RBC ALLOIMMUNIZATION ON POST-HSCT OUTCOMES IN PEDIATRIC PATIENTS WITH SCD

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Background: Red blood cell (RBC) alloimmunization, a complication of transfusion, can cause hemolytic transfusion reactions and is associated with reduced survival in patients with sickle cell disease (SCD). Despite prophylactic matching for certain RBC antigens, alloimmunization still occurs. While transfusion burden, defined as the cumulative number of RBC units received, is associated with RBC alloimmunization, alloimmunization can develop with low transfusion burden. Relationship between RBC alloimmunization status and adverse outcomes after allogeneic hematopoietic stem cell transplant (HSCT) is unknown.

Objectives: To evaluate the impact of pre-HSCT RBC alloimmunization status on post-HSCT transfusion burden, graft-versus-host disease (GVHD) incidence, donor engraftment, and survival outcomes.

Design/Method: Data was obtained from the Sickle Cell Transplant Advocacy and Research Alliance (STAR) retrospective registry of pediatric patients who received a matched related donor (MRD) HSCT for SCD between 1993-2017 at 13 centers in North America. We compared patients with and without a pre-HSCT history of an RBC alloantibody ('alloimmunized = AI" and "non-alloimmunized = non-AI") using Wilcoxon rank-sum and Pearson's Chi-squared tests ($p<0.05$ as significant). Time-to-event analyses were followed for 5 years (censored thereafter); survival outcomes were estimated using Kaplan-Meier method. Severe GVHD-free/disease-free-survival (GDFS) was defined as survival without grade III-IV acute GVHD, extensive/severe chronic GVHD, graft failure, SCD reoccurrence, or death.

Results: In a cohort of 236 patients that received mostly myeloablative conditioning (75%), 42 patients (17.8%) had a history of ≥1 RBC alloantibody. The AI group was older (median age 10.6 vs 8.0 years, $p=0.018$) than the non-AI group; other baseline characteristics as well as time to neutrophil and platelet engraftment were similar between groups. Median post-HSCT transfusion requirements for AI vs non-AI patients were 5 vs 3 RBC units ($p=0.084$) and 15 vs 11 platelet transfusions ($p=0.084$). The incidence of grade III-IV acute GVHD was higher in the AI vs non-AI groups (6/42, 14.3% vs 7/194, 3.6%; $p=0.006$). Graft failure was not significantly different for the AI vs. non-AI groups (4/42, 9.5% vs 6/194, 3.1%, $p=0.082$); median donor myeloid chimerism at last follow-up was 100%. When controlling for age, RBC alloimmunization status was significantly associated with an inferior 5-year GDFS, $p=0.047$. 5-year GDFS for AI vs non-AI patients was 72% vs 88% among those <13 years and 66% vs 83% in those ≥13 years.

Conclusion: In pediatric patients undergoing myeloablative HSCT for SCD, pre-HSCT RBC alloimmunization is associated with an increased risk of high-grade acute GVHD, driving a lower GDFS. The pathobiology underlying this association warrants further study.

Plenary Paper # 2002

PIVOTAL PHASE 2 RESULTS OF AUGMENT-101 FOR REVUMENIB IN KMT2Ar ACUTE LEUKEMIA: PEDIATRIC EXPERIENCE

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Background: Revumenib is a small-molecule inhibitor of the menin–KMT2A interaction being investigated in relapsed/refractory (R/R) *KMT2A*-rearranged and nucleophosmin 1–mutated acute leukemias. Phase 1 results showed preliminary antileukemic activity in children.

Objectives: To evaluate safety and efficacy of revumenib in children (aged ≥30 days to 18 years) with R/R *KMT2Ar* acute leukemia included in the phase 2 AUGMENT-101 study (NCT04065399).

Design/Method: Revumenib was administered orally every 12 hours in 28-day cycles at a recommended phase 2 dose (with strong cytochrome P450 3A4 inhibitor) of 163 mg, or 95 mg/m^2 (if body weight <40 kg). Patients aged ≥30 days with R/R *KMT2A*-rearranged acute leukemia were eligible. Primary efficacy endpoint was rate of complete remission or complete remission with partial hematologic recovery (CR+CRh). Safety was evaluated in patients with *KMT2A*-rearranged acute leukemia who received at least 1 dose of revumenib; prespecified efficacy interim analysis (IA) for the *KMT2A*-rearranged population was conducted 6 months after 57th efficacy-evaluable patient enrolled.

Results: At IA (data cutoff July 24, 2023), 94 patients received ≥1 dose of revumenib; 23 (24.5%) were aged <18 (median [range] 4.0 [1.3–17.0]) years. Pediatric patients had a median (range) 3 (1–11) prior lines of therapy, with 52.2% receiving prior hematopoietic stem cell transplant (HSCT). Of the 57 patients in the prespecified efficacy IA, 13 (22.8%) were children. The primary endpoint in the adult plus pediatric population was met and exceeded the protocol-defined null hypothesis of 10%: CR+CRh rate was 22.8% (13/57; 95% CI, 12.7–35.8; 1-sided *P* value 0.0036). Three of 13 children achieved CR+CRh (23.1%; 95% CI, 5.0–53.8); median (range) time to first CR/CRh in children was 2.27 (1.0–3.9) months. Among children, overall response (CRc+MLFS+partial remission) rate was 46.2% (6/13; 95% CI, 19.2–74.9); CRc (CR+CRh+CRi+CRp) rate was 38.5% (5/13; 95% CI, 13.9–68.4), with 60% (3/5) achieving MRD negativity. Median overall survival was 6.9 (95% CI, 2.3–not reached) months. Of 6 pediatric responders, 4 (67%) proceeded to HSCT; 2 resumed revumenib after HSCT. Differentiation syndrome and QTc prolongation (grade ≥2) were reported in 8/23 and 1/23 children, respectively. No dose reductions were reported in children; one discontinuation occurred due to treatment-emergent adverse events (4.3%; febrile neutropenia).

Conclusion: AUGMENT-101 met its primary efficacy endpoint in an aggregate population of adults and children with R/R *KMT2A*-rearranged acute leukemia, validating phase 1 results. Safety and efficacy were similar in adults and children.

Young Investigator Paper # 2003

LONGITUDINAL OVARIAN RESERVE IN ADOLESCENTS WITH LYMPHOMA: CHILDREN'S ONCOLOGY GROUP STUDY ALTE 11C1

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Background: Most adolescent and young adult (AYA) cancer survivors desire biologic children after cure. While many cancer therapies increase risk of future fertility problems, not all patients develop infertility. Factors underlying risk variation are largely unknown. Furthermore, effects of contemporary treatments (e.g., immunotherapy) on fertility are unknown. Anti-Mullerian Hormone (AMH) is a sensitive marker of ovarian reserve and fertility potential in female AYA cancer populations. Therefore, this Children's Oncology Group (COG) study ALTE11C1 prospectively evaluated longitudinal markers of ovarian reserve (AMH) in female AYA patients with lymphoma.

Objectives: 1. Compare AMH from female, post-menarche AYA patients with lymphoma to non-cancer controls: (1) Prior to treatment initiation (e.g., "baseline"), and (2) 12 months post-treatment.
2. Describe AMH trajectory in female, post-menarche AYA patients with lymphoma from baseline to 12 months post-treatment.

Design/Method: This prospective cohort study recruited female patients newly diagnosed with lymphoma at COG institutions, who were <30 years old with first menses ³6 months before enrollment. Demographically comparable non-cancer controls were simultaneously recruited. At study entry, participants completed demographic and medical history questionnaires and underwent AMH blood draws. Patients completed four additional AMH blood draws at: (1) Third cycle of chemotherapy, (2) End of treatment, (3) Six months post-treatment, and (4) 12 months post-treatment. Descriptive statistics summarized demographics. Fisher's exact tests compared AMH between patients and controls. Paired t-tests compared baseline and 12-month post-treatment AMH among patients.

Results: We recruited 203 patients (64.04% white/non-Hispanic, median age 16.44 years) and 170 controls (66.47% white/non-Hispanic, median age 22.63 years). Median AMH in patients at baseline (2032.15 pg/mL) and 12 months post-treatment (1660.40 pg/mL) was lower compared to controls (4031.98 pg/mL; $p<0.01$). Most patients experienced a precipitous drop in AMH during chemotherapy with improvement post-treatment, though to a lower level than baseline ($p<0.01$). Median AMH decreased from baseline to 12 months post-treatment in patients who received a total cyclophosphamide equivalent dose (CED) >3800 mg/m2 ($p<0.01$) or Brentuximab/Rituximab immunotherapy ($p<0.01$).

Conclusion: Patients had lower baseline AMH compared to controls, possibly reflecting ovarian dysfunction from lymphoma. This could impact fertility preservation success at diagnosis, given low AMH is associated with difficult egg retrievals. Off therapy, AMH did not return to baseline – possibly representing a new post-treatment level. While our results confirm high CED exposure impacts fertility, immunotherapy may also prolong ovarian dysfunction. Longer term studies linking our data to reproductive outcomes are necessary to identify individuals at risk of clinically significant ovarian dysfunction and infertility.

Young Investigator Paper # 2004

TARGETING THE UREA CYCLE TO PREVENT AND TREAT METASTATIC OSTEOSARCOMA

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Background: Osteosarcoma (OS) is the most common primary malignant bone tumor in adolescents and young adults. Intensive multimodal treatment cures almost 75% of patients who present with localized disease. However, only 25% of patients who present with metastases become long term survivors, and those who suffer a metastatic relapse are almost never cured. Polyamine metabolism and signaling play important roles in multiple cancers including neuroblastoma and breast cancer but have not previously been studied in osteosarcoma. D, L-alpha-difluoromethylornithine (DFMO) is an irreversible inhibitor of ornithine decarboxylase (ODC), the initial, rate-limiting enzyme within the polyamine biosynthetic pathway, and has been studied in a number of different cancers and investigated as a chemopreventive agent.

Objectives: We investigated the role of polyamines in OS proliferation and metastasis and whether blocking the polyamine synthetic pathway with DFMO had therapeutic potential in the treatment of OS.

Design/Method: Established OS lines were used for all in vitro experiments. We performed proliferations assays to determine IC-50, caspase assays, and clonogenic growth and spheroid assays to measure functions critical to the ability of metastatic cells to colonize distant organs. To determine the effect on tumor growth in vivo, we implanted fragments of a patient derived xenograft into the tibias of NOD/SCID/IL-2Rγ null (NSG) mice. Upon confirmation of tumor growth, mice were randomized to either receive drinking water or drinking water supplemented with 2% DFMO. A third cohort of mice received 2% DFMO after hindlimb amputation.

Results: DFMO profoundly inhibits the proliferation of OS cell lines in vitro. Utilizing caspase assays, we determined that DFMO does not induce apoptosis, but is cytostatic and induces a G1 cell cycle arrest. We found that DFMO prevents the clonogenic growth of 3 different OS cell lines in soft agar and prevents spheroid formation as well. Importantly, established spheroids were not disrupted after the addition of DFMO. Finally, drinking water supplemented with 2% DFMO decreased local recurrence and limited metastasis (p=0.02) in vivo.

Conclusion: DFMO prevents clonogenic growth in vitro and decreases both local recurrence and distant metastasis in vivo. These findings justify a clinical trial of this well-tolerated, FDA-approved drug to prevent metastatic recurrence in patients with osteosarcoma.

Leukemia/Lymphoma Paper # 2005

DETERMINING BIOLOGIC RISKS THAT DRIVE HIGH-RISK OUTCOMES IN B-ALL OF HISPANIC/LATINO CHILDREN

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Background: Health disparity is typically associated with socioeconomic determinants of health however, the risk of developing Acute Lymphoblastic Leukemia (B-ALL) in Hispanic/Latino (HL) children is 1.2-1.75 greater that Non-Hispanic whites (NHW) and after correcting for socioeconomic factors, mortality is 40% higher in HL children. H/L children have a higher incidence of high-risk genetic variations: a 2-fold greater rate of IKZF1 deletion (IKZF1-del) and a 4-fold greater rate of CRLF2 translocations. IKZF1-del is associated with chemotherapy resistance and CRLF2 translocations represent Ph-like status. These two genetic alterations are concomitant in H/L children. 94% of H/L patients with CRLF2 translocation had a coexisting IKZF1-del. Evidence to explain the disparity between H/L and other ethnicities is lacking.

Objectives: Using transcriptomic and genomic analysis, biological differences were discovered in high-risk B-ALL from H/L patients that give insight regarding mechanisms for increased genetic variants and chemotherapy resistance.

Design/Method: RNA-seq was performed on B-ALL from 42 H/L and 18 NHW children and differential gene expression patterns were compared between the two ethnic groups. We performed separate analysis and compared both ethnic groups with wild-type status of IKZF1 (IKZF1-WT). Gene set enrichment analysis (GSEA) and Ingenuity pathway analysis (IPA) were performed. We performed DNA methylation signature analysis using reduced representation bisulfite sequencing on 8 H/L and 8 NHW B-ALL samples.

Results: H/L B-ALL samples have downregulation of genes critical to maintenance of genome integrity compared to NHW samples. GSEA showed downregulation of genes involved in DNA replication and repair. It also showed decreased expression of DNA templated transcription elongation regulators that are active during cell stress. IPA showed upregulated oncogenes including FLT3 and interferon signaling. When comparing IKZF1-WT, H/L B-ALL had downregulated genes involved in DNA replication, DNA damage signaling, and Glutamate/Aspartate synthesis pathways. IPA for this comparison showed upregulated interferon, HDAC, TREM1, and Tec Kinase signaling. IPA showed upregulation of prooncogenic Ephrin and CDK5 signaling. DNA Methylation patterns differed for several relevant cancer genes and long non-coding RNAs.

Conclusion: H/L B-ALL has altered regulatory pathways that govern genome maintenance including dysregulated DNA damage signaling, replication, and repair. This provides evidence for various mechanisms that result in a disparity of high-risk genetic variants for H/L children with B-ALL. In addition, these data provide further insight for chemotherapy resistance and tumor vulnerability with various upregulated oncogenic pathways and dysregulated glutamate/aspartate synthesis pathways.

Leukemia/Lymphoma Paper # 2006

AML CARE AT HOME: EVIDENCE-BASED GUIDELINES FOR OUTPATIENT ACUTE MYELOID LEUKEMIA (AML) MANAGEMENT

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Background: Pediatric cooperative group AML guidelines recommend post-treatment hospitalization until resolution of severe neutropenia (<200/uL). However, roughly 20% of patients are discharged before neutrophil recovery. Patients meeting strict clinical criteria (no fever, documented infection, or ICU-level care within 3 days of chemotherapy completion) had similar bacteremia rates and mortality with inpatient or outpatient recovery.[a] We used these data and published adult recommendations to develop "AML Care at Home" guidelines for outpatient post-chemotherapy management.

Objectives: To evaluate lengths-of-stay (LOS), course durations, and toxicity rates after AML chemotherapy by early-discharge and inpatient-only setting in a pilot implementation at CHOP

Design/Method: We implemented AML Care at Home as a clinical change on 11/15/2022. Pediatric patients with newly diagnosed AML were eligible for early-discharge evaluation if treated with standard frontline chemotherapy, ≥6 months old, and without constitutional trisomy 21. Patients were not eligible for discharge during Induction 1. Discharge eligibility was determined using standardized clinical and psychosocial criteria. Inpatients and outpatients with severe neutropenia received standard anti-infective prophylaxis.

Bidirectional chart abstractions of all patients receiving frontline AML treatment at CHOP from 6/1/2022—12/15/2023 were used to ascertain LOS, readmissions, and significant toxicities. Demographics and LOS were compared using chi-square and Mann-Whitney U tests. Only treatment cycles where patients met clinical discharge eligibility criteria were included in the analyses, irrespective of actual discharge, to mitigate confounding by indication.

Results: During the study period, 18 patients had ≥1 discharge-eligible cycle by clinical criteria, with 30 discharge-eligible cycles and 16 early discharges. Inpatient-only and early-discharge patients had similar age, race-ethnicity, and insurance distributions. Median total LOS was significantly less for early-discharge cycles than inpatient-only: 6 days (range 4-26) versus 24.5 days (21-35), $P<0.0001$. Median course duration was also shorter: early-discharge 33 days (23-49) versus inpatient-only 41 (31-49), $P=0.02$. Severe neutropenia durations were similar. Among 16 early-discharge cycles, there were 4 non-elective readmissions and 3 emergency visits not requiring admission. All readmissions were for neutropenic fever, two of which had documented infections: COVID and polymicrobial central line-associated bacteremia. Events during discharge-eligible inpatient-only cycles were S mitis bacteremia (n=1) and typhlitis (n=1).

Conclusion: Pilot implementation of AML Care at Home had lower LOS and fewer readmissions than expected based on prior studies of outpatient neutropenia management, possibly reflecting the utility of the evidence-based guidelines used to identify optimal early-discharge candidates. We are currently developing a multi-institutional hybrid type II implementation trial.

Funding: CHOP Healthcare Delivery Science Research Grant (Seif)

[a]Getz *JAMA Network Open* 2021

Leukemia/Lymphoma Paper # 2007

UNDERSTANDING TRADITIONAL AND E-CIGARETTE SMOKING METABOLITES EFFECT ON ACUTE MYELOID LEUKEMIA

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Background: Recent research highlights a link between cigarette smoking and diminished survival in patients with acute myeloid leukemia (AML). Tobacco products: cigarettes, smokeless tobacco, and E-cigarettes, contain nitrosamines such as N'-nitrosonornicotine (NNN) and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK). They may contribute to tumor growth and lead to oxidative stress. FMS-like tyrosine kinase 3 (FLT3) mutant AML, which confers a poor prognosis, comprises 25% of AML cases in adolescents and young adult (AYA) patients. AYA cancer patients engage in unhealthy behaviors such as smoking and vaping which may worsen FLT3 AML outcomes, therefore there is a need to understand the impact of nicotine metabolites on AML.

Objectives: 1-Evaluate impact of cigarette smoke condensate (CSC), NNN, NNK on oxidative stress in FLT3 mutant AML.2-Evaluate impact of CSC, NNN, NNK on FLT3 AML progression in vivo.

Design/Method: Human cell lines FLT3 AML (MOLM13, MV411) and non-FLT3 (OCI-AML3) treated with 10 ug/mL CSC, 1 uM NNN, 1 uM NNK or diluent (DMSO or methanol) for 2 weeks. Viability and cell proliferation measured at each cell passage using the trypan blue dye exclusion. Oxidative stress (intracellular glutathione (GSH), peroxide and superoxide levels) were assessed on days 2, 5, 9, and 14 of treatment. Male and female NOD-SCID mice between 6-8 weeks old were engrafted intravenously with 0.1 million luciferase-tagged MOLM13 cells incubated with CSC vs. DMSO or NNN/NNK vs. methanol. Non-invasive imaging performed twice weekly. Mice were euthanized by day 22 and tissues (bone marrow, spleen, liver) collected for immunohistochemistry (IHC) analysis, and western blot.

Results: There was no difference in cell proliferation and viability with CSC, NNN or NNK exposure compared to control, however, there was an early decrease in GSH suggesting oxidative stress followed by an increase in GSH indicating an adaptive response. In vivo, there was an increase in leukemia burden in CSC compared to control. Leukemia burden was increased in female mice receiving NNN and NNK compared to control. Heme oxygenase-1(HO-1) known to be increased in response to cellular oxidative stress, was found to be increased in spleen tissues (males & females) treated with NNN and NNK compared to control.

Conclusion: Increased leukemia burden was observed in mice exposed to nicotine metabolites but not in vitro suggesting microenvironment effect. Leukemia progression was associated with an increase in HO-1 suggesting oxidative stress as possible mediators in leukemia burden. Future studies is to answer how tobacco products influence outcome in AML and if oxidative stress is a mediator for accelerated leukemia growth.

Leukemia/Lymphoma Paper # 2008

SIX1 KNOCKDOWN AND SMALL MOLECULE INHIBITION IMPAIR PROLIFERATION OF T-ALL AND AML

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Background: The t(10;11) *CALM-AF10* translocation is found in aggressive pediatric T-cell acute lymphoblastic leukemias (T-ALL) and acute myeloid leukemias (AML) and induces expression of proleukemic *HOXA* genes. We previously identified and validated the *SIX1* homeobox gene as a novel direct target in *CALM-AF10* leukemias. SIX1, with its cofactor Eyes Absent 2 (EYA2), a protein phosphatase, transcriptionally activates developmental genes. Overexpression of *SIX1* is seen in mesenchymal malignancies (e.g. breast, ovarian, gliomas), and *SIX1*/*EYA2* knockdown impairs proliferation of these tumors. In addition, two novel small molecule SIX1 inhibitors – **8430** (SIX1/EYA2 complex inhibitor) and **9987** (EYA2 phosphatase inhibitor) – replicate the effects of *SIX1*/*EYA2* knockdown in solid tumors. The SIX1/EYA2 axis has not previously been studied in leukemias. We determined that CALM-AF10 localizes to the *SIX1* locus and SIX1 overexpression immortalizes hematopoietic stem cells in methylcellulose, implying a role in leukemic transformation. We hypothesize that *SIX1* and the SIX1/EYA2 interaction are necessary for leukemia cell proliferation.

Objectives: Determine the effect of *SIX1* knockdown and inhibition in *CALM-AF10* leukemia and a panel of established leukemia cell lines.

Design/Method: *CALM-AF10* leukemia cells were obtained from irradiated mice that developed leukemia following transplant with retrovirally transduced HSCs. Jurkat, OCI-M2, and SHI-1 cells lines were obtained commercially. Each leukemia cell line was retrovirally transduced with a panel of 5 *SIX1* shRNAs. RT-qPCR measured mRNA expression. SIX1 (Cell Signaling) and EYA2 (AbCam) antibodies were used for immunoblotting. Cell-Titer-Glo assays and liquid culture were used to assess effects of shRNAs, 8430, or 9987 on cell proliferation and growth.

Results: Using The Broad Institute Database, we identified established leukemia cell lines with increased *SIX1* expression. We validated increased SIX1 protein expression in three leukemia cell lines: SHI-1, OCIM2 (both AML), and Jurkat (T-ALL). shRNA knockdown in these SIX1-expressing leukemias and *CALM-AF10* leukemia cells resulted in impaired leukemia cell proliferation. We also confirmed a direct SIX1/EYA2 interaction in *CALM-AF10* leukemia cells and all three leukemia cell lines. Finally, we found the 8430 and 9987 inhibitors slowed leukemia cell proliferation in a dose-dependent manner in *CALM-AF10* leukemia cells and all three leukemia cell lines.

Conclusion: Using a *CALM-AF10* leukemia model system, we demonstrated involvement of SIX1 and the SIX1/EYA2 axis in both T-ALL and AML. Furthermore, we showed that both *SIX1* knockdown and inhibitors of the SIX1/EYA2 interaction and of EYA2 reduce proliferation of *SIX1*-expressing leukemias. These observations suggest that pharmacologic inhibition of SIX1 is a novel therapeutic approach for aggressive T-cell and myeloid leukemias.

Solid Tumor Paper # 2009

RCM1 DOWNREGULATES ATP2B4 EXPRESSION AND ENHANCES VENETOCLAX-MEDIATED APOPTOSIS IN RHABDOMYOSARCOMA

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Background: Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children. Multimodal therapy has improved outcomes in localized rhabdomyosarcoma. However, the survival outcome for metastatic or recurrent RMS remains very poor. Newer targeted therapies with less toxicity are urgently needed. The oncogenic transcription factor FOXM1 is highly expressed in RMS and correlates with tumor growth and metastasis. RCM-1 is a small molecule-specific inhibitor of FOXM1 with established efficacy and safety in RMS mouse xenografts. RCM-1 encapsulated nanoparticles with folic acid (RCM-1-NP^{FA}) allow systemic administration and targeted drug delivery. Combination therapy is utilized in the clinic to maximize anti-tumor efficacy and overcome drug resistance.

Objectives: To determine the antitumor activity of RCM-1 and venetoclax in rhabdomyosarcoma cell lines and mouse xenografts.

Design/Method: For *in vitro* assays, murine-derived (76-9) and human fusion-negative (RD) RMS cells were treated with half-maximal inhibitory concentrations (IC50) of RCM-1, venetoclax, or a combination of both. For *in vivo* studies, $1x10^6$ 76-9 cells were injected into the flank of C56Bl/6J wild-type mice. Mice were then treated with either RCM-1-NP^{FA}, venetoclax or a combination drug therapy for 21 days. Paraffin-embedded tumor sections were used for immunostaining. Extracted RNA from the control and treated 76-9 tumor cells were used for sequencing. RNA sequencing was performed using NoveSeq6000. Reads were aligned to the GRCm38 mouse genome. We used DEseq2 software for differential gene expression and Altanlyze for Venn diagrams. siRNA transfection was used to deplete *Atp2b4* in 76-9 cells.

Results: RCM-1 synergized with venetoclax to increase tumor cell death compared to each single treatment *in vitro*. In a mouse model of RMS, the combination treatment further reduced tumor burden, suppressed tumor cell proliferation and enhanced caspase-mediated apoptosis compared to single agent treatments. To determine the molecular mechanism of synergy between RCM-1 and venetoclax, RNA-seq was done. Compared to venetoclax alone, combination therapy downregulated critical oncogenic pathways in RMS, including Wnt/β-catenin, angiogenesis, TGF-beta, and PI3K-AKT-mTOR pathways. Next, RCM-1 significantly decreased ATP2B4 expression, an ATPase plasma membrane calcium transporter critical for intracellular calcium homeostasis. The knockdown of ATP2B4 in RMS cells inhibited cell proliferation, migration, and colony formation. ATP2B4 deficient RMS cells have a significant increase in intracellular calcium, likely triggering the intrinsic apoptotic pathway. Finally, venetocalx treatment significantly enhanced caspase-mediated apoptosis in ATP2B4-deficient cells.

Conclusion: Combination therapy of RCM-1 and venetoclax has superior anti-tumor effects. RCM-1 downregulates ATP2B4 expression, increases intracellular calcium, and enhances venetoclax's caspase-mediated apoptosis in RMS cells in culture and in mouse xenografts.

Solid Tumor Paper # 2010

COMBINATORIAL MACROPHAGE INDUCED INNATE IMMUNOTHERAPY AGAINST EWING SARCOMA

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Background: Tumor associated macrophages (TAM) are the predominant immune cell type in Ewing sarcoma (ES) [1]. Macrophages play important roles in phagocytosing tumor cells [2]. However, we found that ES cells utilize dual mechanisms to evade macrophage clearance by simultaneously over-expressing CD47, the "don't eat me" signal, and down-regulating cell surface calreticulin (csCRT), the "eat me" signal. Doxorubicin (DOX) is one of the first line chemotherapy utilized in ES patients and is known to enhance translocation of intracellular CRT to the surface of cancer cells [3]. Magrolimab (MAG) is a humanized anti-CD47 monoclonal antibody designed to block the "don't eat me" signal [4] and is currently under clinical investigation.

Objectives: Here, we aim to overcome TAM resistance in ES by simultaneously enhancing csCRT expression and blocking CD47 signal and investigate the in vitro and in vivo anti-tumor efficacy and mechanisms of action of the combination of MAG and DOX.

Design/Method: Macrophages were derived from human peripheral blood monocytes by GM-CSF and M-CSF induction. Flow cytometry- and microscopy-based in vitro phagocytosis assays were performed to evaluate macrophage phagocytosis of ES cells. Annexin-V assay was performed to evaluate apoptosis. CD47 and CRT were knocked out by CRISPR/Cas9 approach. An ES orthotopic mouse model was utilized to assess the effect of DOX and MAG on ES tumor growth and metastasis and animal survival. RNA-Seq combined with tumor infiltrating immune cell profiling was utilized to identify mechanisms of response/resistance to the MAG and DOX combinatorial therapy.

Results: We found that MAG alone significantly increased phagocytosis of ES cells by macrophages in vitro ($p<0.05$) but had limited effects on reducing tumor growth in vivo ($p<0.01$). The csCRT level on ES cells was significantly enhanced by DOX mediated apoptosis in a dose- and time-dependent manner ($p<0.01$). Importantly, MAG combined with DOX further enhanced macrophage phagocytosis of ES cells in vitro ($p<0.01$) and had a synergistic effect on significantly decreasing tumor growth ($p<0.001$) and lung metastasis ($p<0.0001$) and extending animal survival in vivo ($p<0.0001$). Furthermore, we identified CD38, CD209, CD163 and CD206 as potential markers of ES-phagocytosing macrophages. Mechanistic studies revealed that increased M2 macrophage infiltration and decreased phagocytic activity of tumor infiltrating macrophages are in part key mechanisms of resistance to the MAG and DOX combinatorial therapy.

Conclusion: By turning "two keys" simultaneously to reactivate macrophage phagocytic activity, our data demonstrated an effective and highly translatable alternative therapeutic approach utilizing innate immunotherapy against high-risk metastatic ES.

Solid Tumor Paper # 2011

URINARY CYSTATHIONINE IS A BIOMARKER FOR NEUROBLASTOMA

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Background: Since neuroblastomas are catecholamine-secreting tumors, catecholamine metabolites, urinary homovanillic acid (HVA) and vanillylmandelic acid (VMA) have been widely used as diagnostic markers. However, in clinical practice, prognostic markers for neuroblastoma are lacking. Recently, MYCN has been reported to increase cystathionine (CTN) production and ultimately contribute to the vulnerability of ferroptosis in MYCN-amplified neuroblastoma.

Objectives: This study aimed to evaluate the utility of CTN for diagnosis and pretreatment risk assessment of neuroblastoma.

Design/Method: This study was conducted at Nagoya University Graduate School of Medicine in Nagoya, Aichi, Japan.
A total of 16 pediatric participants with neuroblastomas and 32 pediatric participants with no known cancer (controls) were included in this study. The concentrations of urinary cystathionine and conventional markers (HVA/VMA) were measured using liquid chromatography/mass spectrometry (LC/MS). The area under the receiver operating characteristic curves (ROC-AUC) were used to evaluate their diagnostic and pretreatment risk assessment performance according to the International Neuroblastoma Risk Group (INRG) pretreatment risk classification and the revised 2021 Children's Oncology Group (COG) neuroblastoma risk classifier (version 2). Any association with prognostic factors, such as MYCN status, and the histologic prognostic groups according to the International Neuroblastoma Pathology Classification (INPC) were also evaluated.

Results: AUC for diagnosis were as follows: VMA = 0.945, HVA = 0.934, and CTN = 0.928. The respective AUC for pretreatment risk assessment (high-risk vs. intermediate- and low-risk) according to the INRG pretreatment risk classification and COG risk classifier were as follows: CTN = 0.683, 0.750; VMA = 0.619, 0.625; and HVA = 0.571, 0.547. Additionally, respective AUC for the MYCN status and histologic prognostic groups according to INPC were as follows: CTN = 0.897, 0.889; HVA = 0.692, 0.778; and VMA = 0.667, 0.833.

Conclusion: The results of this study indicated that CTN may be a useful urinary marker for both diagnosis and pretreatment risk assessment of neuroblastomas.

Solid Tumor Paper # 2012

FEASIBILITY AND USABILITY OF ELECTRONIC ROADMAP APPLICATION

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Background: Chemotherapy prescribing and administration in pediatrics is a high-risk endeavor. To help mitigate this risk, pediatric centers use chemotherapy roadmaps to guide as well as document a patient's treatment. Despite the adoption of computerized provider order entry, many pediatric centers still rely on paper roadmap documents. This hampers clinician efficiency and leads to patient care delays. Stanford Children's created a custom electronic roadmap (ER) application. The HIPAA compliant web-based application can pull basic patient information from and is accessible through the electronic

medical record Epic. The main functionalities are managing a roadmap template library and displaying and enabling documentation on individual patient roadmap documents.

Objectives: To evaluate the ER application's implementation, useability, and effect on efficiency and safety as compared to paper roadmap system (PRS).

Design/Method: Application usage metrics data was collected. An anonymous online survey was administered to oncology providers, nurses, and pharmacists over a 3-week period with reminders. Survey included the positive System Useability Scale (SUS) questionnaire (1) and additional questions to assess participant's views on the how the application has affected patient care efficiency and safety in comparison to PRS. Compared safety incident submissions regarding chemotherapy roadmaps over a 23-month period.

Results: Since implementation, a total of 241 unique patients with electronic roadmaps, 1,368 unique electronic roadmaps, and 319 roadmap templates. Over 70% of patients receiving chemotherapy are on electronic roadmaps. There were 99 respondents to the survey (5 fellows, 56 nurses, 18 attendings, 11 APPs, and 9 pharmacists). The average SUS score was 79.8 (adjective good, grade A) (1). 90% of participants preferred the application to paper roadmap system. A one-way ANOVA demonstrated a statistically significant difference in mean SUS score between at least two provider category groups ($F(4, 94) = [3.95]$, $p = 0.005$), with average scores of 74 from nurses, 85 from APPs, 85 from attendings, 90 from fellows, and 91 from pharmacists. There was no statistical difference in SUS scores by years out of training. Respondents also ranked the application as being more efficient for patient care and as safer than the paper system. The number of roadmap related safety reports causing delays in patient care decreased from 0.8 reports per month to 0.375.

Conclusion: Conclusions: Adoption of ERs was acceptable and feasible to users at a single academic pediatric center, with a useability score grade A. There was no increase in safety issues with less reported delays in patient care.

1 Sauro, Measuring Usability, 2011

Sickle Cell Disease Paper # 2013

SUCCESSFUL LABORATORY-BASED AND POINT-OF-CARE NEWBORN SCREENING FOR HEMOGLOBINOPATHIES IN HAITI

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Background: Hemoglobinopathy newborn screening (NBS) decreases morbidity and mortality in young children with sickle cell disease (SCD). We have worked in Haiti for six years creating NBS capacity including the use of Sickle SCAN point-of-care (POC) for NBS. This POC was previously validated for NBS by our group with the purpose of increasing access to families in rural areas.

Objectives: To describe the NBS results showing the incidence of SCD in Haiti.

Design/Method: Combined databases of two studies were examined to ascertain hemoglobinopathy incidence. A dedicated nursing staff performed NBS at three hospital settings: Justinien University Hospital (JUH) in Cap Haitien, Saint Damien Hospital (SDH) in Tabarre, an area in Port-au-Prince, and Sacré Coeur Hospital (SCH) in the town of Milot. A nurse coordinator followed positive cases at each center and brought them back for confirmatory testing. Isoelectric focusing (IEF) or high-performance liquid chromatography (HPLC) were performed as laboratory methods. The Sickle SCAN POC, which uses lateral flow immunoassay technology to show the presence of hemoglobins A, S, and C in 5 minutes, was utilized. Whereas NBS was done at SDH with IEF alone, JUH and SCH had the alternative of using POC alone or in combination with laboratory method. The use of POC was dictated by its availability at the time of screening. Both SDH and JUH laboratories were equipped with IEF machines. The Florida NBS Laboratory was the back-up laboratory for samples, utilizing HPLC.

Results: From August 2017-August 2018 and from late May 2020-June 2023, 14,691 newborns were screened. Of those, 9,523 (65%) were screened with IEF alone, 1,281 (8.7%) with POC alone, and 1,252 (8.6%) with both methods. The Florida laboratory contributed to 17.7% of samples. In total, 98% had negative screening including trait, 1% had a positive screening for SCD, and 1% results were undetermined. Sickle cell trait and hemoglobin C trait were observed in 9.5% and 2.8%, respectively. SCD was identified in 154 infants, with hemoglobin SS (N=97), hemoglobin SC (N=41), Sß+ thalassemia (N=15), and FS-other (N=1). Hemoglobin C disease had a frequency of 0.12% (N=17). Having a POC and a back-up laboratory assisted in NBS implementation. The screening activity was limited by the availability of screening materials imported to Haiti.

Conclusion: We found 1% of the children screened for positive for SCD. POC facilitated screening. We plan to expand POC screening to the Port-au-Price site. The availability of screening materials was the most critical limitation for NBS.

Sickle Cell Disease Paper # 2014

PRELVALANCE AND SIGNIFICANCE OF PITUITARY SIDEROSIS IN TRASNFUSION DEPENDENT SICKLE CELL DISEASE

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Background: Iron overload is common in chronically transfused patients such as in thalassemia major (TM) and sickle cell disease (SCD). Pituitary iron (PI) deposition precedes the clinical effects of gland damage by around a decade in TM. If detected early enough, the clinical effects can be reversed by aggressive iron chelation. 50% of transfused SCD patients develop pancreatic iron load by their early 30's and some develop cardiac siderosis. No studies have reported PI deposition in SCD patients.

Objectives: Our goal was to determine the prevalence, predictors, and significance of pituitary siderosis in transfused SCD patients.

Design/Method: A convenience sample of SCD patients who had undergone either clinically indicated or research indicated brain MRI between 2009-2022 was used. MRI was used if it had pituitary volume, R2 in coronal and sagittal planes of the pituitary gland, liver iron concentration (LIC) by R2*, heart R2*, and

pancreas R2*; examinations with missing data were excluded. Ferritin levels, transferrin saturation levels, luteinizing hormone (LH), follicle stimulating hormone (FSH) and testosterone levels were obtained from chart review for the dates closest to the MRI. Bone marrow transplants patients were excluded as conditioning regimen is known to cause HH.

Results: 41 patients were screened; 33 patients met the inclusion criteria. Pituitary iron was detectable (R2 Z>2) in 24 patients (72.7%), and severe (Z>5) in 9 patients (27%). On multivariate linear regression, ferritin, pancreas R2*, and years of transfusion were retained in the model with a combined r^2 of 0.84. Using logistic regression, the best overall predictors of severe pituitary iron loading were LIC and ferritin with an area under the receiver operator curve (AUROC) of 0.92 and 0.91 respectively. The best multivariate predictor was ferritin and years of transfusion with a combined AUROC of 0.96. There was a negative correlation between the pituitary R2* Z and pituitary volume Z (r^2= 0.38, p =0.029). FSH values trended lower for subjects with pituitary iron Z-score > 5 but this relationship did not reach statistical significance (FSH values 5.71 ± 1.42 vs 3.40 ± 1.94, p = 0.06).

Conclusion: Pituitary siderosis is common in transfused SCD who have persistent, severe iron overload. More than one quarter of patients are at risk for HH, with evidence of significant pituitary gland shrinkage and impaired FSH production. We encourage clinicians to keep a high index of suspicion for iron overload mediated HH in patients with risk factors.

Sickle Cell Disease Paper # 2015

PAIN COMMUNICATION IN PEDIATRIC SCD: DATA OF NOVEL PAIN ASSESSMENT TOOL AND PARENT/PROVIDER REPORTS

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Background: Pain is the most common symptom of sickle cell disease (SCD). No pediatric pain assessment tool is valid and reliable across all ages and developmental stages, requiring parents and providers to serve as surrogate communicators. The correlation between patient, parent, and provider pain descriptors has not been studied in pediatric SCD. “Painimation” is a technology-based tool that incorporates conceptual animations, rather than numbers or words, to characterize pain. These animations intend to help clinicians understand pain from the patient's perspective.

Objectives: To determine the feasibility of Painimation as a pain assessment tool in Pediatric Sickle Cell Disease and examine the relationship between patient, parent, and provider reports of pain symptoms.

Design/Method: Patients 10-21 years old with SCD attending clinic in baseline health, patient caregivers, and same-day providers were enrolled in this single-site cross-sectional study. Consented patients completed demographic and clinical questions, VAS Score, McGill pain descriptors, Lansky Play-Performance Scale (LPP), PedsQL General Health, PROMIS Pain Severity/Pain Interference, and Ped-PRO-CTCAE. Parents and providers completed comparable surveys. All participants completed a “Painimation” profile. Descriptive statistics and correlation coefficients were examined as dyads: patient-parent and patient-provider.

Results: We enrolled 44 patients with 31 patient-parent dyads and 32 patient-parent dyads. Mean

ratings of Painimation for 1) …easy to use, 2) …enjoyed using, and 3) …would use Painimation to communicate pain with their provider were favorable at 3.25±0.71 (SD), 3.00±0.85, and 3.08±1.16 (scale 0-4), respectively. The "Stabbing" animation was most chosen at 43%, and correlated with increased VAS score. "Shooting" and "Tingling" exhibited highest agreement with intended descriptors. VAS ratings correlated well with Painimation severity ratings (Pearson r = 0.75). Median VAS ratings for each dyad correlated positively with both parent and provider ratings ($p<0.001$). Parents trended towards higher VAS reports while providers trended towards lower VAS reports compared to patient report. Both parents and providers exhibited positive correlation with patient LPP reports ($p<0.001$). Parents trended closely with patients reported LPP, while providers trended towards higher functionality ratings.

Conclusion: Painimation is a novel and feasible pain assessment tool in pediatric SCD with high user satisfaction; it holds the promise of improving pain communication and transforming care in Pediatric SCD. Painimation severity scores correlate strongly with VAS scores, while adding unique conceptual dimensions. Parent and provider reports of pain severity and functionality correlated well with patient reports; however, parents tended to report higher severity of pain while providers tended to report lower severity and higher functionality than patients.

Sickle Cell Disease Paper # 2016

MITOCHONDRIA DECREASES LIFE SPAN OF RBC AND CONTRIBUTES TO COLD INDUCED PAIN IN MOUSE SICKLE MODEL

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Background: Sickle cell disease (SCD) is an inherited blood disorder caused by a genetic mutation in the beta hemoglobin gene, leading to the production of abnormal sickle hemoglobin (HbS). This results in multiple complications, including recurrent painful event. It is known that red blood cells (RBCs) have reduced life span; however, effects of mitochondrial retention and intracellular calcium have not previously been evaluated. Cold exposure can trigger pain events, typically attributed to vasoconstriction exacerbating cell sickling and vascular occlusion. The underlying pathophysiology may however involve additional mechanisms. Clarifying these mechanisms could help identify therapeutic targets for preventing or reduction of pain events in patients.

Objectives: To further investigate the mechanisms underlying the reduced lifespan of SCD's RBCs and gain more knowledge about cold-induced painful events in SCD

Design/Method: Red blood cell (RBC) life span assessment: In Townes sickle cell mice RBCs labeled with biotin were tracked over 4 days using flow cytometry analysis with conjugated streptavidin. Cold exposure evaluation: Townes sickle cell mice were exposed to 10°C for 60 minutes. Blood samples were evaluated by flow cytometry for RBCs maturity (CD71), mitochondria presence (TMRM), ROS production (CM-H2DCFDA), and exposure of TLR9 receptor (ODN 2006) and intracellular Calcium (FLUO-4AM). Standard complete blood count (CBC) assessment was also performed. Statistical analysis was done using GraphPad

Results: In sickle mouse at baseline there were higher levels of calcium, retention of mitochondria, ROS

and TLR 9 compared to controls. Time-course tracking of streptavidin labeled erythrocytes over 4 days revealed reduction of the fraction of cells with elevated mitochondria, ROS and intracellular calcium, suggesting a shorten lifespan Complete blood count (Hemoglobin, RBC Count, MCV, White cell count with differential, and platelet count); plasma mtDNA and RBC TLR9 receptor assessment were all not statistically significantly different between mice exposed to cold and those not exposed to cold. However, there was a reduction of the mean fluorescence intensity (MFI) for both intracellular calcium (-70%; p = 0.0001) and ROS (-80% ; p = 0.0253) in mitochondria-containing RBCs relative to without mitochondria.

Conclusion: In a sickle cell mouse model decreased lifespan was associated with mitochondrial retention and intracellular calcium. In addition, cold exposure induced significantly reduced intracellular calcium and ROS in mitochondrial retaining RBCs without hemolysis. These findings suggest that these RBC with high intracellular calcium and ROS could be off-loading into the blood stream by mechanism other than hemolysis. Overall, this work enhances our understanding of sickle cell disease pathophysiology.

Oncology Paper # 2017

CIRCULATING TUMOR CELLS IN MEDULLOBLASTOMA: A POTENTIAL NOVEL PERIPHERAL BIOMARKERS FOR CNS DISEASE

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Background: Medulloblastoma is a childhood embryonal tumor of the cerebellum and accounts for most pediatric malignant disease of the central nervous system (CNS). Diagnosis, staging, and disease monitoring require invasive neurosurgical procedures with biopsy or MRI. No peripheral blood biomarkers exist. Here we demonstrate the presence of circulating tumor cell clusters (CTCCs) in patients with Medulloblastoma and use a transcriptomic and machine-learning approach to describe their gene-expression.

Objectives: We capture CTCC from unprocessed patient whole blood using a novel physics-based microfluidic device (Cluster-Well) and perform bulk RNA-sequencing followed by differential gene expression (DGE) analysis, gene-set enrichment analysis (GSEA) to describe the CTCC transcriptome. Additionally, we use a machine-learning based deconvolution to infer immune cell composition.

Design/Method: We enrolled 45 total patients in a longitudinal study: 25 with medulloblastoma, 10 with low-grade glioma, and 10 without malignancy. CTCCs were captured from unprocessed whole blood using the Cluster-Well, a novel physics-based label-free approach to CTCC isolation. Bulk RNA sequencing was performed on 21 samples at time of diagnostic resection from 6 patients with medulloblastoma. Sequencing reads were assessed for quality control, trimmed, and aligned to the human genome. DGE was performed against whole blood from healthy controls using DESeq2 after count normalization. Data visualization and dimensionality reduction is performed through principal component analysis (PCA). Reactome pathway database of curated, peer-reviewed gene sets are used for GSEA. To resolve hematopoietic immune cells as a component of clusters, a machine-learning based approach to immune-cell deconvolution is performed using CibersortX.

Results: The presence of peripherally circulating tumor cell clusters in patients with medulloblastoma is not previously known and was detected in all patients with medulloblastoma whereas none were observed from patients with either low grade glioma or non-malignant hematological conditions. Bulk RNA-sequencing demonstrate separation on PCA and gene-expression heatmap against whole blood healthy control. DGE shows upregulation of genes indicating stem-like state. GSEA show enrichment of medulloblastoma molecular pathways and gene sets defining integrin, extracellular matrix remodeling, and cell adhesion pathways. Immune-cell deconvolution shows predominantly neutrophil signature in clusters.

Conclusion: The finding of peripherally captured CTCCs from parent tumor in the CNS from all patients within our patient cohort suggests their utility as a tumor biomarker. Future sequencing is planned comparing CTCC transcriptome against parent tumor.

Oncology Paper # 2018

TARGETING C-MET: IMPROVING EFFICACY OF CAR T-CELLS FOR TREATMENT OF AGGRESSIVE SOLID & BRAIN TUMORS

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Background: Chimeric Antigen Receptor T-cells (CART), FDA-approved immunotherapy for B-cell malignancies, is hampered by inadequate CAR T-cell infiltration, persistence, and function in solid tumors. Along with immune inhibition, tumor adaptations following CART therapy likely contribute to poor efficacy. In our preclinical studies, we observed aberrant upregulation of c-MET, a receptor tyrosine kinase (RTK) overexpressed in tumor cells, during tumor progression and metastasis following treatment with HER2-targeted CART. Thus, co-targeting c-MET using FDA-approved small molecule inhibitors like cabozantinib could potentially offset tumor survival mechanisms and promote CART function through modulation of the tumor immune-microenvironment.

Objectives: Our objective was to characterize c-MET expression dynamics in CART-treated solid tumors and evaluate the effect of cabozantinib on antitumor activity of HER2-specific CART with/without PD-1 checkpoint reversal receptor expression (CPR).

Design/Method: Primary human T-cells obtained from healthy donors were transduced with HER2-CART using retroviral gene delivery. For functional evaluation, we used a panel of tumor cell lines (commercially sourced), including osteosarcoma (LM7, 143B, U2OS), rhabdomyosarcoma (RH41), glioblastoma (LN229) and medulloblastoma (DAOY). We used immune assays optimized in our laboratory like flow cytometry, Luminex-multiplex, western blot, and xCELLigence for in vitro assessment of c-MET expression and CART function. Proteomic analysis of tumor cells was done using Reverse-Phase Protein-Array (RPPA). For in-vivo functional testing, we used orthotopic xenografts of osteosarcoma established by intratibial injection of 143B-osteosarcoma cells.

Results: Following cocultures with HER2-CART, we found consistent upregulation of c-MET across most tumor cell lines evaluated, in contrast to HER2 and other RTKs which were downregulated; increased

surface expression of c-MET was independent of the antigen targeted with CART. In the presence of the c-MET ligand HGF, CART exhibits lower antitumor activity against HER2+ sarcoma cells. Proteomic analysis of treated osteosarcoma xenografts revealed a higher c-Met expression in lung metastasis. We studied the effect of cabozantinib (2.5-10 μM) on CART viability/proliferation and detected no changes from untreated control T-cells. In in vitro functional assays, CART tumor lysis was enhanced in a dose-dependent manner. In orthotopic xenograft models of 143B-osteosarcoma, combination treatment with HER2-CART and cabozantinib induced tumor regression with improved survival over mice treated with CART or cabozantinib alone. Additional studies are currently underway in brain tumor models and in combination with HER2-CART co-expressing PD-1 checkpoint reversal receptors.

Conclusion: Our results suggest a potential synergy between CART and cabozantinib, warranting further preclinical development of the concept to facilitate clinical translation of the combination approach.

Oncology Paper # 2019

TARGETING MICROENVIRONMENT PATHWAYS TO IMPROVE CAR-T CELL EFFICACY IN B-ALL

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Background: Currently, less than half of pediatric patients with relapsed B-cell acute lymphoblastic leukemia (B-ALL) can be cured with chimeric antigen receptor (CAR) T-cells, often because of lack of persistence and exhaustion of T-cells. While studies have identified microenvironment signals that hinder CAR function, few have explored mechanisms within the microenvironment that promote T-cell function. Bone marrow stromal cells (BMSCs) within the microenvironment regulate the function and survival of hematopoietic and T-cells.

Objectives: To investigate the impact of the microenvironment on CAR-T cell function.

Design/Method: Donor T-cells were activated with CD3/CD28 beads, transduced using a lentiviral vector encoding a FMC63-based CD19-directed CAR with 41BB costimulatory domain, and expanded with interleukin-2 (IL-2) for 7 days before cryopreservation. CAR-T cells were co-cultured with and repeatedly exposed to B-ALL cells (REH), both with and without BMSCs (mouse OP9 irradiated with 30 Gy). To rule out secondary effects of T-cell receptor (TCR) activation due to mouse antigens on CAR-T cell function, the experiments were repeated with TCR knockout CAR-T cells. CAR-T cells cultured in IL-2 for an additional 3 days (total culture duration of 10 days) underwent CRISPR/Cas9 knockout of the TCR-α constant locus.

Results: CAR-T cells cultured with BMSCs compared to without BMSCs exhibited sustained expansion and retained the ability to eliminate B-ALL cells for a significantly higher number of B-ALL exposures in 7 experiments across 4 donors (12 vs 7 exposures; two-sided paired t-test, $p = 0.011$). TCR knockout CAR-T cells plated with BMSCs exhausted later compared to those plated without BMSCs (6 vs 5 exposures), and there was no difference between TCR knockout and non-targeting sgRNA control knockout CAR-T cells, indicating that the positive effect of BMSCs on CAR-T cell function is not due to mouse-human TCR cross-reactivity. The similar but less pronounced trend observed in TCR knockout and non-targeting sgRNA knockout CAR-T cells may be attributed to longer IL-2 exposure. CAR-T cells plated with B-ALL cells and BMSCs demonstrated stromal killing prior to exhaustion, unlike CAR-T cells plated with BMSCs

in the absence of B-ALL cells.

Conclusion: Our findings indicate that BMSCs induce sustained cytotoxicity of CAR-T cells. Transwell, exhaustion marker, and RNA sequencing studies on sorted B-ALL and CAR-T cells are ongoing to answer the following questions: (1) Are BMSCs directly affecting CAR-T cell function or is there an indirect effect through decreased exhaustion ligand expression on B-ALL cells? (2) Is the effect mediated through secreted factors or cell-to-cell contact from BMSCs?

Oncology Paper # 2020

CD22 CART FOR CHILDREN AND YOUNG ADULTS WITH R/R B-CELL ALL: RESULTS FROM A 10-YEAR-EXPERIENCE

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Background: Relapse after CD19 CAR T-cells occurs in approximately 50% of patients with B-ALL within the first year. Treatment options for such patients are limited, particularly for those with CD19 negativity. A CD22 CAR T-cell construct was developed in the Pediatric Oncology Branch, National Cancer Institute and has been tested in an ongoing clinical trial for children and young adults with B-ALL since 2014.

Objectives: We provide a comprehensive report from our single-center, phase I trial testing CD22 CAR T-cells in pediatric and young adult patients with CD22+ B-cell leukemia (NCT02315612). Primary objectives were to assess safety, toxicity, and feasibility. Secondary objectives were to explore efficacy.

Design/Method: This was a 3+3 dose-escalation trial. Patients received lymphodepleting chemotherapy with fludarabine and cyclophosphamide prior to CAR T-cell infusion. The initial experience with dose escalation and impact of manufacturing on dose selection have been previously reported (Fry et al., Nature Medicine, PMID 29155426, Shah et al. JCO, PMID 32286905).

Results: As of 12/1/2023, 79 patients have been infused with 45 (57%) having received prior CD19 or CD19/22 CAR T-cells and 28 (35%) having received prior blinatumomab. Forty-six (58%) patients had CD19 partial or negative disease. 46 (58%) of patients were treated with 3×10^5 CD22 CAR T-cells/kg using a T-cell selection process prior to transduction as the effective dose. Sixty-eight (86%) patients developed cytokine release syndrome with the majority (79%) being grade 1 or 2 in severity. 1 patient had a grade 5 ARDS event related to CRS. Neurotoxicity was limited. Hemophagocytic lymphohistiocytosis (HLH)-like toxicities were seen in 26 (33%) patients. A comprehensive analysis of these HLH-like toxicities led to the development of a consensus statement towards the identification and treatment approach to immune-effector cell associated HLH-like syndrome. Complete remission was seen in 54 (68%) patients with 47 (59%) being in an MRD negative complete remission. Most patients who achieved remission proceeded to a consolidative hematopoietic stem cell transplant. Overall remissions lasted a median of 5.4 months (range 1.43-22.23 months). A total of 18 (22.8%) patients remain alive at a median of 4.1 years (0.1-8.2 years), post CD22 CAR, 9 of whom remain in an ongoing remission.

Conclusion: Our extensive experience confirms the safety and efficacy of CD22 CAR T-cells, while providing novel insights into CAR T-cell toxicities. Based on these results, a pivotal registration study in pediatric B-ALL is in development.

Hematology Paper # 2021

EVALUATING THE BIOPHYSICS OF PLATELET ADHESION AND GEOMETRY-SENSING IN MILD BLEEDING DISORDERS

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Background: A subset of patients with mild bleeding disorders have may have an underlying platelet dysfunction that cannot be evaluated with current lab tests. Among this subset of patients are those with mild type 1 von Willebrand Disease (vWD) which comprises a population that was recently more broadly redefined to capture patients with von Willebrand Factor (vWF) levels between 30-50 IU/dL and abnormal bleeding. There is no diagnostic test or biomarker that can accurately identify which patients are at risk for bleeding within this population which comprises a broad spectrum of patients with varying degrees of bleeding.

Objectives: We have engineered two new assays to assess disorders of primary hemostasis and apply these assays of platelet function testing to potentially define new bleeding disorders, characterize platelet phenotypes in patients with mild bleeding disorders and refine the definition of type 1 vWD.

Design/Method: Platelet spreading area is measured quantitatively through an automated software we developed that is able to detect area spread on images obtained by confocal microscopy. The platelet geometry-sensing assay detects how platelets secrete granules and spread in a spatially dependent manner. This assay is engineered such that the area of the adhesive matrix encompassed by a microdot is less than the spreading area of a platelet and as such, it assesses the capability of the platelet to secrete granular contents to enable adhesion beyond the boundaries of microdot. A platelet can spread on microdots of collagen or fibrinogen substrate and on a range of microdot sizes as platelets sense the surrounding microenvironment.

Results: On average, those with type 1 vWD had 0.07 (SE=0.03) lower circularity of fibrinogen than the control group (p-value=0.04). Microdot size was significantly associated with all stamp assay outcomes except for the area in collagen specimens. An increase in microdot size (measured in microns) was associated with an increase in collagen % area colocalization (B=4.33, SE=0.09, p-value<0.001), collagen circularity (B=0.001, SE=0.0004, P=0.02), fibrinogen area (B=1.01, SE=0.06, P<0.001), fibrinogen % area colocalization (B=2.96, SE=0.09, P<0.001), and fibrinogen circularity (B=0.01, SE=0.0005, P<0.001).

Conclusion: The heterogeneity in platelet spreading and adhesion among patients with type 1 vWD suggests differences in platelet function within this population. Compared with the control group, there was a significant decrease in platelet circularity in type 1 vWD suggestive taht there is a platelet circularity spreading defect with reduced spreading capacity after activation.

Hematology Paper # 2022/Late Breaking Abstract

TARGETING A NOVEL SOX18-MEVALONATE PATHWAY AXIS TO TREAT INFANTILE HEMANGIOMA

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Background: Infantile hemangioma (IH) is the most common tumor in children and a paradigm for pathological vasculogenesis, angiogenesis and regression. Propranolol was discovered serendipitously to be effective for IH. The R(+) enantiomer of propranolol was shown to inhibit IH vasculogenesis via a β-adrenergic receptor independent off-target effect on the endothelial specific transcription factor SRY box 18 (SOX18). Here we show R(+) propranolol downregulates the mevalonate pathway (MVP) which bifurcates into cholesterol biosynthesis and the production of farnesyl diphosphate used for prenylation of proteins, particularly small GTPases in the Ras pathway.

Objectives: The aim of this study was to unravel downstream targets of SOX18 to advance our understanding of central regulators involved in IH pathogenesis. We identified the MVP as a novel target in IH resulting in new opportunities to repurpose drugs along the MVP for IH treatment.

Design/Method: We performed bulk RNA-Seq of patient-derived differentiating hemangioma stem cells (HemSC) (n=6) treated with R(+) propranolol. Testing of statins and tipifarnib testing was performed in vivo by implanting patient-derived HemSC into nude mice and treating for 7 days with simvastatin (n=50), atorvastatin (=26), or vehicle control (n=36) as well as tipifarnib (n=42) or vehicle control (n=17). The R(+) propranolol dependent downregulation of the MVP was validated in functional in vitro studies and in patient tissue samples at different IH stages (n=10 each).

Results: Transcriptomic profiling of patient-derived HemSC undergoing endothelial differentiation and treated with R(+) propranolol revealed a coordinated downregulation of genes in the MVP. Functional assays, including pharmacological inhibition of SOX18 as well as lentiviral knockdown, loss of SOX18 confirmed SOX18-mediated inhibition of the MVP by R(+) propranolol. Further, SOX18 and the mature form of the MVP master regulator sterol response element binding protein-2 (SREBP2) were co-expressed in endothelial cell nuclei of proliferating and rebounding IH samples. The MVP inhibitors, simvastatin and atorvastatin, as well as the FDA-approved prenylation inhibitor tipifarnib suppressed IH vessel formation in a preclinical xenograft model for IH.

Conclusion: We suggest a novel theranostic approach to repurpose statins and inhibitors of prenylation for the treatment of IH and potentially other vascular anomaly entities based on a SOX18-MVP-axis as a central metabolic regulator. Our proposal functionally connects three major drug classes via the transcription factor SOX18 - beta blockers, statins and inhibitors of prenylation - a link that may have potential for broad implications in the fields of vascular anomalies and oncology.

Hematology Paper # 2023

OUTCOMES OF HSCT USING REDUCED INTENSITY CONDITIONING IN PEDIATRIC SEVERE APLASTIC ANEMIA

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Background: Severe aplastic anemia (SAA) is a rare multilineage bone marrow failure disorder. The current standard of care is immunosuppressive therapy (IST) in the absence of a matched sibling hematopoietic stem cell transplant (HSCT) donor; the latter has an overall survival (OS) of >90% in pediatric population. Due to increased risk of disease recurrence and clonal hematopoiesis with IST, an allogeneic transplant can be curative for SAA.

Objectives: To study the outcomes and to report the feasibility of using reduced intensity conditioning (RIC) regimen in allogeneic HSCT for SAA.

Design/Method: We studied 23 patients with a median age of 9 years (range 3-19 years), diagnosed with SAA at St Louis Children`s Hospital (2013-2023). All of them received RIC regimen (alemtuzumab 33 mg for <10 kg or 48 mg for >/=10 kg, Fludarabine 150 mg/$m^{2,}$ Melphalan 140 mg/m^2 with/without Thiotepa 8 mg/kg). Patients received calcineurin inhibitor and abatacept for graft vs host disease (GVHD) prophylaxis.

Results: Out of the 23 patients, 11 patients were males (48%) and 12 were females (52%). 14 patients (60.8%) received IST as initial therapy and subsequently developed serious adverse effects due to the drug or failed/relapsed following discontinuation of therapy. Also, two patients (8%) developed paroxysmal nocturnal hemoglobinuria clones. There were 13 (56%) matched related and 8 (35%) matched unrelated donors. Two of them (8%) received cord blood transplants. Of all the donor types, 18 (78%) were fully HLA-matched (10/10), and 2 received haploidentical transplants. One patient received a transplant from an HLA-matched identical twin. All patients except one were fully engrafted and reached 100% chimerism by day +30. None of the patients developed graft failure or acute or chronic GVHD. Seven of 23 (30%) developed infectious complications (2 bacterial, 5 viral reactivations). Eight of 23 patients (35%) required >10 units of packed red blood cell transfusion and 4 of 23 patients (17%) developed transfusion-related iron overload that required phlebotomy and iron chelating agents. OS for the entire group was 95% and were disease-free at a median follow-up of 48 months (range 12-144 months).

Conclusion: Our study has shown high cure rates and favorable OS following HSCT in SAA, irrespective of the donor types. Prior transfusion burden did not significantly complicate the transplant success, but some of the patients required iron chelation in the posttransplant period. Use of RIC regimen with allogenic transplant in our patient group has demonstrated excellent outcomes with minimal chronic transplant-related complications.

Hematology Paper # 2024

THE CHARACTERISTICS OF PEDIATRIC PATIENTS WITH PYRUVATE KINASE DEFICIENCY AND IRON OVERLOAD

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Background: Pyruvate kinase (PK) deficiency is a rare, congenital hemolytic anemia. Iron overload (FeO) occurs in both transfused and non-transfused pediatric patients with PK deficiency and can cause long-term complications.

Objectives: Describe the characteristics of pediatric patients with PK deficiency and FeO according to transfusion status using real-world data from the Peak Registry (NCT03481738) and PK Deficiency Natural History Study (NHS; NCT02053480).

Design/Method: Data on pediatric (aged 1–<18 years at enrollment) patients with PK deficiency and FeO from the two studies were merged for this analysis. FeO was defined as having ever received chelation/phlebotomy or any of the following in the 3 months prior to enrollment/during follow-up: 1) ferritin >1000 ng/mL; 2) liver iron concentration by MRI >3 mg Fe/g dry weight; 3) cardiac T2 MRI ≤20 ms. Patients were grouped into cohorts by enrollment age (1–<6, 6–<12, 12–<18 years) and by transfusion status 12 months prior to enrollment (regularly transfused [RT, ≥6 transfusions] and non-regularly transfused [NRT, <6 transfusions]). Data available were summarized for each cohort using descriptive statistics.

Results: *Overall*: Of 135 pediatric patients, 92 (68.1%) met the criteria for FeO (as of 13May2022). Median (range) age at enrollment was 6 years (1–17) in those with FeO and 7 years (1–16) in those without FeO.
FeO cohort: Among 92 patients with FeO, 50 (54.3%) were female. Forty (43.5%) patients were aged 1–<6 years, 29 (31.5%) 6–<12 years, 23 (25.0%) 12–<18 years. FeO was common across *PKLR* genotypes (missense [M]/M: 43.5%; M/non-missense [NM]: 31.5%; NM/NM: 25.0%). Being RT was less common among older age groups (1–<6 years: 32/40, 80.0%; 6–<12 years: 12/29, 41.4%; 12–<18 years: 5/22, 22.7%). Median (Q1, Q3) ferritin was 880 ng/mL (492, 1356). In total, 55 (59.8%) patients had undergone splenectomy, including 20/49 (40.8%) RT and 34/42 (81.0%) NRT patients. Across age groups, the most common chelator was deferasirox (80/82, 97.6%). Median (range) age at first chelation was 3 years (1–14) and 4 years (0–18) in RT and NRT patients, respectively. Chelation was ongoing in 26/33 (78.8%) RT and 16/28 (57.1%) NRT patients. Overall, patients experienced complications such as gallstones (14/49, 28.6%), extramedullary hematopoiesis (14/87, 16.1%), hepatomegaly (15/56, 26.8%), and pulmonary hypertension (4/56, 7.1%).

Conclusion: FeO is common in pediatric patients with PK deficiency. In this population from the NHS and Peak Registry, history of FeO occurs across age range, transfusion status, splenectomy status, and genotypes.

General Hematology and Bone Marrow Failure/Immune Dysregulation (001-070)

Poster # 001

VARYING PREMEDICATION AND ITS IMPACT ON TRANSFUSION REACTIONS IN PEDIATRIC BMT AND HEME-ONC PATIENTS

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Background: Transfusion reactions are potentially serious complications of blood product administration. The pediatric hematology, oncology and bone marrow transplant patients are a group that receive numerous transfusions during their treatment, placing them at higher risk for reaction. This study focuses on the most common transfusion reactions: febrile nonhemolytic reactions (FNHTRs) and allergic transfusion reactions (ATRs). Acetaminophen and diphenhydramine are commonly administered pre-medications for transfusions, but there is insufficient evidence showing true benefit for reactions. There is risk of hepatotoxicity and sedation, respectively, as well as delay in blood product administration, with use of these medications. Our practice was changed from routine premedication with acetaminophen and diphenhydramine to no pre-medications and found no difference in the incidence of allergic reactions between groups, but a statistical difference in FNHTRs between groups. We then changed our routine premedication policy to include only acetaminophen unless history of reaction.

Objectives: To compare the incidence of FNHTRs and ATRs in patients who were routinely premedicated with acetaminophen and diphenhydramine, acetaminophen alone, or no pre-medications to determine clinical benefit of routine premedication for transfusions.

Design/Method: IRB-approved retrospective chart review study of all hematology, oncology, and bone marrow transplant patients ages ≥ 6 months and ≤ 25 years, who received a transfusion of packed red blood cells or platelets across two phases, pre-medication with acetaminophen and diphenhydramine, then with acetaminophen alone ranging from January 2017 – May 2022. Patients were excluded if they had a history of prior transfusion reaction. Data was collected on patient demographics, blood products, pre-medications, transfusion reaction occurrence and type.

Results: There were 1769 total transfusions analyzed. Based on premedication standard of care at each time of data collection: 644 transfusions were premedicated with acetaminophen/diphenhydramine, 649 transfusions were not premedicated, and 366 transfusions were premedicated with acetaminophen alone. 1.9% (7/366) of reactions occurred in the acetaminophen only group, 3.2% (21/649) in the no premedication group, and 1.1% (7/644) in the acetaminophen/diphenhydramine group. There was no significant difference across groups for ATRs. There was a significant difference in FNHTR occurrence between acetaminophen/diphenhydramine group and no medication ($p = <0.01$) and acetaminophen versus no medication ($p = 0.03$). There was no significant difference between the acetaminophen/diphenhydramine and acetaminophen alone groups ($p = 0.15$).

Conclusion: This study supports that there may be a practical use of pre-medicating with acetaminophen to prevent febrile nonhemolytic transfusion reactions and there does not appear to be any benefit of additional pre-medications in our patient population.

Poster # 002

A QUALITY IMPROVEMENT INITIATIVE USING THE ELECTRONIC MEDICAL RECORD TO REDUCE BLOOD ORDER ERRORS

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Background: Pediatric hematology and oncology (PHO) patients frequently require blood product transfusions essential for their successful treatment. These blood products, most often red blood cells and platelets, require special processing for immunocompromised patients. Ordering blood products can be challenging and prone to error, and inaccurate orders can lead to serious, and even life-threatening, adverse events.

Objectives: In collaboration with the blood bank, we aimed to decrease blood product ordering errors by modifying existing electronic medical record (EMR) blood product order sets.

Design/Method: All blood product special processing errors were tracked from January 2020 through October 2023. Intervention 1 occurred in April 2021. We worked with the informatics team to modify the appearance of special processing options for prescribers. Separate questions were created for both irradiated and Cytomegalovirus (CMV) seronegative blood, with readily visible indications, rather than requiring providers to click into a box. In April 2022, we implemented intervention 2, modifying the order set to display the patients prior special processing requirements allowing providers to be aware of previous needs. Additionally, in May 2022, a hospital wide decision was made to deimplement CMV serostatus special processing, and the order set was updated. Data was tracked on run charts with both total events and excluding CMV related errors.

Results: During the project period, 396 prescribing errors occurred out of 33,901 dispenses of red blood cells and platelets, of which 126 (31.8%) were CMV serostatus related. Error rate was tracked monthly. Prior to April 2021, the special processing mean monthly error rate was 1.69%, excluding CMV serostatus events, which decreased to 0.61% after intervention 1 and to 0.27% following intervention 2. One way ANOVA showed a statistically significant difference in mean error rate between at least two groups ($F(2,42) = [47.73]$, $p<0.001$) with post hoc Tukey HSD demonstrating significant difference in pairwise comparison of pre-intervention 1 vs post-intervention 1 and with post-intervention 1 vs post-intervention 2 ($Q = 9.74$, $p<0.001$ and $Q = 12.72$, $p<0.001$, respectively). On run chart analysis, centerline downward shifts occurred in February 2021, June 2021, and October 2022.

Conclusion: Appropriate blood product administration is essential to support PHO patients. The EMR system can be harnessed as a tool and by enhancing and standardizing order sets, we demonstrated a subsequent decrease in prescribing errors, reducing risk, enhancing patient safety, and consistency in care.

Poster # 003

ANALYSIS OF ALLERGIC TRANSFUSION REACTIONS AT A CHILDREN'S TERTIARY CARE CENTER

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Background: Transfusion reaction adverse events are a relatively rare occurrence in the United States. This is due to specific blood safety measures such as appropriate collection, preparation, testing, storage, and distribution of blood components as well as appropriate monitoring of patients receiving

these transfusions. Here we describe the rate of transfusion-associated adverse events in pediatric patients at Children's Hospital of Michigan from 2018-2022.

Objectives: The aim of this retrospective chart review was to assess the rate of allergic blood transfusion complications and reactions among pediatric patients at Children's Hospital of Michigan in Detroit, Michigan.

Design/Method: An institution-based retrospective chart review was conducted for a total of 43,210 transfusions over five years from 2018-2022.

Results: There were a total of 43,210 transfusions. A total of 26,669 of these products were red blood cell (RBC) transfusions, 10,447 were apheresis platelets, 4,392 were plasma, and 1,702 were cryoprecipitate A reaction was reported in 176 of the 43,210 transfusions but only 116 were true transfusion reactions (0.268%), 66 of these (56.9% of all reactions or 0.153% of all transfusions) were classified as allergic reactions. (61% only skin manifestations such as urticarial or itching, 39% respiratory or airway symptoms, with or without skin manifestations).

Allergic reaction rate was 35 (0.131%) for RBCs, 19 (0.182%) for platelets and 11 (0.250%) for plasma and 1 (0.059%) for cryoprecipitate.

Conclusion: ATRs were observed in 0.268% of total transfusions (allergic reactions (0.153%) and other reactions (0.115%)) that occurred over the course of five years at our institution. This is about 1 in 655 blood components transfused that was associated with an allergic reaction (more commonly with plasma > platelets > packed RBCs). The rate of allergic reactions is less than what was reported by National Blood Collection and Utilization Survey 2017 (0.282%). It is also less than rates reported for children (0.53%) and adults (0.26%) in reviewing meta-analyses. These lower rates could be secondary to changes in blood processing and under-reporting.

Poster # 004

HYPERTENSION AND ENCEPHALOPATHY IN A PEDIATRIC PATIENT FOLLOWING RED BLOOD CELL TRANSFUSION

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Background: Reversible cerebral vasoconstriction syndrome (RCVS) and posterior reversible encephalopathy syndrome (PRES) are rare complications of packed red blood cell (pRBC) transfusions, primarily reported in adults with severe chronic anemia. This literature of encephalopathy after pRBCs lacks sufficient details to clearly distinguish between RCVS and PRES, and there is likely some diagnostic overlap between these entities. The postulated mechanisms include altered cerebral autoregulation and endothelium damage. Clinically, both are characterized by severe headaches as well as other neurological symptoms including aphasia.

There are few reports in pediatric patients with pRBC transfusion-associated encephalopathy, usually in children with underlying vasculopathy. Here we present a case of a previously healthy 4-year-old male child that developed encephalopathy after pRBC transfusion for severe iron deficiency anemia (sIDA).

The potential severity of these syndromes warrants better awareness by pediatric hematology providers.

Objectives: To describe potential post-pRBC transfusion neurologic sequelae.

Design/Method: Case report

Results: Our patient presented with sIDA after not having any routine pediatric care for several years. Echocardiogram demonstrated cardiomegaly, pericardial effusion, moderate left ventricular dilation, and moderate coronary artery dilatation. His history was notable for an extremely selective diet and consumption of >50 ounces/day of cow's milk. He received 43 mL/kg of pRBCs (602 mL total) in 8 aliquots over 3 days; his hemoglobin increased from 1.4 g/dL to 11.4 g/dL. His family declined intravenous iron treatment.

He then re-presented 5 days after discharge with altered mental status and hypertension. Brain MRI/MRA showed luminal irregularities in multiple anterior and posterior circulation intracranial arteries creating a beaded appearance, concerning for RCVS/PRES. He was treated supportively with aggressive blood pressure control and made a complete neurologic recovery 8 days after presentation. At hematology clinic follow-up 2 months post-discharge, he remained at his typical neurologic baseline.

Conclusion: Several features of this case are similar to the reported adult cases of transfusion-related encephalopathy: 1) severe chronic anemia with cardiac dysfunction and 2) the large volume of transfused pRBCs over a short period. Adult case series have suggested that $\geq$5 g/dL hemoglobin increase is associated with RCVS.

RCVS/PRES should be considered in patients recently transfused for chronic severe anemia presenting with headaches or other neurological symptoms. Prompt recognition may prevent unnecessary treatment and potentially limit risk of neurologic compromise. The role of volume and rapidity of the pRBC transfusions in the development of encephalopathy warrants further study.

Poster # 005

REFRACTORY ITP RESPONSIVE TO JAK INHIBITION WITH BARICITINIB IN AN INFANT WITH A NEW TLR-7 MUTATION

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Background: Immune thrombocytopenia (ITP) is a heterogeneous autoimmune disorder characterized by a decreased platelet count and variable bleeding symptoms. Response to treatment is often unpredictable and while many children will respond to standard ITP therapy, there is a subset of patients that will be refractory to first-line treatments. Immune dysregulation in ITP is difficult to measure and refractory patients often need trials of multiple agents. Additionally, some children may have an underlying inborn error of immunity that warrants evaluation and may help in guiding therapy.

Objectives: We describe here an infant with challenging to treat ITP. Her treatment was ultimately

guided by the results of her primary immune deficiency testing as well as correlative functional lab testing that helped in identifying a novel treatment approach.

Design/Method: A 10-month-old infant with severe symptomatic ITP and mild nonhemolytic anemia failed treatment with corticosteroids, IVIG, thrombopoietin agonists (eltrombopag, romiplostim), sirolimus and rituximab. An extensive work up including bone marrow evaluation was unrevealing. Her genetic testing showed a novel heterozygous TLR-7 mutation (Exon 3, c.2453G>T pGly818Val) reported as a VUS (Variant of Unclear Significance) on a primary immune deficiency panel (Invitae). This was not found in population databases and was predicted to disrupt function. Trio testing (Gene Dx) was sent on both parents and neither were carriers of the mutation. An expanded platelet antibody panel revealed very high platelet antibody titers (Versiti). An elevated Type 1 Interferon score of 373 was reported on a research basis (Cincinnati). Her lack of response to multiple therapies and elevated interferon score in the context of a novel TLR-7 VUS, led us to begin a trial of a Jak inhibitor, baricitinib. Functional testing of her TLR-7 mutation is ongoing on a research basis.

Results: TLR-7 mediated upregulation of interferon has been documented in autoimmune diseases. Baricitinib, a selective JAK1 and JAK2 inhibitor, has been shown to reduce IFN signaling. A trial of baricitinib in our patient showed a positive response with normalization of platelet counts and resolution of bleeding symptoms. She currently remains in remission on baricitinib and eltrombopag with no adverse side effects. Repeat anti-platelet antibody titers and an interferon score are underway.

Conclusion: Identification of mutations in immune regulatory genes in children with difficult to treat ITP might be helpful in choosing novel therapies. Our patient's discovery of a novel possibly pathogenic TLR-7 mutation, a high type 1 interferon activity, and ultimately response to Jak inhibition with baricitinib illustrates this approach.

Poster # 006

NEONATAL ALLOIMMUNE THROMBOCYTOPENIA: CONSIDERATIONS REGARDING SURROGACY AND USE OF ORAL STEROIDS

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Background: Neonatal alloimmune thrombocytopenia (NAIT) occurs when alloantigens on fetal platelets induce antibodies produced by the individual carrying the fetus. NAIT is a major cause of thrombocytopenia in the neonate, and can cause significant bleeding issues including intracranial hemorrhage. Standard treatment includes random-donor platelet transfusion (ideally HPA-compatible) or maternal platelet transfusion, and/or IVIG. IV corticosteroid use can be considered, though data is limited. Use of outpatient oral steroids (in situations where suitable platelets are not readily available) has not been reported in the literature. Adjustments to NAIT approach may be needed in situations of surrogacy.

Objectives: To present our experience with diagnosis and management of NAIT in the setting of surrogacy.

Design/Method: Case Report

Results: A female born at 39 weeks, carried by Surrogate Mother (wife of Biological Mother), had significant bruising and petechiae on initial exam. Biological Mother and Sperm Donor are both Caucasian (no additional information available for Sperm Donor), and the Surrogate Mother is Hispanic. CBC showed platelets of 3000. The neonate had coffee-ground emesis on day of life 1, no other bleeding issues. She received IVIG 1g/kg/dose (3 doses total) but platelet count did not improve. She had very short-lived response to random-donor platelets. Due to delays in ability to test Surrogate Mother (and inability to test Sperm Donor), platelet antibody testing done on neonate. While awaiting results, IV methylprednisolone 1mg every 8 hours for 3 days was given with good response. Testing on neonate (and ultimately on Surrogate Mother) showed anti-HPA1a antibodies (and Surrogate Mother's platelets were HPA1a-negative). Neonate had good response to HPA1a-negative platelets.
As an outpatient, she received 3 transfusions of HPA1a-negative platelets. It appeared that she would require a 4th transfusion but there was difficulty obtaining HPA1a-negative platelets in time, and so she was given oral prednisolone (1.3 mg/kg/dose every 8 hours) for a three-day course after which platelet count stabilized. Platelet count then improved and ultimately normalized (no relapse of thrombocytopenia).

Conclusion: Corticosteroids (including oral course) induced good platelet response after IVIG failure. In absence of timely, appropriate platelets in the outpatient setting, oral steroids may allow for at least temporary stabilization of platelet count. In cases of surrogacy, race/ethnicity of Biological Parents and potential Surrogate should be evaluated (and consider pre-pregnancy platelet antigen typing). While false negatives can occur with platelet antibody testing of neonate, it should be done to potentially expedite diagnosis/optimal care when testing of the Surrogate cannot be done promptly.

Poster # 007

LINKING EOSINOPHILIA TO BLEEDING: A PEDIATRIC CASE OF TOXOCARA INFECTION AND PLATELET DYSFUNCTION

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Background: Acquired platelet dysfunction with eosinophilia has been described in a few observational studies and case reports, predominantly from Asia. This clinical syndrome is characterized by a transient tendency to mucocutaneous bleeding in the setting of a high eosinophil count. It is typically caused by parasitic infection and resolves upon treatment of the primary cause. Proposed mechanisms include the formation of immune complexes that bind to platelets, resulting in abnormal secondary aggregation. Additionally, eosinophil cationic protein, a basic protein in the eosinophil primary matrix, can act as an inhibitor of platelet aggregation.

Objectives: To recognize a rare, acquired bleeding diathesis associated with eosinophilia.

Design/Method: Case report

Results: A seven-year-old male from Tonga in Oceania presented to Rady Children's Hospital in San Diego with a year of weekly self-limited nosebleeds and mild gum bleeding with brushing teeth,

associated with intermittent gastrointestinal symptoms and malaise. Three weeks prior to presentation, he was hospitalized in Tonga for diffuse ecchymoses. His complete blood count (CBC) from that time showed mild leukocytosis; additional testing results were unavailable. On physical examination, patient had multiple bruises at different stages of healing, with the largest, located on the lower back, measuring 15 centimeters. The initial CBC at our institution showed a white blood cell count of 18.3 K/uL, an absolute eosinophil count of 6.5 K/uL, and a platelet count of 264 K/uL. Prothrombin time, activated partial thromboplastin time and fibrinogen were within normal limits. Testing for von Willebrand disease was negative. Platelet aggregation tests showed a decreased response to ADP and epinephrine, borderline normal response to collagen and a normal response to ristocetin. An extensive infectious, hematologic and immunologic work-up for eosinophilia was performed. Positive serologic testing confirmed the diagnosis of Toxocara infection. Eosinophil count normalized upon therapy with albendazole. Platelet aggregation study repeated one month after initial presentation showed normal values. Bleeding and bruising symptoms have resolved.

Conclusion: We present a case of a patient from Oceania with ecchymoses and epistaxis in the setting of Toxocara infection. Acquired platelet dysfunction with eosinophilia is a condition described mostly in the context of parasitic infections. Knowledge of this clinical entity can help avoid unnecessary testing in patients with a high eosinophil count and new-onset symptoms of mucocutaneous bleeding. Although this condition is uncommon and has been reported predominantly in Asia, it can be encountered worldwide.

References:
1. Chotsampancharoen T et al, Acta Haematol. 2018.
2. Maziero AM et al, Life Sci. 2013.

Poster # 008

SUCCESSFUL USE OF CAPLACIZUMAB IN A 13-MONTH-OLD WITH iTTP REFRACTORY TO STANDARD TREATMENT.

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Background: Thrombotic thrombocytopenic purpura (TTP) is exceedingly rare in pediatrics with an annual incidence of <1 case per million children. Immune TTP (iTTP), comprising of 90% of all TTP cases, is a life-threatening emergency with a 9% mortality rate in children, neccesitating early recognition and prompt management. First line treatment requires daily plasma exchange, along with steroids as an adjunctive therapy. Immunomodulation with Rituximab and other agents like mycophenolate mofetil is generally reserved for patients with refractory iTTP. Caplacizumab is a novel therapy, approved by the FDA in 2019 for adults with iTTP in combination with plasma exchange and immunosupression, however, there is limited data on its use in pediatric patients.

Objectives: To report the successful use of Caplacizumab in a pediatric patient with iTTP refractory to standard interventions.

Design/Method: Case report with literature review.

Results: A 13-month-old female presented with febrile seizures and easy bruising. Laboratory evaluation demonstrated severe thrombocytopenia 5 x 10^3/uL, anemia (Hgb 9.4 g/dL), reticulocytosis, unconjugated hyperbilirubinemia, elevated LDH, undetectable haptoglobin, normal renal function, and schistocytes on peripheral blood smear. She initially received multiple FFP infusions due to familial situation, and methylprednisone as adjunctive therapy without improvement. iTTP was confirmed with ADAMTS13 activity <5% and ADAMTS13 inhibitor level >8 units/mL. Daily total plasma exchange (TPE) was initiated on day 5, with a suboptimal response, and weekly Rituximab 375mg/m2/dose was added to daily TPE from day 14, with normalization of platelet count after its second dose. Multiple attempts at spacing TPE resulted in thrombocytopenia. Caplacizumab 5mg was intiated on day 58 and continued for 30 days, in which TPE was sucessfully discontinued, steroids and mycophenolate were slowly weaned and patient has since been in complete remission for more than one year.

Conclusion: Caplacizumab, although initially approved for adults with iTTP, has now been extended to patients from 12 years of age weighing at least 40kg. To date, there are a few cases demonstrating a favorable response to caplacizumab in children and our patient is the youngest reported case in the literature. Caplacizumab was proven safe and effective in our patient based on dosing derived from model-based simulations in the literature. Caplacizumab, in combination with daily TPE and immunosupression, induced remission in our patient, and should be considered for future pediatric patients with refractory TTP.

Poster # 009

PLATELET INVESTIGATIONS IN A CHILD WITH FLNA GENE VARIANT

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Background: Filamin A (FLNA) gene mutations have been associated with GPIIb/IIIa activation. However, the clinical implications and risk of thrombosis due to FLNA variants are not well characterized. We describe a 7-year-old female with a novel heterozygous FLNA variant of uncertain significance and recurrent thrombosis of her mechanical mitral valve.

Objectives: We aimed to investigate the effect of the novel FLNA variant on platelet function and thrombotic risk and evaluate a potential therapy in preventing thrombosis in this child.

Design/Method: Citrated whole blood was obtained and analyzed by mass cytometry (CyTOF) for platelet activation markers PAC-1 (i.e., GPIIb/IIIa activation) and P-selectin (i.e., granule release) both at baseline and with agonist stimulation. Whole blood impedance aggregometry was performed to assess platelet physiologic function *ex vivo*. Peripheral blood samples were treated with platelet agonists (i.e., ADP, thrombin, and collagen analogs) and/or inhibitors (i.e., Dasatinib) as indicated. All samples were obtained while the child was on aspirin and clopidogrel.

Results: Several peripheral blood samples were analyzed from the child during inpatient hospitalization for management of mitral valve thrombosis and subsequently repeated as an outpatient. Initial CyTOF analysis of blood samples collected as an inpatient showed increased platelet GPIIb/IIIa activation measured by PAC-1 at baseline and with ADP stimulation, whereas granule release measured by P-selectin was similar to controls, including the child's mother who does not have the FLNA variant.

Following discharge, additional CyTOF analysis of peripheral blood collected as an outpatient did not show increased platelet activation in this child. Finally, treatment of whole blood *ex vivo* with increasing doses of Dasatinib, a tyrosine kinase inhibitor that has previously been shown to inhibit downstream signaling of platelet GPIIb/IIIa, significantly decreased platelet activation and aggregation in the child's blood sample especially at higher drug doses. No significant effects of Dasatinib on platelet activation was observed on a control sample at the indicated doses.

Conclusion: Functional testing of the child's platelets is not consistent with persistent GPIIb/IIIa activation due to the heterozygous FLNA variant. However, findings are confounded by ongoing dual antiplatelet therapy. Dasatinib offers a potential targeted intervention for platelet inhibition in cases where conventional antiplatelet therapy may be insufficient.

Poster # 010

A UNIQUE CASE OF AN ADOLESCENT WITH GLANZMANN THROMBASTHENIA AND SPONTANEOUS GASTROINTESTINAL BLEED

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Background: Glanzmann Thrombasthenia (GT) is a rare bleeding disorder caused by defects of alpha IIb beta3 in platelets. Patients with GT can have lifelong bleeding episodes. Patients with GT rarely have spontaneous gastrointestinal (GI) bleeding, which occurs even less likely in young patients and rarely without an inciting cause such as H. pylori or polyps.

Objectives: We present a unique case of a 16 year old male with a known diagnosis of GT presenting with spontaneous hemoptysis and upper GI bleed causing hemorrhagic shock.

Design/Method: Single subject case report

Results: A five year old male was followed by hematology after experiencing severe bleeding following a lip laceration with noted anemia. Flow cytometry revealed platelets deficient in CD61 and positive for CD42B, confirming the diagnosis of GT. He was followed annually and complained of intermittent epistaxis and minor bleeding following dental procedures that resolved with oral aminocaproic acid. However, at 16 years of age, he presented with spontaneous and sudden onset of hemoptysis and melena. Labs were notable for hemoglobin of 8g/dL and he received fluids and aminocaproic acid in the ER. His hemoglobin further decreased to 5.8g/dL and platelets were $143x10^3/\mu L$. Endoscopic evaluation revealed friable, oozing mucosa in addition to hematin and a large clot. There were no ulcers, polyps, or malformations and biopsies were negative for H. Pylori.
He ultimately required intensive care unit admission for hemorrhagic shock with drop in hemoglobin to 4.8g/dL. Though platelet transfusions are typically avoided in GT, he required platelet transfusions for stabilization and multiple transfusions of packed red blood cells, fresh frozen plasma, intravenous aminocaproic acid and recombinant factor VIIa. Ultimately his bleeding subsided and cytopenias stabilized. He was discharged on hospital day 10 and continued on aminocaproic acid for one additional week.

Conclusion: Although GI bleeding occurs in adult patients with GT, occurring in 12% of cases, there are

fewer cases describing this complication in pediatric patients. Additionally, many cases of GI bleeding are linked to an underlying etiology, unlike in our patient. The cause of this patient's thrombocytopenia was possibly related to consumption in the setting of significant hemorrhage. Despite requiring multiple platelet transfusions, there was no evidence of isoantibodies against platelets. He is now 3 months from the event with no further episodes of spontaneous hemorrhage. This is a rare and unique case of a significant GI bleed in GT given his young age and unclear etiology for the spontaneous hemorrhage.

Poster # 011

TWO HIT THEORY FOR THE PATHOGENESIS OF TYPE 3 CONGENITAL AMEGAKARYOCYTIC THROMBOCYTOPENIA

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Background: Congenital amegakaryocytic thrombocytopenia (CAMT) is an autosomal recessive disorder characterized by thrombocytopenia with absence of megakaryocytes. It can lead to aplastic anemia or myelodysplastic syndrome (MDS). CAMT is linked to a mutation in the c-MPL gene on chromosome 1, which encodes the thrombopoietin receptor.

Objectives: We report a case of a patient with CAMT-like symptoms, without a c-MPL gene mutation, suggesting the presence of an alternative genetic defect.

Design/Method: Multi-institutional collaboration and review of medical records

Results: Twelve-year-old male with severe thrombocytopenia initially observed at age 2 years. Bleeding complications included scalp hematoma, excessive bleeding during adenoidectomy, petechiae, epistaxis, and gum bleeding. Platelet count ranged between 30-80,000 $x10^3$/uL. At age 10, bleeding worsened with platelet counts of 6-20,000 $x10^3$/uL. Simultaneously there was a decline in hemoglobin and the emergence of macrocytosis. Clinical presentation made immune thrombocytopenia, autoimmune disorders, and immune dysregulation-induced platelet destruction unlikely. Inherited thrombocytopenia panel testing for 42 germline variants was negative. Bone marrow biopsy showed 60% cellularity and a decrease in megakaryocytes. Cytogenetic analysis revealed trisomy 6 in 7/20 metaphases. Molecular hematopathology identified a GATA2 variant in 50% of the alleles. Inherited BMF panel revealed heterozygosity for multiple variants of unknown significance (VUS), including c.5096A>G (p.Asp1699Gly) in BRCA2 gene, c.3898A>G (p.Ile300Val) in LYST gene, 1408A>G (p.Thr470Ala) in PALB2 gene, and c.7240G>A (p.Val2414Met) in tVPS13B gene. Testing for Fanconi anemia and dyskeratosis congenita were negative. Whole exome sequencing revealed heterozygosity for a 1.57 Mb duplication on chromosome 3q29.Repeat bone marrow testing demonstrated a progressive decrease in cellularity to 5-30% with trilineage hypoplasia. With extensive yet inconclusive diagnostic workup, worsening clinical presentation, and progressive hypocellularity of the bone marrow, he underwent an ABO incompatible stem cell transplantation (9:10, A HR) from a mismatched unrelated donor. The conditioning regimen was myeloablative with busulfan, cyclophosphamide, anti-thymocyte globulin, and post-transplant cyclophosphamide. Currently, he is 270 days post-transplant with peripheral blood chimerism demonstrating 97% donor engraftment. Platelet counts have normalized, and he has not required a transfusion for nearly 220 days.

Conclusion: This case highlights the concept of a "double hit" hypothesis. While homozygous mutations of PALB2 and BRCA2 are individually associated with Fanconi anemia and BMF syndromes, no pathology has been reported in their heterozygous forms, raising the question of whether the co-expression of these variants in a heterozygous state could result in a similar disease phenotype as their homozygous counterparts. This finding prompts exploration into the potential impact of combined variants on disease manifestation.

Poster # 012

NOT ALL MICROCYTIC ANEMIAS ARE IRON DEFICIENCY ANEMIAS

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Background: Hypochromic, microcytic anemias are commonly attributed to iron deficiency. Here we present a rare autosomal dominant familial case of chronic microcytic anemia with normal iron stores, hemoglobin A2, and absence of Barts on newborn screen.

Objectives: To describe the clinical presentation and work-up leading to the diagnosis of Gamma-Delta-Beta thalassemia minor.

Design/Method: Case Report

Results: We present a case of a 7-year-old girl with chronic hypochromic, microcytic anemia. At birth, the patient experienced severe microcytic anemia requiring a red cell transfusion on day 1 and day 40 of life for a hemoglobin of 6.5 g/dL. The father and paternal grandfather were also affected with chronic microcytic anemia although neither had required transfusions. The patient was growing appropriately at the 5th percentile. Upon examination, there was mild pallor noted, but no hepatosplenomegaly or jaundice. Laboratory findings revealed a hemoglobin of 9.9 g/dL, iron saturation of 24%, ferritin of 57 ng/mL, reticulocyte count of 1.8%, haptoglobin of 46 mg/dL, and hemoglobin A2 of 2.7%. The remarkably low mean corpuscular volume (MCV) of 59.2 fl and red blood cell (RBC) count of $5.27x10^6$ uL yielded a Mentzer index of 11.2, strongly suggesting thalassemia over iron deficiency. A peripheral blood smear showed relatively uniform microcytosis. Based on the need for transfusion at birth, persistent anemia resistant to iron supplementation, microcytosis, normal ferritin levels, and Mentzer index < 13, iron deficiency anemia was ruled out as a differential diagnosis. No hemoglobin Barts was detected on the newborn gel electrophoresis and her hemoglobin A2 levels remained normal, proving that alpha and beta thalassemia trait were unlikely. Given findings consistent with a thalassemia trait associated with severe microcytic anemia at birth, we explored the possibility of a multi-gene B cluster deletion. A multiplex ligation-dependent probe amplification (MLPA) assay was performed yielding one copy of a pathogenic deletion in the beta globin cluster. This multi-gene deletion was diagnostic of Gamma-Delta-Beta thalassemia trait.

Conclusion: Multiple gene deletion thalassemia minor should be considered in the differential diagnosis for persistent microcytic anemia in children with a history of severe microcytic anemia at birth in the absence of hemoglobin Barts on newborn screen, normal A2, and normal iron stores. As the deletion also involved the gamma chain, the patient had severe microcytic anemia at birth requiring neonatal

transfusions. Identifying cluster gene deletions are critical for genetic counseling as the trait would be predicted to cause severe blood disorder if co-inherited with other mutations.

Poster # 013

TRANSFUSION-DEPENDENT ANEMIA DUE TO LEVETIRACETAM: A NOVEL HEMATOLOGIC COMPLICATION OF A COMMON DRUG

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Background: Levetiracetam (LEV) is a commonly prescribed anti-seizure medication (ASM) generally considered to have low risk of hematologic adverse effects. There are case reports of LEV-induced pancytopenia, but no prior description of severe isolated anemia due to this medication.

Objectives: We present a case of medication-induced, transfusion dependent hypo-proliferative anemia attributed to LEV.

Design/Method: Single case report with relevant history, laboratory and pathology results obtained from the patient's medical record.

Results: A 7- year-old boy with history of cardiofaciocutaneous syndrome and epilepsy presented to the emergency department for fatigue and pallor and was found to have severe normocytic anemia with hemoglobin (Hb) 5.7g/dL requiring blood transfusion. He had a history of one prior transfusion due to severe anemia three months earlier which was attributed to oxcarbazepine with return to normal counts after discontinuation of that medication. Hematology was consulted for further investigation of recurrent anemia. Home medications at admission included LEV, perampanel, clobazam, cetirizine, polyethylene glycol, and topical triamcinolone. Further laboratory testing revealed severely depressed reticulocyte count of 0.7%. No leukopenia, neutropenia, lymphopenia or thrombocytopenia was noted on multiple CBC evaluations. Peripheral smear demonstrated normocytic, normochromic anemia with moderated anisocytosis and rare ovalocytes with no evidence of hemolysis. Erythropoietin level was appropriately elevated, with iron, B12, folate, thyroid, and renal function testing all within normal limits. Marrow evaluation revealed normocellular marrow (90-95%) with trilineage hematopoiesis and negative flow cytometry and cytogenetics with no concern for leukemia or myelodysplasia. M:E ratio of 8.1:1 indicated erythroid hypoplasia. Whole genome sequencing revealed no additional mutations related to hypo-proliferative anemia.
After extensive hematologic evaluation, concern was raised for possible medication suppression. Due to the patient's history of difficult to control seizures, ASM wean was initiated after collaboration with pediatric neurology. The patient received eight transfusions in total prior to the LEV wean. Within four weeks of LEV discontinuation, Hb increased from 7.8 g/dL to 10.5 g/dL and reticulocyte count increased from 0.2% to 7.9%. Complete resolution of anemia and related symptoms has persisted for greater than six months off LEV therapy with seizures controlled on increased doses of other ASMs.

Conclusion: Severe normocytic anemia is a rare and not-previously reported adverse effect of the ASM LEV. Clinicians should consider medication-induced suppression in the evaluation of hypo-proliferative anemia especially in the setting of polypharmacy. Further study may reveal the mechanism by which LEV induces erythroid suppression.

Poster # 014

SEVERE MIXED WARM AND COLD AUTOIMMUNE HEMOLYTIC ANEMIA TREATED WITH SUTIMLIMAB AND SIROLIMUS

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Background: Autoimmune hemolytic anemia (AIHA) is a rare disease process found in pediatrics with an estimated incidence of 0.8-1.25 cases per 100,000 children per year. Only 6-8% of cases present as a mixed warm and cold agglutinin autoimmune hemolytic anemia (mAIHA). While warm AIHA is typically treated with steroids, severe anemia (Hgb <6gm/dl) and mAIHA, are risk factors for relapse and increase the risk of mortality. mAIHA may require more aggressive therapies both to initially induce remission, but also to recapture after relapse.

Objectives: A 14-year-old girl presented with pallor, fatigue, dizziness, and constipation. Her hemoglobin was 4.5gm/dl, MCV 126fl, RDW 24%, and reticulocytes 20%. Direct antiglobulin testing of red blood cells was positive for IgG, IgM and complement. In addition, she had evidence of autoimmune thyroiditis with TSH of 176mcIU/ml and thyroxine 0.28ng/dl. Thyroglobulin antibodies were positive at 171 IU/ml. Other autoantibodies associated with rheumatologic disorders were negative. Furthermore, she also had severe deficiency of vitamin D. Lymphocytes demonstrated normal FAS mediated apoptosis, and a flow cytometry panel did not support the diagnosis of autoimmune lymphoproliferative syndrome. There was a strong family history of autoimmune disease, including Sjogren's syndrome in the father.

Design/Method: Case Report

Results: The patient was initially treated with high dose intravenous steroids with minimal effect. Subsequent therapies included intravenous immune globulin, rituximab, and cyclophosphamide. In addition, patient was placed on synthyroid and high dose vitamin D. Due to partial response, the patient was treated with sutimlimab with resolution of her anemia. Transition to maintenance therapy was achieved with sirolimus. Next-generation sequencing of a panel of 345 genes associated with primary immune deficiencies, and inflammatory and immune dysregulatory pathways was non-contributory.

Conclusion: This patient had severe mixed-type warm and cold agglutinin AHIA, as well as autoimmune thyroiditis, a family history of autoimmune disease and severe vitamin D deficiency. The anemia was initially refractory to steroid therapy, requiring aggressive immune modulation including the humanized monoclonal antibody sutimlimab which targets and inhibits the complement cascade. Furthermore, maintenance therapy has been successful using the mTOR inhibitor sirolimus, allowing for reduced exposure to chronic steroids. The use of sutimlimab has not been reported in children, but complement inhibition may warrant an expanded role in immune cytopenias such as immune thromobocytopenia and AIHA, particularly cold agglutinin disease.

Poster # 015

VARIABLE CLINICAL OUTCOMES IN CONGENITAL ANEMIA DUE TO MUTATIONS IN ERYTHROID TRANSCRIPTION FACTORS

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Background: Fetal anemia is a potentially life-threatening condition, although the most common cause is maternal alloimmunization; numerous genetic conditions are also implicated.

Objectives: The aim of this case series is to highlight the importance of upfront genetic testing and molecular characterization in patients with fetal anemia.

Design/Method: Retrospective chart review.

Results: The first case is a female infant diagnosed with fetal hydrops at 20 weeks of gestational age. Prenatal exome sequencing identified compound heterozygous mutations in *KLF1* (P171Rfs*66 and H361Y) inherited from each parent. She required one fetal transfusion at 23 weeks gestation for a hemoglobin of 5 g/dl and eventually born at 34 weeks due to worsening fetal anemia. Postnatally, her hemoglobin was 7.9 g/dl necessitating blood transfusion. Hemoglobin electrophoresis revealed 1.9% Hb Bart along with 3.2% of embryonic hemoglobins. Her pyruvate kinase level was low at 2.5 U/g Hb. Due to ongoing hemolysis, she developed jaundice requiring phototherapy. She currently remains transfusion dependent every 3-4 weeks. *KLF1* encodes for master transcription factor that plays a pivotal role in erythropoiesis. It regulates erythroid lineage commitment, γ to β globin gene switch and transcription activation or suppression of certain erythroid specific genes. Over 60 genomic variations in *KLF1* exist with distinct phenotypes including congenital dyserythropoeitic anemia and congenital non-spherocytic hemolytic anemia. Based on her genotype, it was expected that she would be transfusion dependent.
The second case is a male infant with fetal hydrops whose prenatal exome sequencing identified a novel heterozygous variant in *GATA1* (E200K)**.** Additional investigation using RNA sequencing showed aberrant *GATA1* transcript formation. Post-natal evaluation revealed dysmorphic features including low set ears, webbed neck and hypospadias. CBC performed after birth showed normal Hb but thrombocytopenia (50,000 k/ul). Platelet electron microscopy study showed decreased platelet dense granules. Repeat CBC throughout admission showed improvement in his platelet counts. At 1 month of age, he was found to have anemia of 9.5 g/dl and neutropenia of 0.87 k/ul, despite of which he remains well without bleeding or need for transfusion. *GATA1* is another master regulator of erythropoiesis, in its absence, erythroid progenitors undergo apoptosis. These mutations give rise to a spectrum of disorders, including congenital dyserythropoetic anemia, congenital erythropoietic porphyria and rarely Diamond-Blackfan anemia.

Conclusion: These cases highlight the genetic heterogeneity of non-immune causes of fetal anemia, and the importance of genetic testing to evaluate for specific genotypes that may result in a variety of clinical presentations and outcomes.

Poster # 016

NEXT-GENERATION SEQUENCING (NGS) IN HEREDITARY SPHEROCYTOSIS (HS)- IDENTIFICATION OF NOVEL MUTATIONS

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Background: HS is the most commonly inherited red blood cell (RBC) membrane disorder with broad genetic and phenotypic heterogeneity. HS has historically been diagnosed using clinical and family history (FH) along with osmotic fragility and eosin-5'-maleimide dye binding. The advent of NGS has made accurate genetic diagnoses attainable, with an increasing number of studies reporting its clinical utility in HS. However, there is limited data on the use of NGS to characterize HS in the Hispanic population.

Objectives: To report a series of four Hispanic children with novel HS mutations along the US/Mexico border and characterize their clinical phenotype.

Design/Method: Four pediatric patients with HS who had NGS performed were selected to comprise a descriptive case series.

Results: Case 1:14-month-old male with FH of HS received an RBC transfusion during his first week of life with multiple transfusions until the age of 6 months. Baseline hemoglobin after this was 9-10g/dL. NGS showed ANK1(c.3563_3564del). His mother reported having only an early cholecystectomy but no transfusions.
Case 2:8-year-old male with FH of HS. His baseline hemoglobin has remained 9-10g/dL with no history of neonatal jaundice, transfusions or splenectomy. NGS showed ANK1(c.3629+1G>C). Both mom and his older brother had splenectomies but no history of transfusions.
Case 3:10-year-old male with no FH of HS. Baseline hemoglobin between 6-7g/dL and he is requiring 2-3 transfusions/year. Due for splenectomy with increasing transfusion requirements and problems with growth. NGS showed compound heterozygous inheritance of both SPTA1(c.4339-99C>T) and SPTA1(c.4632dup).
Case 4: 14-year-old male with no FH of HS with baseline hemoglobin of 6-7g/dL. Maternal FH of early cholecystectomies but no transfusions/splenectomies. He had an emergent splenectomy for sequestration with subsequent hemoglobin of 14-15g/dL. Compound heterozygous inheritance of ANK1(c.3808del) and PKLR c.1456C>T.

Conclusion: These results show that HS in the Hispanic population is characterized by complex molecular interactions and a high prevalence of novel mutations in RBC cytoskeleton/enzyme genes. Due to its heterogeneity, understanding the association between gene variants and modifiers with corresponding disease phenotype is valuable for a better understanding of the disease. NGS has clinical utility and should be considered for accurate diagnosis.

Poster # 017

SEVERE HEMOLYTIC DISEASE OF THE FETUS AND NEWBORN DUE TO ANTI-U ANTIBODIES.

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Background: Hemolytic disease of the fetus and Newborn (HDFN) predominantly occurs with rhesus incompatibility from anti-D antibodies but can also occur from antibodies against rare/minor variants such as the "U". The U-negative phenotype is seen in ~1% individuals of African descent. Anti-U HDFN is a potentially fatal condition. Neonatal clinical presentation ranges from mild anemia to erythroblastosis fetalis. Preemptive antenatal management with intrauterine transfusion support to prevent fetal mortality has become standard practice worldwide for HDFN, however, rarity of anti-U HDFN increases fetal and maternal risk for detection failure and undertreatment.

Objectives: To describe a case of severe Hemolytic Disease of the Fetus/Newborn due to minor U antigen.

Design/Method: Case report

Results: A male neonate born at 36weeks due to reduced fetal movement developed moderate hypoxic ischemic injury requiring body cooling and invasive respiratory support in the initial newborn period. He developed disseminated intravascular coagulation and frank bleeding within the first 8 hours of life (HOL) with prolonged coagulation profile (PTT 45.9, PT 60, INR 6.8, Fibrinogen 183, D-dimer 10.95) and thrombocytopenia (Platelets 75,000cells/microliter), likely from anoxic insult. He received multiple units of fresh frozen plasma, cryoprecipitate, and platelets. Serum bilirubin peaked at 13mg/dl within 24 HOL requiring intensive phototherapy. Labs showed HB 8.6g/dL, Retic count 17%, and maternal and newborn blood-group was O-positive. Baby had a positive DAT with IgG anti-U antibody. Of note, mother was also positive for anti-E and anti-C in pregnancy with a titer <1:1. Baby did not have anti- C or E antibody. The eluate prepared from the newborn's RBCs reacted with the reagent RBCs positive for the U antigen in a pattern similar to that present in his mother's plasma indicating that his positive DAT is due to his mother's anti-U which crossed the placenta and bound to his RBCs, consistent with HDN due to anti-U antibody. He received IVIG 1g/kg every 12 hours for a total of 7 doses before hemolysis stabilized. He received appropriately matched blood products with no worsening hemolysis and was subsequently discharged.

Conclusion: Anti-U HDFN is rare and can be missed, posing a significant risk for fatal outcomes, if left untreated. Management of anti-U HDFN is similar to Rh incompatibility including intra-uterine and post-natal transfusions with careful crossmatching. Anti-U antigen negative blood products is ideal but is not always possible. More research is needed to protect mothers from exposure to minor red blood cell antigens to prevent sensitization and fetal demise in subsequent pregnancies.

Poster # 018

TWO ISN'T ALWAYS BETTER THAN ONE: A RARE CASE OF HDFN DUE TO ANTI-C AND ANTI-LITTLE E

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Background: Hemolytic disease of the fetus and newborn (HDFN) can be caused by incompatibility of the Rh blood group between a mother and infant. The most common Rh antigen known to trigger hemolytic disease is the D antigen; however, other Rh antigens can also precipitate disease.

Objectives: To describe the clinical course of an infant born with congenital anemia due to HDFN secondary to maternal anti-C and anti-e antibodies.

Design/Method: Case Report

Results: A newborn, born at 37 weeks, 3 day gestation, was delivered via repeat C-section with tight nuchal cord and required vacuum for extraction. Apgars 8/8, admitted to newborn nursery; however, noted to be pale at delivery and CBC was performed. Initial hemoglobin (Hgb) and hematocrit (HCT) was 9.9 g/dL, 29% respectively, with reticulocyte count of 5.51% with confirmatory repeat with Hgb 9.4 g/dL, HCT 27.6%. Infant was transferred to the neonatal intensive care unit (NICU) for higher level of care. First-trimester maternal antibody screening negative, however, noted to be positive prior to delivery. Maternal blood type A positive, infant blood type A positive, with positive direct antiglobulin test (DAT) with anti-C and anti-e antibodies identified on eluate. Infant was transfused with 10 mL/kg of packed red blood cells (pRBC) in total. Empiric phototherapy was started due to ongoing hemolysis with bilirubin level maximum of 16.1 mg/dL and 9.6 mg/dL at discharge. Infant remained hemodynamically stable throughout admission with discharge Hgb 11.4 g/dL, HCT 31.9%. Infant had close follow up with persistent jaundice noted at 19 days of life (DOL) with Hgb 9.0 g/dL, HCT 24.7% and reticulocyte count 0.99%. Labs performed at 35 DOL revealed severe anemia though the infant remained asymptomatic with Hgb 5.9 g/dL, HCT 16.3% and reticulocyte count 3.51% requiring admission for transfusion. Infant received a 15 mL/kg pRBC transfusion with improvement of Hgb to 11.1g/dL, HCT 31.1% and reticulocyte count 2.80% prior to discharge.

Conclusion: HDFN is an immune-mediated red blood cell (RBC) disorder which occurs secondary to maternal blood group antibodies attacking fetal or newborn RBCs causing destruction. Administration of RhIg has significantly decreased cases secondary to anti-D antibodies, but does not decrease development of other Rh antibodies. This report represents a case of severe anemia from a rare form of HDFN due to minor blood group maternal antibodies anti-C and anti-e found late in pregnancy.

Poster # 019

HEREDITARY OROTIC ACIDURIA: AN UNCOMMON PRESENTATION IN A PEDIATRIC PATIENT

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Background: Hereditary orotic aciduria (HOA) is an exceedingly rare diagnosis due to an inborn error in metabolism. One modality of this disease is the result of uridine monophosphate synthase (UMPS) enzyme dysfunction, impacting the final two steps of de-novo pyrimidine metabolism. Typically, this disease presents with progressive lethargy and failure to thrive with evidence of megaloblastic anemia. If quickly diagnosed the detrimental effects of persistent orotic acidosis can be mitigated. This disease is not currently tested for on newborn screening and is not commonly screened for during work up for non-nutritional anemia.

Objectives: Describing a case of hereditary orotic aciduria presenting with normocytic anemia and neutropenia.

Design/Method: Case report

Results: A previously healthy 9-month-old female born at term presented with incidental findings of neutropenia and normocytic anemia. The patient did not respond to a two-month trial of oral iron. She was referred to Pediatric Hematology at age 11 months for evaluation The patient was meeting normal developmental and growth milestones. She had no systemic symptoms. A comprehensive hemolysis workup was done and was negative. No evidence of iron deficiency, vitamin B12, or folate deficiency. A bone marrow sample was collected and showed evidence of hypercellularity, marked dyserythropoiesis, mild myeloid dysplasia, and increase in myeloblasts. Overall, concerning for myelodysplastic syndrome (MDS) and congenital dyserythropoietic anemia. Bone marrow chromosome analysis, MDS FISH panel, and Myeloid Malignancy Panel by Next Generation Sequencing (NGS) were normal. Blood Bone Marrow Failure Panel detected a heterozygous mutation of uncertain significance in SAMD9L gene. Whole Exome Sequencing done on patient and parents detected compound heterozygous mutations in the UMPS gene. The patient's orotic acid level was found to be 2,986 mmol (normal: 0.7 to 5.1 mmol) The patient started uridine triacetate. After roughly one month of treatment the patient's level dropped to 1,277 mmol, and 3 months later to 348 mmol. Anemia and neutropenia resolved 3 weeks after starting uridine triacetate.

Conclusion: A thorough work up was completed for this patient with initial symptoms of neutropenia and normocytic anemia. After preliminary testing, a diagnosis of MDS was heavily considered with the potential for a bone marrow transplant. A definitive diagnosis was found after whole exome sequencing. Although an exceedingly rare diagnosis, screening for HOA should be considered during work up for dyserythropoiesis. Especially given the recent introduction of an effective treatment. Notably, this helped the patient's younger sister receive treatment for the same illness starting at birth.

Poster # 020

HEMOGLOBIN PERTH: A RARE CASE OF HEMOLYTIC ANEMIA DUE TO AN UNSTABLE HEMOGLOBIN VARIANT

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Background: An amino acid substitution in the beta globin gene alters the sustainability of the hemoglobin molecule, leading to an unstable hemoglobin that precipitates and hemolyzes. Unstable hemoglobin variants are rare and can be a diagnostic challenge. We present a case of a two-year-old girl of Hispanic ancestry who presented with severe anemia and was diagnosed with a rare unstable hemoglobin, Hemoglobin (Hb) Perth. Hb Perth is defined as the replacement of leucine by proline, displacing the connection between the adjacent leucine and the heme molecule, clinically resulting in severe hemolytic anemia.

Objectives: To highlight the importance of including unstable hemoglobin variants in the differential diagnosis of hemolytic anemia.

Design/Method: Case report.

Results: A two year old girl was referred for a hemoglobin of 6.7g/dL. Her history was significant for neonatal jaundice requiring phototherapy, and normocytic anemia (Hgb 8.7g/dL) at two weeks of age.

She was treated unsuccessfully for presumed iron deficiency. She had no known family history of anemia. Her labwork revealed a MCV of 75fL and her absolute reticulocyte count was elevated at 530k/Ul. Her haptoglobin was <10mg/dL, LDH was 1,187U/L, and total bilirubin elevated at 4.1mg/dL. She had normal iron studies, negatve Coombs and G6PD. Her exam showed scleral icterus, frontal bossing, and massive splenomegaly. A peripheral smear revealed marked basophilic stippling, poikilocytes, spherocytes, and schistocytes. Due to her longstanding hemolysis and anemia, a genetic hereditary hemolytic anemia panel was sent which resulted positive for a heterozygous unstable beta globin variant, HBBc98.98T>C, pLeu33Pro, Hemoglobin Perth.

Conclusion: Unstable hemoglobinopathies are a rare form of hemolytic anemia and distinguishing Hb Perth from other variants requires guided diagnostics including gene sequencing of the β-globin gene. It may occur as a de novo mutation, making clinical presentation important, even in the absence of family history. In neonates, jaundice is common however is not usually associated with anemia, therefore a high index of suspicion for hemolysis should be had in the setting of neonatal jaundice with concomitant anemia. Older children may present with signs and symptoms of severe hemolysis, including splenomegaly, jaundice, and evidence of extramedullary hematopoiesis such as frontal bossing. The presence of an unstable hemoglobinopathy should be considered by a pediatric hematologist when considering hemolytic anemia of unknown etiology and otherwise unrevealing testing. Genetic testing is required to confirm the diagnosis. Once diagnosed, treatment options may vary depending on severity but can include chronic transfusions, splenectomy, or possible use of Hydroxyurea.

Poster # 021

MANAGEMENT OF SEVERE HDFN DUE TO MATERNAL ANTI-RH17: SUPPORTING INFANTS WITH INCOMPATIBLE BLOOD

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Background: The main antigens in the Rh blood group system are D, C, c, E and e[1]. D-- is a rare type that involves the complete absence of the C,c,E,e antigens and the elevated expression of D on RBC surface[2]. Mother's who are D– can be sensitized to RH17, an antigen common to nearly all RHCE alleles. Alloimmunization to anti-Rh17 has been shown to cause severe HDFN4[4].

Objectives: Here we report the case of an infant diagnosed prenatally with Rh17 alloimmunization who developed severe HDFN and was treated primarily with incompatible blood.

Design/Method: Case Report.

Results: The patient's mother was AB D-- blood type. At 18 weeks gestation, the fetus was noted to have signs of anemia. Prenatal testing in the mother confirmed an anti-Rh17 titer of 1:64. The mother was treated prenatally with plasma exchange, intravenous immunoglobulin (IVIG) and five intrauterine transfusions (IUTs). The fetus developed severe anemia and signs of hydrops and required emergent delivery at 32 weeks of gestation. Following delivery, the infant was noted to have significant hyperbilirubinemia and anemia. She was treated with IVIG and received an exchange transfusion, was started on phototherapy and remained in the neonatal intensive care unit. In total, she received three exchange transfusions with least incompatible blood, three simple transfusions from a compatible blood

unit, one transfusion from an incompatible unit, eight platelet transfusions and two doses of IVIG and epogen.

Conclusion: Rh17 alloimmunization has been reported mainly in a few case reports because of the rarity of its condition. These cases have resulted in high severity of HDFN. When identified, screening for fetal anemia is imperative to begin treatment early to avoid fetal death. Treatment during pregnancy involves intrauterine transfusion. Finding compatible blood is an issue for these patients given the rarity of D-- phenotype. Clinical decision-making in the setting of blood incompatibility required a multidisciplinary effort between neonatology, hematology, transfusion medicine and the blood suppliers to avoid the sequelae of significant hyperbilirubinemia. With early identification and aggressive management, severe HDFN cases can be treated with collaborative efforts as seen in our case despite the lack of compatible blood availability.

Poster # 022

A RARE DISEASE RE-EMERGING: HEMOLYTIC DISEASE OF THE NEWBORN

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Background: Hemolytic Disease of the Fetus and Newborn (HDFN), though much less common in higher income countries with Rhesus immunoglobulin (RhIg) prophylaxis in Rh(D)-negative mothers, is re-emerging as women from lower- and middle-income countries migrate to the United States (US) and in women who can't access health care reliably. While HDFN remains uncommon in the US, it is important for hematologists to keep up to date with this disease and its management.

Objectives: We describe a case of HDFN born to a mother with multiple minor red blood cell (RBC) antibodies leading to severe anemia and jaundice in a newborn.

Design/Method: Case presentation

Results: A 4-month-old male presented to our clinic with a history of severe HDFN. Mother, who is Rh(D)-negative, had 2 prior pregnancies. She reportedly received RhIg prophylaxis with her first pregnancy, and that child is now a healthy 15-year-old. She had no prenatal care with her 2nd pregnancy until 7 months gestation due to intravenous drug use, and this fetus was severely anemic, requiring periumbilical sampling (PUBS) and intrauterine transfusion (IUT). This fetus died due to complications from the IUT. Mother was then diagnosed with cirrhosis and required two RBC transfusions for severe anemia from esophageal varices.

Mother didn't receive prenatal care with our patient until he was 23-weeks' gestation and at that time was found to have anti-D, anti-C, and anti-Fya antibodies. Infant blood type was group O Rh(D)-postive. Doppler ultrasound of the fetus showed normal middle cerebral artery (MCA) velocities, and it's unclear if this testing was repeated. Our patient was born with severe HDFN at 38-weeks requiring a two-week neonatal intensive care (NICU) stay where he required RBC transfusion and phototherapy. When we met him, we confirmed maternal antibodies against Rh(D), Rh(C) and Fya antigens in his circulation, resulting in a positive direct antiglobulin (DAT) test with 2+IgG. He had a normal hemoglobin (12.1g/dL) and bilirubin (0.3mg/dL).

Conclusion: New advances, including the detection of fetal RBC antigens with cell-free fetal DNA (cffDNA) in maternal blood is increasingly used early in pregnancy to predict fetal risk of HDFN. Maternal management, including intravenous immunoglobulin (IVIg) and steroids at regular intervals throughout pregnancy, and as-needed PUBS/IUT are relevant to the care of the infant after birth. Phototherapy and IVIg can be used in the neonate to prevent exchange transfusion, which is increasingly only done at centers with NICU expertise in this rare procedure.

Poster # 023

PATHOLOGIC MUTATION OF SEVERE GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY (G6PD)

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Background: G6PD deficiency is an enzymatic mutation with variable symptoms, most commonly newborn jaundice and episodic hemolytic anemia, often as a result of oxidative stress, medications, or diet. This well studied enzyme has yielded as many as 400 different genetic variations, with 186 known precise mutations[1-2].

(1.Cappellini, Lancet 2008; 2. Beutler, Blood 2008)

Objectives: To describe the clinical and genomic findings of a patient with severe neonatal G6PD.

Design/Method: Case Report

Results: An 8 week old male presented with anemia. Born at 35 weeks to a G4P3 Chinanteco speaking mother with pregnancy complicated by preeclampsia, gestational diabetes and intrauterine growth retardation. He was found to have a micropenis, hypospadias, grade I IVH, patent foramen ovale and atrial septal defect. Lab work at birth was concerning for hemolytic anemia with a hematocrit of 29.1%, MCV 151.6fl, retic >17.9% and total bilirubin of 13.1mg/dl. Peripheral blood smear showed atypical erythrocytes including stomatocytes, codacytes and dacrocytes. TORCH titers, DAT were negative. The patient was transfused with packed red blood cells four times during their 5 week stay in the neonatal intensive care unit. Whole exome sequence analysis (GeneDX) revealed a likely pathologic variant in the G6PD gene, p.Arg387Gly (CGC>GGC): c.1159 C>G in exon 10 inherited from the mother. WES analysis failed to reveal co-existing diagnoses such as congenital dyserythropoietic anemia and other RBC membrane/enzyme disorders Enzymatic activity of G6PD was quantified at 54 x 10e12 RBC units/L.

Conclusion: The World Health Organization has established a class system based on G6PD enzymatic function. This genetic mutation shows a more severe form of G6PD for the tested enzymatic activity. There is striking severity in the mutation reported, as seen in the need of 10 pRBC transfusions during the first 13 months of life. The clinical picture is very similar to the rare Guadalajara variant of G6PD deficiency caused by the c.1159C>T;p.Arg387Cys) which is known for causing severe non-spherocytic hemolytic anemia. [3-4]
(3.Vaca Hum Genet 1982; 4. Keller Prenatal Diagnosis 2015)

Poster # 024

HEMOGLOBIN SE: GENOTYPE VS. PHENOTYPE

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Background: Hemoglobin (Hb) SE is a hemoglobinopathy resulting from a compound heterozygosity of Hemoglobin S (*HBB Glu6Val)* and Hemoglobin E (*HBB Glu26Lys)*, the two most common variants in the world. Hb S is commonly found in Africa, Eastern Saudi Arabia and Central India, while Hb E is found in Sri Lanka, Eastern India, Southeast Asia, and Southwest China. Hb SE can be phenotypically similar to Sickle B+ thalassemia presenting commonly with mild anemia, vaso-occlusive crisis, and enlarged spleen. We present two patients with different phenotypes of Hemoglobin SE disease despite similar genotypes.

Objectives: Review the presentations of two patients with Hemoglobin SE disease.

Design/Method: Case report obtained by comprehensive chart review.

Results: Patient 1 is a 6-year-old male with Hb SE found on newborn screen with Hb F 83.4%, Hb S 11.6% and Hb E 36%, and no Hb A. Hemoglobin electrophoresis obtained at nine months of age showed Hb S 53.6%, Hb E 28.2%, Hb A2 3.3%, Hb F 14.9% with a Hb/Hct of 8.6/27.0 and MCV of 53 fL. In his first two years of life, he was hospitalized for acute chest syndrome (ACS) requiring treatment with antibiotics, albuterol and steroids. Given his low baseline hemoglobin of 7.8 – 8.3 g/dL and recurrent ACS, he was started on Hydroxyurea (HU) at 20 months of age. With continued Hydroxyurea, his hemoglobin significantly improved to hemoglobin of 11 – 12 g/dL with MCV of 78 fL and minimal admissions for ACS. He has maintained a hemoglobin of 11 g/dL on a dose of 300 mg (~14 mg/kg) of Hydroxyurea. Patient 2 is a 5-year-old male with Hb SE with mother from Cambodia and father from St. Lucia. His hemoglobin electrophoresis showed Hb F 84.5%, Hb S 12.3%, Hb E 3% and trace hemoglobin Barts. He has a baseline hemoglobin 10.5 g/dL with no significant symptoms or ACS. He has had no complications.

Conclusion: Hemoglobin S and Hemoglobin E are the most common variant hemoglobins worldwide. Hemoglobin SE commonly presents phenotypically and symptomatically similar to Sickle B+ thalassemia. We describe two disparate cases of hemoglobin SE with vast variation in presentation. Our patient with marked anemia and complications in the first year of life has responded well to Hydroxyurea therapy. Longitudinal follow up of these patients are uniquely modeled for patients based on their presentation.

Poster # 025

A NARRATIVE OF TWO PATIENTS GLUCOSE PHOSPHATE ISOMERASE GENE MUTATIONS AND HEMOLYTIC ANEMIA

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Background: Glucose-6-phosphate isomerase (GPI) is an enzyme found in red blood cells that mediates the second reaction step of glycolysis. GPI deficiency is considered the second most common erythro-

enzymopathy of anaerobic glycolysis. Currently, only approximately 70 cases of GPI deficiency have been reported. GPI deficient patients are affected by chronic, non-spherocytic hemolytic anemia however severity of anemia has been variably reported.

Objectives: Describe the clinical courses of two patients with GPI deficiency

Design/Method: Case Series

Results: PATIENT A: Patient A is a now two-year-old female born term, found to have significant jaundice requiring phototherapy. At two months of age, the patient began to require transfusions for symptomatic macrocytic anemia with hemoglobin of 6.1 g/dL and a mean corpuscular volume of 107.3. She was found to have an elevated reticulocyte percentage greater than 21.6% though the patient had no evidence of jaundice. ADA was negative and a hereditary hemolytic anemia panel was obtained showing two previously described pathogenic variants in GPI, c.1039C>T (p.Arg347Cys); NM_000175.5 and c.1144G>T (p.Glu382Ter); NM_000637.5. The patient continues to require red blood cell transfusions every two to four months. Hemolytic episodes are often preceded by viral infection however not solely isolated to times of infection.

PATIENT B: Patient B is a now four-year-old consanguineous male who presented at 7 months of age with profound hemolytic anemia with a hemoglobin of 2.0 g/dL and mean corpuscular volume of 112.4 requiring multiple red blood cell transfusions. Reticulocyte percentage was found to be greater than 21.6%. The patient was found to have coronavirus infection, hyperuricemia, and elevation of LDH. Bone marrow biopsy showed dyserythropoesis without malignancy. A congenital dyserythropoesis anemia panel was negative while a hereditary hemolytic anemia panel showed a homozygous variant for c.1010C.T (pAla337Val); NM_000175.3, a variant of unknown significance at the GPI gene. The patient required PRBC transfusions every one to four months the first four years of life for symptomatic anemia often preceded by viral infection. The patient's course has been complicated by short stature, poor weight gain, and severe iron overload in the liver requiring chelation therapy with 14 milligrams per kilogram of Deferasirox.

Conclusion: GPI deficiency is a previously underrecognized form of hereditary nonspherocytic hemolytic anemia which can require chronic transfusion dependence and management of iron overload.

Poster # 026

CLINICAL SIGNIFICANCE OF VARIANTS OF UNKNOWN SIGNIFICANCE IN DIAMOND BLACKFAN ANEMIA

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Background: Diamond-Blackfan anemia (DBA) a congenital erythroid aplasia that typically presents in infancy is diagnosed as classical DBA if: There is onset of anemia at age <1-year, macrocytic anemia with no other significant cytopenias, reticulocytopenia and normal marrow cellularity with a paucity of erythroid precursors.
Nonclassical DBA can be made if there is presence of a known genetic variant despite not meeting all classical clinical criteria. With genetic testing becoming more prevalent, genetic variants of unknown

significance become difficult to interpret for patients who may experience some, but not all of the classical clinical criteria.

Objectives: To contribute to the existing data on Variants of Unknown Significance (VUS) in DBA associated genes.

Design/Method: Four year old female with macrocytic anemia without other cytopenias presented with an MCV of 102, hemoglobin of 8.5mg/dl, white blood cells of 8.4mg/dl and platelets of 475mg/dl. She had a history of congenital bilateral thumb hypoplasia and short stature with no family history of diamond blackfan anemia, increased reticulocyte count at 3.29% as a response to her macrocytic anemia, normal hemoglobin F at 1.4%, elevated adenosine deaminase at 2414. A bone marrow failure panel was sent which identified a VUS c.3+5G>c (intronic) heterozygous in RPL5 gene. A presumed diagnosis of DBA based on physical exam and laboratory findings was made and a bone marrow evaluation deferred at that time.

Results: A trial of prednisone was attempted to monitor for improvement in her hemoglobin. She was noted to respond with a max hemoglobin of 10.3mg/dL on a low daily dose of prednisone. After weaning off, she was found to return to her baseline hemoglobin of 9.2mg/dL.

Conclusion: Mutations in RPL5 have been identified as one of the genes associated with DBA. While our patient harbors a mutation within a known ribosomal protein in RPL5, the variant,c.3+5G>c (intronic), has not been previously described in published case reports. The sequence change does not directly affect the coded amino acid sequence within the RPL5 protein thus its exact mechanism is unclear on clinical phenotype. Caution should be exercised with VUS, however, when patients fit clinical criteria, it becomes unclear how clinicians are to best counsel patients with DBA in terms of follow up and risk for malignancies associated with classical DBA. It is imperative that on-going data collection pertaining to VUS in DBA associated genes continue so we can broaden our knowledge of the vast genetic and clinical implications for better patient care.

Poster # 027

ZNF699-DEGCAGS DIAGNOSIS IN A PEDIATRIC PATIENT WITH ANEMIA, THROMBOCYTOPENIA, AND LYMPHOPENIA

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Background: DEGCAGS (Developmental delay with Gastrointestinal, Cardiovascular, Genitourinary and Skeletal abnormalities) syndrome is a recently described, multisystem disorder due to biallelic pathogenic variants in *ZNF699* (OMIM 619488). Hematologic findings, including anemia and pancytopenia, are noted in 8 of the 14 patients described to date, but have not been well characterized. Here we report on the hematologic findings of a patient initially evaluated for possible Diamond Blackfan anemia (DBA), who was later diagnosed with DEGCAGS syndrome.

Objectives: Describe the hematologic findings in a pediatric patient with DEGCAGS syndrome, bring awareness to this diagnosis in patients being evaluated for suspected inherited marrow failure syndromes.

Design/Method: Retrospective review of medical records and emerging *ZNF699* literature

Results: The patient presented to hematology at age 10y in 2018 for mild macrocytic anemia, thrombocytopenia, and lymphopenia. Reticulocyte count was normal. Her history included multiple congenital abnormalities with developmental delay, poor growth, facial dysmorphism, Shone's complex, bilateral renal dysplasia, bilateral thumb abnormalities (polydactyly, hypoplasia), shortened ulnae, hearing loss and esotropia. Family history was notable for consanguinity, parents are second cousins. Given the constellation of findings suggested an IMFS, evaluation included chromosomal breakage studies, hemoglobin F and eADA. Abnormal findings included elevated Hgb F (4%) and eADA (2.05 iU/g of Hb). Bone marrow biopsy showed mild hypocellularity, but otherwise appropriate trilineage hematopoiesis with normal cytogenetics. Exome trio was non-diagnostic. The patient reestablished in 2023, for planned cardiac surgery. Blood counts were unchanged. Reanalysis of the prior exome identified novel homozygous frameshift variants in *ZNF699*, interpreted as likely pathogenic. *ZFN699* variants were described in association with DEGCAGS syndrome in 2021; this finding felt to explain her phenotype.

Conclusion: Hematologic abnormalities including anemia and pancytopenia have been reported in DEGCGAS syndrome but few data are available to characterize them further. The anemia in our patient had overlapping features with DBA, with macrocytic red cells, elevated eADA and increased hemoglobin F. In contrast to DBA her marrow did not show deficiency of erythroid progenitors and her reticulocyte count was preserved; additionally, no genetic variants in ribosomal protein genes were identified. *ZNF699* is a zinc finger protein with wide tissue expression, but its function is unknown. Other zinc finger protein genes, including *GATA1*, have key roles in hematopoiesis. With identification of additional patients, the role of *ZNF699* in hematopoiesis might be better defined. *ZNF699* should be included in the evaluation of patients with suspected IMFS.

Poster # 028

CHALLENGING DETECTION OF A NOVEL FANCA DELETION MUTATION

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Background: Fanconi anemia (FA) is an inherited bone marrow failure syndrome with increased risk of both hematologic malignancy and solid tumors due to the defects in DNA interstrand crosslink repair. Twenty-three genes have been reported involved in the pathogenesis, with FANCA the most mutated. Varied clinical presentations often delay the establishment of the initial diagnosis.

Objectives: We present a patient whose novel FANCA pathogenic variant required several genetic testing approaches to uncover, emphasizing the crucial role that chromosomal breakage studies continue to play in establishing the diagnosis of FA.

Design/Method: Case report

Results: An 8-year-old male with short stature and atrial septum defect presented with fatigue and pallor. Pertinent physical findings included a hypoplastic right thumb and multiple café-au-lait macules.

He was found to be pancytopenic with hemoglobin 2 g/dL, absolute neutrophil count 0.51 x 10^3/µL and platelet count 6 x 10^3/µL. Bone marrow aspirate and biopsy showed a hypocellular marrow without dysplasia or increased blasts.
Fanconi anemia was suspected and was supported by a positive chromosome breakage analysis. His initial genetic evaluation included trio exome sequencing (ES) (patient and parents), which reported an inconclusive result of variants of unknown significance in genes not associated with FA, and a chromosomal microarray analysis (CMA), which did not report any copy number changes though did report significant amounts of absence of heterozygosity (AOH) consistent with the known parental consanguinity. A dedicated FA gene panel was next obtained, which did not report any known variants; however, it did note poor coverage in exons 1 and 2 of FANCA. This finding raised suspicion for a homozygous deletion of this region. Upon re-analysis of the ES FANCA data, a 0.76 kb homozygous deletion including exon 1 and partially exon 2 was identified, which was confirmed by additional multiplex ligation-dependent probe amplification and PCR testing. This copy number variant has not been previously described.
After the confirmatory genetic diagnosis, the patient underwent a 9/10 HLA matched related donor hematopoietic stem cell transplantation with successful engraftment.

Conclusion: Due to the complexity of FA, collaboration between hematologists and genetic laboratory personnel and genetic counselors is imperative for precise diagnostics, especially in cases exhibiting a high index of suspicion. While the rapid advancement in genetic testing has provided deeper insights into pathogenesis, chromosomal breakage analysis remains central to the diagnosis of FA.

Poster # 029

NOVEL MUTATION OF FANCI GENE LEADING TO EARLY BONE MARROW FAILURE

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Background: Fanconi anemia (FA) is an autosomal recessive disease characterized by defects in the DNA repair pathway often leading to bone marrow failure (BMF), congenital and developmental abnormalities, and various malignancies. FA complementation group I (FANCI), a protein encoded by the FANCI gene, is a rare subset of FA not well described in the literature.

Objectives: To describe a novel FANCI mutation (C.2890-11T>G), that in combination with a known pathogenic FANCI mutation, resulted in progressive BMF at 3 years of age.

Design/Method: Single-subject case report.

Results: At birth, our patient had microcephaly, small, curved right arm, absent right thumb, hypopigmented skin lesions and imperforate anus. X-RAYs confirmed absent right radius and right thumb, bowing of the right ulna, and bilateral hip dislocations. Further work up showed a solitary right kidney and atrial septal defect. He had mild thrombocytopenia (130K/CUMM) and elevated serum creatinine (1.3mg/dL).

Given concern for FA due to the anatomical, physical, and lab findings, chromosome breakage testing was sent and resulted as abnormal. Further genetic testing showed two heterozygous mutations in the

FANCI gene. The first mutation AR c.2946_2947del is known to be pathogenic. The second mutation AR C.2890-11T>G was noted as a variant of uncertain significance not previously described in FA.

During the first year of life, he was diagnosed with failure to thrive, global developmental delay and chronic kidney disease stage 3. Platelet count normalized until 12 months of age when he developed mild thrombocytopenia (120K/CUMM). By age 2, platelet count decreased to 30-40K/CUMM, and then to 16K/CUMM 6 months later. A trial of thrombopoietin-mimetic (Romiplostim) with dose escalation to 12mcg/kg maintained his platelet account 20-25K/CUMM for 1 year. While treated with Romiplostim, his hemoglobin improved from 9g/dL to 11g/dL and absolute neutrophil count remained only mildly low (800-1300K/CUMM). At age 4, he had an acute drop in platelet count to <10K/CUMM and became transfusion dependent. Bone marrow evaluation showed 20% cellularity, but no evidence of malignancy or fibrosis. Bone marrow transplant planning is currently underway.

Conclusion: This case describes a patient with phenotypical characteristics findings of FA, abnormal chromosome breakage study, and two heterozygous mutations in FANCI. Additionally, he developed progressive BMF, which is a known outcome of FA. His clinical course indicates that the previously unreported FANCI mutation (C.2890-11T>G) is likely pathogenic. Our patient with FANCI FA developed transfusion dependent bone marrow failure at an early age.

Poster # 030

Novel pathogenic variants in DNAJC21 discovered after allogeneic transplant for bone marrow failure

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Background: Bone Marrow Failure Syndrome 3 (BMFS3) is a recently described recessive disorder characterized by pancytopenia in early childhood, with fewer than 20 cases reported in the literature. BMFS3 includes features that overlap with Shwachman-Diamond syndrome (pancreatic insufficiency and short stature) and Dyskeratosis Congenita (telomere attrition, dental and hair abnormalities). Additional variable features include joint and skeletal abnormalities, impaired development, growth hormone deficiency and retinal dysplasia.

Objectives: Describe novel genetic findings in a patient with BMFS3 and his journey to accurate diagnosis while highlighting the importance of both archival DNA analysis after HSCT and multidisciplinary reappraisal of evolving symptoms for optimal management of long-term care.

Design/Method: Case description and literature review.

Results: The proband is a now 13-year-old Hispanic male who presented at 18 months with pancytopenia and ichthyosis. Initial work up for inherited bone marrow failure syndromes was negative. He was successfully treated with HLA-matched unrelated bone marrow transplant after failing Immune suppressive therapy. He subsequently developed additional features including coarse facial features, broad/short neck, kyphosis, abnormal tooth enamel, developmental delay, exocrine pancreatic insufficiency, growth hormone deficiency and insulin-dependent diabetes. His evolving clinical features showed overlap of multiple bone marrow failure syndromes, warranting further work up.

We performed a whole-exome sequencing on DNA extracted prior to BMT, which provided a definitive diagnosis of BMFS3, with compound heterozygous mutations in trans in *DNAJC21* (p.V114F fs*4, p.D145G). He is currently receiving multi-disciplinary services for GI and endocrine abnormalities. The patient and his family received appropriate genetic counselling.

Neither variant has been described with BMFS3 syndrome, but both are reported at low frequency in individuals of Hispanic descent (allele frequency 0.01 - 0.02 in gnomAD). While nonsense mutations are common in BMFS3, rare missense changes are nearly exclusively in the DnaJ domain. The D145G variant lies between the DnaJ and coiled-coil domains in a region lacking known protein homology, suggesting an important role for this region in *DNAJC21* function.

Conclusion: Bone marrow failure syndromes are heterogeneous group of diseases impacting multiple genetic pathways and displaying a wide range of genotypic-phenotypic variability and phenotypic overlap. At the time of presentation and treatment, BMFS3 was not a known entity thus the initial genetic work up was negative. This case emphasizes the importance of careful multidisciplinary follow-up with repeat genetic evaluation proving helpful in patients with idiopathic bone marrow failure who have multi-system involvement. Further, this case demonstrates novel *DNAJC21* variants for genotype/phenotype correlation.

Poster # 031

WHOLE GENOME SEQUENCING IDENTIFIES NOVEL VARIANTS IN TWO PATIENTS WITH DIAMOND-BLACKFAN ANEMIA

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Background: Diamond-Blackfan Anemia (DBA) is an inherited bone marrow failure (iBMF) syndrome characterized by congenital pure red cell aplasia. Heterozygous allelic variations are found in ribosomal protein (RP) genes in ~80% of patients; most commonly *RPS19*. In ~20% of cases, no known pathogenic variant is identified.

Objectives: We describe two patients with clinical phenotypes consistent with DBA without identifiable pathogenic variants in DBA-associated genes performed on standard genetic testing. Whole genome sequencing (WGS) identified previously undescribed variants in *RPS7* and *RPS19.*

Design/Method: Trio (Patient 1) or Quad (Patient 2) whole genome sequencing (WGS) was performed from buccal or blood samples obtained from probands and family members. Genomic DNA was extracted for Illumina sequencing platform. WGS data were analyzed by Emedgene software with etiological attention to RP-related genes.

Results: Patient 1 is a 17-month-old female who presented at 7 weeks with a hemoglobin (Hb) of 2.1 g/dL, MCV 110 fL, and low reticulocyte count 8.7 K/mcL. Erythrocyte adenosine deaminase (ADA) was normal. Bone marrow was normocellular with nearly absent erythroid progenitors. Patient 2 is a 22-month-old male who presented at 8-weeks with initial Hb 4.4 g/dL, MCV 106.7 fL, and low reticulocyte

count 4.9 K/mcL. Erythrocyte ADA was markedly elevated at 2,138 mU/g Hb. Bone marrow was hypocellular with markedly decreased erythroid progenitors and increased hematogones. Both patients were transfusion dependent every 3-4 weeks. Neither patient had physical anomalies except Patient 1 had ventricular and atrial septal defects. In both cases, targeted genetic testing by next generation sequencing (NGS) for iBMF syndromes and whole exome sequencing (WES) for patient 2 revealed no pathogenic variants, so whole genome sequencing (WGS) was obtained through the University of Utah Penelope Program for rare and undiagnosed diseases.

In Patient 1, WGS revealed a heterozygous *de novo* intronic splice-site variant in *RPS19* (chr19:41861562 C>T). In Patient 2, WGS revealed a maternally inherited, heterozygous allelic variant in the 5' untranslated region of *RPS7* (c.172+350C>T). Neither patient responded to glucocorticoid trials and both remained transfusion-dependent. Both patients had HLA-matched siblings who tested negative for the identified variants and were referred for hematopoietic stem cell transplant.

Conclusion: DBA should be suspected in all patients with pure red cell aplasia identified at <5 years of age. WGS may identify allelic variants of interest in non-coding regions of RP genes that would be missed by other genetic testing methods, including WES, highlighting its clinical utility in the care and treatment of undiagnosed rare genetic disorders.

Poster # 032

AUTOSOMAL RECESSIVE SHWACHMAN-DIAMOND SYNDROME DUE TO A HOMOZYGOUS PATHOGENIC DNAJC21 MUTATION

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Background: Shwachman-Diamond Syndrome (SDS) is an inherited bone marrow failure disorder characterized by cytopenia, exocrine pancreatic insufficiency, and metaphyseal dysplasia. Over 90% of cases are attributed to biallelic pathogenic variants in the *SBDS* gene involved in ribosomal biogenesis; however, mutations in the *DNAJC21* gene have also been implicated. SDS may progress to bone marrow failure or myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML). These patients typically have a poor prognosis and hematopoietic stem cell transplantation (HSCT) is the only curative option.

Objectives: Present a case of autosomal recessive SDS and bone marrow failure due to a homozygous pathogenic *DNAJC21* mutation.

Design/Method: Case Report

Results: An 18-month-old girl with failure to thrive, transfusion-dependent thrombocytopenia, exocrine pancreatic dysfunction, and developmental dysplasia of the hip was referred to our BMT clinic for HSCT evaluation after developing bone marrow failure. The patient was noted to have an abnormal newborn screen for mucopolysaccharidosis type 1 (MPS-1), prompting extensive work-up with multiple subspecialists. Alpha-L-Iduronidase (IDUA) gene testing was done to evaluate for MPS-1. She was found to have a homozygous mutation; however, urine glycosaminoglycans (GAG) testing was normal, making MSP-1 very unlikely. At her 15-month well-child visit, the patient had diffuse bruising and petechiae. A CBC revealed severe pancytopenia, prompting hospitalization for evaluation. Initial bone marrow

aspiration and biopsy demonstrated a normocellular marrow with erythroid hyperplasia and left shifted erythropoiesis and granulopoiesis without evidence of blasts or dysplasia. Cytogenetics and flow cytometry were unremarkable. Invitae genetic panel identified a homozygous pathogenic *DNAJC21* mutation without evidence of an *SBDS* mutation, consistent with autosomal recessive SDS. Repeat bone marrow aspiration and biopsy several months later revealed bone marrow failure with marked hypocellularity (< 15%) and mild dyserythropoietic without blast population. Given the rarity of her mutation, the patient's microarrays were run at two different labs for comparison. Both reported about 16% genomic region of homozygosity (ROH), a degree of shared genomic regions that would be expected for individuals known to be related. Thus, consanguinity was presumed. On pre-transplant evaluation, the patient's mother was identified as a 10/10 phenotypic human leukocyte antigen (HLA) match and served as her donor for peripheral blood stem cell (PBSC) transplantation despite being a presumed carrier.

Conclusion: *DNAJC2* and *SBDS* are genes involved in ribosomal assembly. This case report describes a patient with SDS due to a homozygous pathogenic mutation of *DNAJC2* without an *SBDS* mutation, highlighting an association between ribosomal dysfunction and bone marrow failure.

Poster # 033

ACTIVATED CD8+ T-CELL HEPATITIS AND EVOLVING APLASTIC ANEMIA: A POTENTIAL THERAPY APPROACH

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Background: Activated CD8+ T-cell hepatitis has recently been reported in the context of indeterminate pediatric acute liver failure and is associated with IFN-γ pathway immune dysregulation. Hepatitis-associated AA is a well-recognized and distinct variant of AA with similar immune dysregulation. Research has shown that CD8+ T-cells and IFN-γ both may contribute to hepatitis and marrow failure. The use of emapalumab, a monoclonal antibody against interferon-γ, has been studied in refractory hemophagocytic lymphohistiocytosis, however has not been described in this unique setting.

Objectives: To report a case of activated $CD8^+$ T-cell hepatitis with evolving AA, to review known pathophysiology, and to discuss the use of emapalumab in this patient as initial therapy.

Design/Method: Case report.

Results: A healthy 10-year-old male presented with abdominal pain and jaundice. His evaluation revealed severe acute hepatitis (aspartate aminotransferase 2446 U/L, alanine transaminase 1740 U/L, total/direct bilirubin 19.2/16.6 mg/dL, gamma-glutamyl transferase 150 U/L, and negative infectious hepatitis evaluation). Inflammatory work up revealed: Ferritin 269 ng/mL, triglycerides 208 mg/dL, fibrinogen 197 mg/dL, soluble interleukin (IL)-2 receptor 3329 pg/mL, IL-18 5521 pg/mL, and CXCL9 9340 pg/mL. Cell blood count was notable for isolated mild neutropenia (1200 cells/uL). Liver biopsy demonstrated a CD8+/CD103+ T-cell predominant inflammatory infiltrate, suggesting the diagnosis of activated $CD8^+$ T-cell hepatitis. Immunosuppressive therapy (IST) was initiated with steroids and a dose of intravenous immunoglobulin with subsequent gradual improvement of liver function, however patient did not tolerate steroid wean and progressed with recurrence of hepatitis and moderate

cytopenias with peak CXCL9 level of 14,848 pg/mL. Thus, tacrolimus was incorporated into IST. Bone marrow biopsy demonstrated a hypocellularity without dysplasia, normal cytogenetics, and no pathogenic somatic mutations identified by next generation sequencing. Screening for inherited bone marrow failure syndromes was negative. Emapalumab was initiated with sequential steroid wean and tacrolimus discontinuation. Effective IFN-γ blockade occurred after two doses (CXCL9 336 pg/mL), with resolution of hepatitis however persistent moderate AA.

Conclusion: Activated $CD8^+$ T cell hepatitis is associated with AA and immune dysregulation, as demonstrated in our patient by elevated CXCL9 and evolving cytopenias. We present the rationale of incorporating targeted therapy to IST. This patient received multiple interventions for the initial management of his immune dysregulation and despite the chronology of INF-γ blockade and resolution of hepatitis, we are unable to attribute this outcome to emapalumab itself. Further study of this approach should be pursued in the context of a clinical trial. Persistent cytopenias support the need for consolidative therapy.

Poster # 034

IDIOPATHIC PAPILLEDEMA IN PAROXYSMAL NOCTURNAL HEMOGLOBINURIA WITH SEVERE APLASTIC ANEMIA

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Background: Paroxysmal Nocturnal Hemoglobinuria (PNH) leads to a heterogenous disease process that ranges from hemolysis to bone marrow failure and severe aplastic anemia (AA). There have been several reported cases of papilledema in AA, though none with PNH, in pediatric patients. In cases of acquired AA and papilledema, the ophthalmologic findings often improved and even resolved after anemia was corrected.

Objectives: Report a case of a pediatric patient with findings of papilledema in setting of PNH with severe AA, which persisted until definitive treatment with matched unrelated donor transplant.

Design/Method: Case Report

Results: A 17 year old female presented with headache and transient visual obscurations after a syncopal event. Ophthalmology evaluated and found bilateral optic nerve head edema, so urgent workup was performed to rule out leukemic optic neuropathy, and ophthalmologic emergency. On initial workup, she was found to have pancytopenia, with a hemoglobin of 4.3g/dL. She was ultimately diagnosed with paroxysmal nocturnal hemoglobinuria (GPI deficient granulocytes of 89.39%) with aplastic anemia (marrow cellularity 20%). Computerized tomography with angiography of the head revealed distal transverse sinus compression, though otherwise negative, implicating anemia as the etiology of neurologic symptoms. After 3 units of packed red blood cell transfusion, the patient improved clinically with stable neurologic exam. She received transfusion therapy to maintain hemoglobin >7 g/dL and eculizumab. Her aplastic anemia later progressed to severe range and she was treated with a matched unrelated bone marrow transplant. Her papilledema was slow to resolve until after transplant, and finally, at 130 days post-transplant, her papilledema had resolved completely without ophthalmologic sequalae.

Conclusion: We present a rare finding of papilledema in the setting of PNH with severe AA that persisted despite relative correction of this patient's anemia with transfusion support and eculizumab. Prolonged papilledema can lead to deleterious nerve damage. In this patient's case the nerve edema ultimately did not resolve until after bone marrow transplant. Without the presenting visual changes, an ophthalmologic exam may not have been pursued to identify her papilledema; and if left uncorrected could have led to more permanent vision loss. This case would suggest that eye examination should be considered in any patient with severe anemia, especially in the setting of any reported visual complaints. If papilledema is identified in these patients, this may be an indication for definitive treatment if transfusion support does not correct the papilledema.

Poster # 035

ATYPICAL PRESENTATION OF DIAMOND-BLACKFAN ANEMIA WITH UNBALANCED TRANSLOCATION OF CHROMOSOME 3 AND 5

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Background: Pure red cell aplasia (PRCA) is a syndrome defined by normochromic and normocytic or macrocytic anemia with inappropriately low reticulocyte count and marked reduction or absence of erythroid precursors from the bone marrow. The congenital form of PRCA is Diamond-Blackfan anemia (DBA).

Objectives: DBA is due to a defect in the ribosomal RNA (rRNA) maturation as a consequence of a heterozygous mutation in ribosomal protein (RP) genes. An allelic variation, always in a heterozygous state in a RP, is found in approximately 70% to 80% of classic DBA cases. This indicates that 20-30% of patients do not have known mutations and are being identified as atypical presentations.

Design/Method: Herein, we present a case with persistent macrocytic anemia with severe reticulocytopenia and an unbalanced translocation of chromosome 3 and 5.

Results: An 11-month-old female was referred to hematology for further evaluation of severe anemia with reticulocytopenia requiring multiple transfusions. Blood smear revealed large red blood cells that were decreased in number. Hb electrophoresis was normal with a negative Coombs test. Bone marrow biopsy revealed a cellular marrow, marked erythroid hypoplasia, adequate myeloid and megakaryocyte maturation. Chromosomal breakage studies were normal, effectively ruling out Fanconi anemia. Chromosome analysis found an unbalanced translocation 46,XX,dert(3,5)(p22.2;q35.3), a partial trisomy on chromosome 3, and partial monosomy on the distal portion of chromosome 5. After genetic consultation, whole genome sequencing (WES) was performed on the bone marrow and did not reveal a DBA causative mutation. She has been transfusion dependent, unresponsive to steroid therapy, and given her comorbidities, is not a candidate for bone marrow transplantation. Her 8-year-old brother has the same unbalanced translocation derivative without hematologic abnormalities.

Conclusion: DBA is a rare inherited bone marrow failure syndrome and complex erythroid disorder that can present with varying phenotypes and genotypes. The bone marrow aspiration shows a severe paucity of red blood cell precursors, while the rest of the cell lineages are normal and individuals with

the similar mutation may exhibit a very different clinical phenotype, even within the same family, as in the presented case. Our extensive literature search did not find a known association between our patient's unbalanced chromosomal translocation and refractory anemia which supports the notion that this case is an atypical presentation of DBA with an unbalanced translocation.

Poster # 036

H3K27M DIFFUSE MIDLINE GLIOMA IN A YOUNG PATIENT WITH FANCONI ANEMIA: A CASE REPORT

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Background: Fanconi Anemia (FA) is known to predispose pediatric patients to childhood cancers, most commonly leukemias, some solid tumors, and only rarely CNS tumors. FA is caused by mutations of several known genes, including BRCA2 and PALB2 (alternatively termed FANCN). Patients with biallelic BRCA2 mutations are those most associated with development of pediatric cancers. More recently, patients with biallelic PALB2 mutations have also been suggested to have increased predisposition for childhood cancer. Brain tumors in pediatric patients with FA are typically medulloblastomas, and very rarely pediatric high-grade glioma (pHGG), with none identified in prior literature having DMG characteristic H3K27M mutation. DMG is very difficult to treat with very few options for therapy and poor prognosis. EGFR mutations in DMG are associated with a bithalamic location and resistance to Onc201 therapy, but may have response to EGFR-targeting agents.

Objectives: We report a novel case of H3K27M diffuse midline glioma in a three-year-old patient with FA and two affected copies of the PALB2 gene, one of which was a maternally inherited copy of unknown significance, the other of which was a paternally inherited pathogenic copy.

Design/Method: Case Report.

Results: A three-year-old female was noted to have microcephaly, mixed hearing loss, short stature, and café-au-lait macules. Whole exome sequencing was significant for mutations in the PALB2/FANCN gene, a paternally inherited pathogenic variant and a maternally inherited variant of unknown significance. She developed symptoms of tremor and right leg weakness, and on brain MRI was found to have a large bithalamic mass. Sterotactic biopsy was consistent with diffuse midline glioma, including diffusely positive H3K27M mutant protein and loss of H3K27me3. Tumor cytogenetics were significant for overexpression of EGFR missense mutation (likely activating) at the p.A289V site to 59.2% VAF, with overexpression of the EGFR transcript as well. Chromosomal breakage testing was within normal limits. Treatment included localized hypofractionated photon radiation to 4005 cGy, with plans for EGFR-targeted therapy with cetuximab, given the known association of EGFR mutation with Onc201 resistance.

Conclusion: To our knowledge, this is the first reported case of a pediatric patient with H3K27M diffuse midline glioma with FA. While patients with FA and biallelic PALB2 variants are at risk for childhood cancers, this case suggests that high grade gliomas may be one of these cancer types. Annual abdominal ultrasound and brain MRI are recommended for patients with biallelic BRCA2 mutations, however screening in patients with biallelic PALB2 mutations may also be warranted.

Poster # 037

DIAGNOSIS AND MANAGEMENT OF ACUTE INTERMITTENT PORPHYRIA IN TEENAGE FRATERNAL TWINS

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Background: Porphyrias encompass a family of rare inherited disorders characterized by autosomal dominant mutations in enzymes involved in the heme biosynthesis pathway. These mutations result in excessive buildup of porphyrin precursors triggering episodes of debilitating neurovisceral symptoms. Among these disorders, acute intermittent porphyria (AIP) is the most prevalent, arising from mutations in the hydroxymethylbilane synthase (*HMBS*) gene resulting in the overaccumulation of 5-aminolevulinic acid (ALA) and porphobilinogen (PBG).

Objectives: To describe the clinical management of AIP in dizygotic twins who presented five months apart with similar symptoms.

Design/Method: Patient A is a 15-year-old previously healthy girl who presented with five days of acute hip and abdominal pain, anorexia and dark urine correlating with the start of her menses. She presented in hypertensive crisis with electrolyte derangements including hyponatremia consistent with SIADH. She was treated with labetalol infusion, fluid restriction and morphine via patient-controlled analgesia. Family history was notable for AIP in father and eldest sister. She was empirically started on a 4-day course of hemin which led to significant resolution of her symptoms. Urine studies investigating ALA (34.7 mg/g creat, reference 1.5 – 5.3 mg/g creat) and PBG (85.145 mg/g creat, reference < 0.36mg/g creat) were elevated, confirming a biochemical diagnosis for AIP. Since her initial presentation, she experienced three additional attacks associated with menses with each episode requiring hospitalization. Five months later, patient A's dizygotic twin sister (patient B) presented with similar abdominal pain and hypertension requiring inpatient hemin infusion. Subsequent workup similarly revealed marked elevation of urinary markers ALA and PBG. Upon genetic evaluation, both patients were found to have a pathogenic mutation leading to a premature translational stop signal in *HMBS* (c. 730_731del; p.Leu244Alafs*6).

Results: After experiencing her third neurovisceral attack, Patient A was started on monthly outpatient hemin infusions as a prophylactic measure. Subsequently, she was approved to start monthly injection of small interfering RNA drug, givosiran, which targets *ALAS1* (gene encoding rate-limiting enzyme in the heme biosynthetic pathway). She was hospitalized for a fourth attack one day after receiving her first injection of givosiran requiring inpatient treatment, although onset of pain symptoms began 48 hours earlier. Patient B was similarly started on monthly prophylactic hemin injections and later transitioned to givosiran.

Conclusion: With the presentation of AIP in these twin siblings, we hope to highlight our approach to management of AIP, particularly the utilization of prophylactic treatments which requires highly individualized management due to limited data in the pediatric population.

Poster # 038

NOVEL VON HIPPEL-LINDAU VARIANT IDENTIFIED IN SIBLINGS CAUSING CHUVASH POLYCYTHEMIA

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Background: Chuvash polycythemia is a rare, autosomal recessive disorder of erythropoiesis prevalent in the Chuvashia Republic, Russia. It is caused by homozygous or compound heterozygous pathogenic variants in the von Hippel-Lindau (VHL) gene, a negative regulator of hypoxia sensing. Although Chuvash polycythemia lacks an association with tumorigenesis seen in primary myeloproliferative disorders, adult cohort studies report an increased risk of life-threatening stroke and other thromboembolic events. The most common *VHL* variant reported is c.598C>T (p.Arg200Trp), a founder mutation within the Chuvash population, a Turkic ethnic group, responsible for the majority of Chuvash polycythemia cases. However, other rare biallelic *VHL* variants have been reported.

Objectives: Present the clinical and genetic evaluation of siblings in Colorado, USA with symptomatic polycythemia found to carry a novel heterozygous *VHL* variant of unknown significance.

Design/Method: With local IRB approval, de-identified data was extracted from electronic medical records. Gene variant pathogenicity was determined according to American College of Medical Genetics guidelines.

Results: A 17-year-old male presented with dizziness and headache, persistently elevated hemoglobin (22-25g/dL) and mild thrombocytopenia (90-100,000/mcL). Bone Marrow demonstrated normocellularity (90%) with erythroid hyperplasia. Peripheral evaluation: reticulocyte 1.4%, erythropoietin 15.6mIU/mL, ferritin 15ng/mL. He is a long-distance runner and swimmer. His 15-year-old sister reported similar headaches, demonstrating a hemoglobin 20-22g/dL, normocellular marrow (80%) with erythroid and megakaryocytic hyperplasia. Peripheral evaluation: reticulocyte 1%, an elevated erythropoietin 46.4mIU/mL, a decreased ferritin 8.3ng/mL and additionally has type 1 diabetes mellitus. She swims as well and reports that both can hold their breath for ≥ 5 minutes. Genetic testing identified a paternally-inherited heterozygous pathogenic c.598C>T (p.Arg200W) variant in *VHL* and previously undescribed frameshift variant in *VHL* (c.460_467dup, p.Asp156Glufs*11).

Conclusion: We present two siblings living at altitude with symptomatic Chuvash polycythemia. This frameshift variant has not been previously reported amongst those with Chuvash polycythemia and recognizes the important of full *VHL* gene analysis in suspected cases. Few children have previously been reported and, despite headache and dizziness, they anecdotally demonstrate increased athletic capability. Unfortunately, adult cohorts report increased mortality after age 25 from thromboembolic events. The siblings will undergo, scheduled surveillance including neuroimaging, ECHO, peripheral blood monitoring, and have initiated low dose aspirin therapy. The impact of phlebotomy and suppression of erythropoiesis in adult cohorts has not proven beneficial with some additional concern that reduction in hemoglobin results in further upregulation of HIF-1, worsening the thromboembolic risk. The cases further expand the genotypic and phenotypic spectrum of Chuvash polycythemia.

Poster # 039

SAFE ADMINISTRATION OF GENDER-AFFIRMING HORMONE THERAPY IN A TEEN WITH ERYTHROPOIETIC PROTOPORPHYRIA

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Background: Literature is limited to guide hematologic monitoring during gender-affirming hormone therapy (GAHT) in transgender individuals. Administration of estrogen and testosterone risk thrombosis and polycythemia, respectively. Even less reported is the safety of such therapy on patients with congenital blood disorders.

Objectives: We present the case of a transgender female adolescent with erythropoietic protoporphyria (EPP) receiving high-dose estrogen and spironolactone GAHT.

Design/Method: We prospectively followed administration of GAHT for 1 year with scheduled clinical (history of photosensitivity events and exam) and laboratory evaluations (including liver function, ferritin, hemoglobin, alkaline phosphatase, and free and zinc protoporphyrin levels) at baseline, 1, 4, 5, and 12 months on therapy. Liver ultrasound was obtained prior to therapy and at 12 months. With local IRB approval, data was extracted from the electronic medical record and compared to annual visit data for the four years prior to GAHT. T-tests were used to compare mean lab values pre- and post-initiation of GAHT.

Results: Hepatic function, measured pre- and post-therapy, remained unchanged and within normal limits (Total bilirubin 0.7 vs 1.1 mg/dL, p: 0.06; AST 43 vs 23 U/L, p: 0.12; ALT 20 vs 18 U/L, p: 0.94). Hemoglobin was unchanged as well (12.5 vs 12.7 g/dL, p: 0.41). Free protoporphyrins, stably elevated at baseline, remained unchanged during GAHT (1323 vs 1777 mcg/dL, p: 0.41). Zinc protoporphyrins, within normal limits pre-therapy, demonstrated an initial mild elevation that normalized quickly without intervention. Mean zinc protoporphyrin levels were unchanged post-therapy (46 vs 52 mcg/dL, p: 0.52). Alkaline phosphatase, although decreased on therapy, remained within a normal range (141 vs 75 U/dL, p: 0.03). Ferritin, mildly decreased pre-therapy, demonstrated an overall increase post-therapy (9.27 vs 12.05 mg/mL, p: 0.04). Liver ultrasound and exam remained unchanged pre- and post-therapy. Frequency of major photosensitivity reactions (diffuse rash & blistering requiring therapy) at baseline was 0-1 episodes/year and 1 episode/year on therapy. No thrombotic events were reported on therapy.

Conclusion: We report the safe administration of high-dose estrogen based GAHT in a patient with EPP without negative impact on hepatic function, worsening of systemic protoporphyrin levels or photosensitivity events, and without thrombotic complications. Anecdotally, the patient reported significant improvement in mental health and quality of life on therapy emphasizing the importance the need for safe hematologic monitoring protocols for GAHT In transgender patients.

Poster # 040

IMPACT OF INTERFERON-GAMMA BLOCKADE IN CHILDREN WITH SEVERE IDIOPATHIC HEPATITIS AND CYTOPENIAS

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Background: Children with severe idiopathic hepatitis and immune dysregulation, likely driven by cytotoxic T-cells, face risks of liver and bone marrow failure, often necessitating liver and hematopoietic cell transplants. Steroids are the conventional treatment for this disease, anti-thymocyte globulin has been used in more severe cases who progress to acute liver failure. However, the potential of interferon-gamma blockade in halting the progression toward liver and bone marrow failure remains unexplored.

Objectives: Exploring the impact of interferon-gamma blockade on immune - mediated hepatitis in children with severe liver injury and cytopenias.

Design/Method: A single-institution case series.

Results: This pediatric case series documents the clinical course of four boys (3-11 years) between 2021-2023 with severe acute hepatitis who presented with jaundice, abdominal pain but no fever. One patient was EBV IgM+, otherwise the laboratory testing was negative for infections, metabolic and auto-immune processes. At presentation, AST ranged from 3000-5000 IU/ml, ALT 2000->6000 IU/ml, total bilirubin 11-23 mg/dl, INR -15-2.2, and ferritin 755 -1763 ng/ml. Liver biopsies were consistent for acute hepatitis with a predominant CD8+ T-cell infiltrate. Alongside the liver injury, patients had occurrences of progressive cytopenias. 50% of cases showed pancytopenia, while 50% showed anemia with thrombocytopenia. 75% patients had a bone marrow biopsy that showed mild to severe marrow hypoplasia with 50% of patients showing hemophagocytic cells and CD8+ T Cell predominance. All patients were initially treated with 2 mg/kg of systemic steroids for 1-3 months with additional therapies like IVIG. In the setting of suboptimal response to steroids and worsening cytopenias, inflammatory markers were analyzed and most notably, CXCL9 (interferon-gamma inducible cytokine) was found to be elevated in all patients (6300-32000 pg/ml, normal levels<647picogram/ml). Given this finding, interferon-gamma blockade with emapalumab was initiated. Starting dose of emapalumab was 1-3 mg/kg and patients received a total of 6-11 doses. All patients achieved complete resolution of hepatitis in 1-3 months and cytopenias in 1-4 months after initiation of emapalumab therapy. Additionally, CXCL9 values normalized in 1-3 months. In this case series emapalumab administration was found to be safe with only one documentation of line infection with staph aureus.

Conclusion: Interferon-gamma-induced immune dysregulation in severe idiopathic acute hepatitis highlights the need for targeted immunotherapy, which can potentially prevent the need for liver and hematopoietic cell transplantation. CXCL9 can potentially be used as a biomarker for diagnosis and treatment response.The dose, duration of treatment, and efficacy of Emapalumab should be studied in a clinical trial.

Poster # 041

RECALCITRANT CYTOPENIAS AS EARLY AND INITIAL PRESENTING FEATURES OF ACTIVATED PI3Kδ SYNDROME (APDS)

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Background: Recalcitrant cytopenias may be early warning signs of underlying inborn errors of immunity (IEI) such as activated PI3Kδ syndrome (APDS). However, IEIs may be overlooked when missing canonical features (eg, infections).

Objectives: Use APDS to highlight the importance of early genetic evaluation for patients with recalcitrant cytopenias, which may change diagnosis and alter management/outcomes.

Design/Method: Chart review of 3 male patients across 3 institutions.

Results: Patient 1: 3-year-old White male who presented with low platelets (25×10^9/L) and diffuse petechiae at 3 months. He received intravenous immunoglobulin (IVIG) for immune thrombocytopenia (ITP) that resolved at 1-month follow-up with a pediatric hematologist/oncologist. ITP at young age, history of hospitalizations for respiratory infections, and family history of recurrent sinopulmonary infections and common variable immune deficiency (CVID) prompted genetic testing, revealing a pathogenic variant in *PIK3CD* (E1021K) that resulted in an APDS diagnosis. Infections and asthma persist. Patient 2: 23-year-old White male who was referred to a pediatric hematologist/oncologist at 5 years for ITP. Initial examination revealed lymphadenopathy and petechiae. He was diagnosed with CVID requiring IVIG at 3 years and autoimmune lymphoproliferative syndrome (ALPS)-like features at 11 years. Thrombocytopenia persisted from ages 8 to 20 years (platelets, $6\text{-}37\times10^9$/L), occasionally requiring high-dose IVIG and rituximab infusions. These and other manifestations such as splenomegaly, asthma, infections—some with a family history—prompted genetic testing at 14 years, revealing apathogenic variant in *PIK3CD* (N334K). He received sirolimus for 4 years prior to bone marrow transplantation to treat refractory cytopenias and lymphoproliferation. Splenectomy at 21 years resolved thrombocytopenia. IVIG and antimicrobial treatment discontinued at 22 years. Patient 3: 5-year-old Black male who was referred to a pediatric hematologist/oncologist at 3 years for anemia (hemoglobin, 4 g/dL) and thrombocytopenia (platelets, 100×10^9/L). Leukemia, HIV, ALPS, and other diagnoses were excluded. Persistent anemia, colitis, infections, lymphoproliferation, and family history of autoimmunity prompted genetic testing, revealing a pathogenic variant in *PIK3CD* (E1021K). Sirolimus and IVIG resolved anemia (12.7 g/dL) and reduced spleen size (865 mL to 313 mL); fluctuating lymphadenopathy persists.

Conclusion: These cases illustrate recalcitrant cytopenias as an early feature of APDS and demonstrate challenges in differential diagnosis, highlighting the importance of genetic evaluation at initial presentation. Changes in management and outcomes can follow a definitive diagnosis. IP's opinions expressed in this abstract are her own and do not reflect views of the FDA, Department of HHS, or US government. Supported by Pharming Healthcare, Inc.

Poster # 042

NEXT GENERATION SEQUENCING-INFORMED MANAGEMENT OF PEDIATRIC AUTOIMMUNE CYTOPENIAS

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Background: Pediatric autoimmune cytopenias are a group of variable but closely related conditions defined by immune-mediated destruction of hematologic cell lineages. The causes may be primary or secondary to coexisting conditions such as immunodeficiency, immune dysregulation, malignancy, or rheumatologic disorders**.** While treatment typically involves nonspecific immune suppression or modulation, recent insights into disease biology have paved the way for targeted therapies, such as thrombopoietin mimetics in immune thrombocytopenic purpura (ITP) and sirolimus for cytopenias associated with autoimmune lymphoproliferative syndrome. Spleen tyrosine kinase (SYK) is an important regulatory molecule of signal transduction pathways involved in the pathogenesis of autoimmune diseases such as ITP, and the SYK-signaling pathway has emerged as a potential target for treatment.

Objectives: To discuss targeted treatment for autoimmune cytopenias in Casitas B lineage lymphoma *(CBL)* syndrome

Design/Method: Case Report

Results: A 16-year-old male presented with a past medical history of speech delay, acute disseminated encephalomyelitis, autoimmune thyroiditis, hepatosplenomegaly with portal hypertension, and complex immune cytopenia. Despite initial identification of a heterozygous variant of uncertain significance (VUS) in *CTLA4*, further functional studies did not support its pathogenicity. However, during the investigation of cytopenia, a somatic hematologic malignancy next generation sequencing panel revealed a VUS in the *CBL* gene (p.H398R) with a high variant allele frequency. Further analysis, including germline testing using skin fibroblast and parental studies identified this variant as de-novo, aligning with the diagnosis of *CBL* syndrome.

The patient's complex immune cytopenia was initially managed with rituximab and steroid therapy. When sirolimus failed to raise counts, fostamatinib, a SYK inhibitor, was initiated given the regulatory connection between the SYK pathway and the *CBL* gene. Mildly elevated liver function tests were noted prior to starting fosfamatinib which was thought to be immune-mediated and is now improving after treatment. Despite mild epistaxis, the patient did not require dose adjustment. No hypertension, nausea, abdominal pain, or diarrhea was noted. Due to suboptimal platelet rise initially, adjusting the fosfamatinib dosage to 150 mg twice daily resulted in increased platelet count and reduced spleen size, indicating decreased peripheral platelet destruction.

Conclusion: In conclusion, this case report highlights the intricate landscape of managing secondary complex immune cytopenias. In this patient, the identification of a de-novo *CBL* gene variant led to initiation of a SYK inhibitor, fostamatinib, after traditional treatment with rituximab and steroids. Our patient's positive response on fostamatinib suggests that SYK inhibition in *CBL*-associated autoimmune cytopenias may be a viable treatment for this patient population.

Poster # 043

AUTOIMMUNE LYMPHOPROLIFERATIVE RELATED DISORDER IN PATIENT WITH TRISOMY 21 AND AN IL-10RB MUTATION

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Background: Autoimmune Lymphoproliferative Syndrome (ALPS) is a rare condition characterized by a failure of lymphocyte apoptosis with resultant lymphoproliferation. Non-specific symptoms and variations in clinical presentation can lead to a diagnostic challenge. The criteria for ALPS diagnosis include chronic, non-malignant, non-infectious lymphadenopathy with elevated double negative T cells and either defective lymphocyte apoptosis or a pathogenic mutation. Patients with clinical and laboratory evidence concerning for ALPS who do not strictly fulfill the diagnostic criteria may have an ALPS-related disorder. Treatment is guided by clinical presentation and includes immunosuppressive agents such as corticosteroids, IVIG, and sirolimus.

Objectives: We report the case of a two-year-old male with a history of trisomy 21 who underwent extensive evaluation for chronic fever, lymphadenopathy, and urticarial rash and was subsequently diagnosed with ALPS-related disorder.

Design/Method: Case report.

Results: We present a 2-year-old male with trisomy 21, congenital hypothyroidism, several months of viral illnesses with fever, and associated urticarial rash with new onset bilateral edema of the hands and feet. Diffuse lymphadenopathy was noted on exam and confirmed with full body MRI. Infectious evaluation was remarkable for IgM/IgG positive for CMV, but noted to have thrombocytopenia, normocytic anemia, and elevated ESR, CRP, procalcitonin, and ferritin. Diagnostic evaluation was negative for malignancy but remarkable for lymph nodes with paracortical expansion due to infiltration by polyclonal TCRαβ+ CD4/8 negative T-cells.

The patient met 3 of 4 criteria for ALPS. Other pertinent labs showed elevated IL-5, IL-10, IL-6, soluble IL-2r (CD25), markedly elevated IL-18, and CXCL9, elevated CD4/8 negative T-cells. Genetic evaluation revealed several VUS, including a mutation for the gene encoding for IL-10RB duplication. The patient was successfully treated with IVIG, and corticosteroids followed by the addition of sirolimus due to persistently elevated inflammatory markers.

Conclusion: The complex and varied symptoms seen in ALPS can present a diagnostic challenge that requires a comprehensive evaluation. Despite efforts to redefine ALPS diagnostic criteria in 2010, there remain patients who demonstrate a clinical picture consistent with ALPS without strictly meeting the diagnostic criteria. The lymphocyte apoptotic pathway may be broader then yet understood and the role of IL-10RB mutations within this pathway should be explored. Aberrance in the IL-10RB pathway can manifest as an ALPS-related disorder. The unique presentation of this patient, and his response to ALPS treatment highlights the need for further research into ALPS and ALPS-related disorders.

Poster # 044

A MYSTERIOUS CASE OF TREATMENT-RESISTANT AUTOIMMUNE LYMPHOPROLIFERATIVE SYNDROME

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Background: Autoimmune lymphoproliferative syndrome (ALPS) is a disorder described as the uncontrolled production of lymphocytes manifesting as lymphadenopathy, splenomegaly, cytopenias, and, rarely, the development of secondary lymphoid malignancy. Multiple diagnostic criteria of ALPS exist, all requiring common ALPS clinical manifestations and elevation of double-negative T-cells in addition to various accessory criteria. ALPS has several genetic causes but is most commonly caused by defects in the apoptotic cell death mechanism via mutation of the Fas-mediated pathway.

Objectives: Describe the case of an 18-year-old male initially diagnosed with Evans syndrome with subsequent lymphoproliferation complicated by splenomegaly, lymphadenopathy, and cytopenias, indicative of ALPS, resistant to numerous treatment modalities.

Design/Method: Case report

Results: The patient presented at 9 years of age with thrombocytopenia and Coombs positive for IgG with no signs of hemolysis. He was unsuccessfully treated with intravenous immunoglobulin (IVIG) and steroids. Following initial hospitalization, he developed fluctuating neutropenia and intermittent immune-mediated hemolysis. Subsequent work-up showed isolated IgA deficiency, splenomegaly, and mildly hypocellular bone marrow with normal morphology. ALPS workup revealed elevated double-negative T-cells, ranging from 4-6%, but with normal FAS-mediated apoptosis and negative ALPS gene panel. Whole exome sequencing was completed with no causative mutations identified upon multiple re-analyses. Many treatments were trialed throughout his clinical course with varying levels of low or temporary success including high-dose steroids, mycophenolate mofetil, IVIG, rituximab, granulocyte colony-stimulating factor, eltrombopag, sirolimus, romiplostim and ultimately splenectomy. Following the splenectomy, he had recovery of counts and was weaned off medication. Unfortunately, about one-year post splenectomy, he presented with pneumonia with ground glass opacities on CT and significant gross adenopathy with biopsy showing follicular hyperplasia. He re-developed thrombocytopenia and neutropenia. He was trialed on hydroxychloroquine for potential B-cell effects with significant improvement of all cell lines.

Conclusion: ALPS consists of various genetic dysfunctions of the immune system and treatment typically entails immunosuppressants, which are not specific and are often complicated by treatment resistance and toxicities. Hydroxychloroquine is a safe and well-tolerated medication often used in the treatment of many autoimmune conditions; however, a clear mechanism of action is unknown. Recent work in murine models as well as limited case reports have shown success in the treatment of ALPS and ALPS-like disorders with the use of hydroxychloroquine, which may work through induction of cell apoptosis[1,2]. This suggests that hydroxychloroquine is a safe and steroid-sparing alternative for treatment-refractory ALPS.

1. Dowdell KC, et al, Blood, 2007.
2. Kiykim A, et al, J Clin Immunol, 2015.

Poster # 045

UNICENTRIC CASTLEMAN DISEASE COMPLICATED BY TRANSIENT PRESENTATION OF PARANEOPLASTIC PEMPHIGUS

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Background: Unicentric Castleman disease (UCD) is a rare lymphoproliferative disorder that can result in the systemic complication of paraneoplastic pemphigus (PNP), where an underlying neoplasm induces antibodies against the mucocutaneous system. Characteristic features include stomatitis, mucositis, and polymorphic cutaneous eruptions. Lesions are typically resistant to treatment, with many cases of UCD incidentally diagnosed through the workup of these lesions. PNP may affect bronchial respiratory epithelium and lead to an obstructive respiratory disease called bronchiolitis obliterans (BO).

Objectives: To report an atypical presentation of paraneoplastic pemphigus in a patient with bronchiolitis obliterans due to unicentric Castleman disease and review the literature.

Design/Method: We report an eight-year-old male with a history of mucosal lesions that resolved months prior to his presentation with BO secondary to UCD. We systematically reviewed Castleman disease cases resulting in PNP and BO on PubMed and MEDLINE databases.

Results: A previously healthy eight-year-old male presented with hypoxic respiratory failure. The patient's mother reported he had mucosal lesions successfully treated with dexamethasone at an outside hospital five months prior. Other than signs of respiratory distress, the rest of the physical exam was normal, with no rashes or mucosal lesions. A pelvic mass was discovered on ultrasound and confirmed as UCD hyaline vascular type by biopsy. Imaging findings suggested BO. Chest computer tomography showed diffuse areas of mosaic attenuation bilaterally, and pulmonary function tests revealed severe air trapping. The patient was treated with high-dose methylprednisolone pulse, hydrocortisone, intravenous immunoglobulin, and tocilizumab. His condition stabilized, and he underwent successful mass resection. Eleven months later, he received lung transplantation. Literature review of Castleman disease complicated by PNP and subsequently BO revealed that 80% of patients with evidence of PNP initially present for mucosal lesions (n=22). We identified two cases reporting adults without active mucocutaneous lesions. This is the first pediatric patient case reported. The rest of the patient's course was consistent with previous reports. At least 69% of survivors' pulmonary functions were stable but remained decreased (n=9). Similarly, our patient's pulmonary status did not improve with treatment and after UCD mass resection. However, he remained stable on supplemental oxygen and inhaled budesonide/formoterol until his lung transplantation.

Conclusion: This is the first pediatric patient reported with BO secondary to UCD presenting with isolated respiratory symptoms and no active mucosal lesions. Our case emphasizes the importance of considering an underlying neoplasm in seemingly healthy patients presenting with rapid respiratory decline due to BO.

Poster # 046

A SUBTLE AND UNUSUAL PRESENTATION OF UNICENTRIC CASTLEMAN'S DISEASE AND PARANEOPLASTIC PEMPHIGUS

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Background: Castleman's Disease (CD) encompasses a group of rare heterogeneous lymphoproliferative disorders with distinct histopathological variants that may present as unicentric (UCD) or multicentric disease (MCD). It is thought to involve clonal expansion of lymph node stromal cells. Individuals with CD are at increased risk of developing paraneoplastic pemphigus (PNP), an autoimmune disease of mucocutaneous lesions diagnosed by positive antiplakin antibodies on immunofluorescence and one or more mucus membranes involved. CD with PNP comprises an even smaller subset of the pediatric population, with very few cases reported, and can significantly impact morbidity and mortality. We present a unique case of a 17-year-old male with UCD and PNP presenting with dysphagia and found to have a hilar mass.

Objectives: To describe a unique case presentation of an individual with UCD and PNP presenting with dysphagia and highlight the diagnostic and therapeutic difficulties encountered.

Design/Method: Case report – A retrospective chart analysis was conducted.

Results: Our case involves a 17-year-old male with 5-6 months of difficulty swallowing solids, leading to a 40-pound weight loss. He denied pain, difficulty swallowing liquids, or airway obstruction. Symptoms were refractory to omeprazole and famotidine. An esophagogastroduodenoscopy revealed ulcerations in the lower third of the esophagus, and the scope could not pass through further. Biopsy consistent with esophagitis. A chest CT revealed a left infrahilar soft tissue mass, and a biopsy confirmed Hyaline Vascular (HV) type Castleman disease. Positive envoplakin IgG confirmed PNP. Further workup confirmed UCD. Although the standard of care for UCD is surgical excision, this was not possible in our case due to the location of the tumor. We gave a course of Rituximab and steroids that led to the resolution of dysphagia. Currently, he is receiving monthly Rituximab as maintenance therapy. As most cases of CD-associated PNP depicted in the literature describe oral lesions and skin findings, dysphagia and acute esophagitis are not commonly reported, thus adding to the limited information available on this presentation in children.

Conclusion: UCD and PNP are rare disorders that can co-occur in individuals of all ages and children more rarely. This case presents a distinctive presenting symptom of dysphagia that is not commonly seen in the literature and was responsive to steroids and Rituximab. Given this presentation is more subtle than oral lesions or visible skin findings oftentimes reported, providers must be vigilant in the prompt evaluation of occult UCD and its management in children.

Poster # 048

TRANSMISSION ELECTRON MICROSCOPY OF PLATELET DENSE GRANULES IN PEDIATRIC PATIENTS HEALTHY DONORS

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Background: PTEM whole mount (WM) is a standard method for evaluating platelet dense granules (pDG). However, a pediatric/adolescent pDG reference range (RR) and prevalence of pDG deficiency in symptomatic patients has not been well-established.

Objectives: This study aimed to establish a pediatric/adolescent RR for mean pDG and determine the prevalence of pDG deficiency in a cohort of patients who had clinical suspicion for platelet disorders (PD)

Design/Method: First, WM-PTEM was performed on healthy donors. A mean pDG RR was calculated by averaging DG of 100 plt per patient. Next, patients undergoing laboratory evaluation of suspected PD were recruited to this study. In addition to routine laboratory testing, their ISTH BAT score (normal <3; abnormal >3) was correlated with mean pDG.

Results: Healthy donors (n=77, 41.6% female), ages 3-18 years, had a mean pDG 2.7 (+/- 0.5) ranging from 1.9 to 3.8. The mean pDG did not correlate with age or gender. The tentative RR was calculated to be 1.9 to 3.8 DG/platelet. Nineteen patients over the age of three (25.3%, n=19/75) had <1.9 mean pDG. Of the 75 symptomatic patients (age 3-18 years, 69.3% female), 42 and 33 patients had BAT scores >3 and <3 (range 0-11), respectively. DG/plt in pt with bleeding scores >3 (mean=2.3 +/- 0.83, n = 42) vs. those with bleeding scores < 3 (mean=2.3+/-0.66, n = 32) (p=.206) were similar. There was no difference in the number of patients with normal or abnormal bleeding scores in groups with normal vs decreased mean DG/plt (p=.595)

Conclusion: In this study, we established a tentative pediatric RR for platelet DG at 1.9 - 3.8 DG/plt. Approximately 25% of patients were found to have DG deficiency. However, pDG did not not correlate with the ISTH BAT.

Poster # 049

CLINICAL STUDY TO DETERMINE THE PATHOGENESIS OF AUTOIMMUNE THROMBOCYTOPENIA

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Background: Immune thrombocytopenia (ITP) is a common pediatric autoimmune disorder that leads to platelet destruction and decreased platelet production. The majority of children with ITP will have spontaneous resolution, but after 6-12 months there remains a small proportion that develop chronic ITP. It is generally accepted that ITP is not only autoantibody mediated platelet destruction, but that cellular immunity and cytokines play a major role in the development and persistence of chronic ITP.

Objectives: The aim of this study is to determine if the immune and genetic profile of ITP patients can help identify factors that increase an individual's risk of developing chronic ITP.

Design/Method: We enrolled patients with newly diagnosed ITP from 9 months to 18 years of age at Children's Hospital of Orange County. Blood samples were drawn at the time of diagnosis, at time of platelet count recovery, and when patients developed chronic ITP. Samples were sent to Stanford University Human Immune Monitoring Center (HIMC). On each sample drawn, mononuclear cell profiles were evaluated using mass cytometry (Flow CyTOF) and cytokine levels were determined using the Luminex Assay. DNA and RNA samples were also collected and stored for future analysis.

Results: On each sample we were able to characterize 125 different parameters for mononuclear cell identification and enumeration along with 80 different cytokines. We collected samples from a total of 10 patients, generating over 3000 unique results on individuals evaluated thus far. Three of ten patients

went on to develop chronic ITP (2 adolescent females, one 2 yr old male). Although the numbers are small in this feasibility study, clear differences are observed between presentation and resolution of acute ITP. In the chronic ITP patients, the adolescents were noted to have lower levels of transitional B cells when compared to controls. Additional analysis in the acute ITP patients shows similar patterns within this group such as persistence of NK cell depression and shifts in Treg populations with resolution.

Conclusion: This study looks at an extensive profile of immune and cytokine markers in ITP. Though our patient cohort is currently small, we are continuing to enroll at least 150 more patients to document trends and identify risk factors that increase the likelihood of a patient developing chronic ITP. With early recognition of biomarkers identifying disrupted immune pathways, we hope to personalize therapy to prevent the persistence of thrombocytopenia.

Poster # 050

NAVIGATING HEALTH SYSTEM BARRIERS IN TREATING CHRONIC IMMUNE THROMBOCYTOPENIA WITH ELTROMBOPAG

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Background: The most recent American Society of Hematology (ASH) Immune Thrombocytopenia (ITP) guidelines for management of pediatric patients recommend thrombopoietin agonists such as eltrombopag as second line therapy for chronic ITP. Despite this recommendation, Canadian children face significant challenges in accessing eltrombopag if they do not have third party or employer insurance. In contradiction to the ASH guidelines, our government pharmacare program continues to recommend treatment with rituximab, mycophenolate mofetil (MMF) or splenectomy before considering coverage for eltrombopag.

Objectives: We reviewed the records of pediatric patients with ITP under our care in British Columbia who received eltrombopag with the objective of evaluating the challenges associated with procurement and documenting clinical outcomes.

Design/Method: Records of pediatric patients followed at British Columbia (BC) Children's Hospital between 2020-2023 with chronic ITP who received eltrombopag were reviewed. Demographic, treatment, payer and outcome data were collected and analyzed.

Results: Sixteen patients with chronic ITP were treated with eltrombopag. Two received coverage through government pharmacare, six through private insurance, five via combined private insurance and pharmaceutical company patient support programs (PSP), three exclusively through a pharmaceutical company PSP, and one via self-pay. Eleven patients received eltrombopag following failure of second-line therapy; two patients were treated with rituximab first without response, three (including the only two who received eltrombopag approval through government pharmacare) were treated with both rituximab and MMF without response. No patients underwent splenectomy prior to eltrombopag. Response (complete or partial) to eltrombopag was documented in twelve patients (75%), four patients (25%) had no response. Two patients have maintained a stable platelet count following an eltrombopag wean. The administrative burden and time delay in starting eltrombopag were

high due to the need to apply and be rejected by the government insurer before seeking approval through alternative supports, or in five patients, needing to treat with third-line treatments before eltrombopag.

Conclusion: Despite barriers imposed by the government payer, pediatric patients with chronic ITP who needed eltrombopag were able to eventually access the medication[RD1] and 75% achieved benefit. Despite consensus guidelines for use of eltrombopag as second-line therapy in pediatric ITP, 73% of our patients were only able to access it following failure of second or third-line therapy. It is hoped that presenting these findings to the government pharmacare program will aid in improving the approval process for future pediatric patients with chronic ITP in British Columbia.

Poster # 051

EVALUATING IRON DEFICIENCY IN PEDIATRIC PATIENTS OBTAINING A HEMOGLOBINOPATHY WORKUP

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Background: Low ferritin levels have been previously described to lower HbA2 percentages on hemoglobinopathy evaluation. Our institution has incorporated serum ferritin levels into an expanded panel test for thalassemia and hemoglobinopathy to assist with interpretation. Some experts have recommended a higher limit for ferritin with a lower threshold of 50 mcg/L. Lower ferritin levels, even in the absence of anemia or microcytosis, cause nonspecific symptoms such as fatigue, weakness, difficulty concentrating, and decreased productivity. A hemoglobinopathy evaluation can serve as a checkpoint to detect iron deficiency allowing for prompt treatment and amelioration of symptoms.

Objectives: To evaluate the relationship between ferritin levels and the occurrence of hemoglobinopathies among pediatric patients in a single institution.

Design/Method: This retrospective, single-center study was conducted through medical chart review and included patients aged 0-18 years who had their first thalassemia and hemoglobinopathy testing between January 1, 2023 and July 28, 2023. Low ferritin was defined as a ferritin level less than or equal to 25 mcg/L. Pearson's Chi Squared test and the Kruskal Wallis test were used for statistical analysis of categorical and continuous variables respectively.

Results: Seventy-seven eligible patients were identified. Thirty-five were found to have low ferritin levels (45.5%) and median ferritin levels were 26.5 (Q1=15.5, Q3=54.5). Among those with a low ferritin level, 15 patients also had a hemoglobinopathy present (41.7%) with no significant difference compared to those with normal ferritin levels (p value = 0.467). Patients with normal ferritin levels were older compared to those with low levels 12.2 years vs 6.8 years (p value = 0.001), 14 (42.4%) patients with low ferritin had no anemia and 29 (82.9%) never received prior iron supplementation. Patients of Asian race were more likely to have received prior iron supplementation 27.3% (p value = 0.004). The average age of hemoglobinopathy diagnosis was 9.1 years (95% Confidence Interval 6.6-11.7 years).

Conclusion: There was no significant difference between those patients having a hemoglobinopathy present and lower or higher ferritin levels. Iron deficiency was more often noted among the younger patients even in the absence of anemia. The majority of patients with iron deficiency detected had

never received prior iron supplementation until the time of their hemoglobinopathy evaluation. This also demonstrates that many providers may not do a stepwise workup but order all the evaluations at once. Our results suggest that enhanced characterization of iron deficiency parameters for patients receiving a hemoglobinopathy evaluation is warranted.

Poster # 052

IRON DEFICIENCY ANEMIA IS ASSOCIATED WITH DEPRESSIVE SYMPTOMS IN ADOLESCENT HEAVY MENSTRUAL BLEEDING

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Background: It is well reported that heavy menstrual bleeding (HMB) in adolescents can cause iron deficiency (ID) with or without anemia (IDA). ID has been associated with depression in two previous studies: among adults with inflammatory bowel disease, and in a self-reported survey-based study of healthy adults. However, this association is not well-studied among patients with HMB. A significant association between high Patient Health Questionnaire scores (PHQ-9; a validated screening tool to assess depression risk) and adolescent HMB has been previously reported in two single-center studies.

Objectives: We aimed to assess the prevalence of depressive symptoms, ID/IDA, and the association between depressive symptoms with/without ID/IDA among adolescents with HMB.

Design/Method: With IRB approval, we conducted a retrospective study by records review of adolescents aged 10-21 years with HMB and a documented PHQ-9 score, from 2019-2023. HMB was defined as menstrual bleeding >7 days, soaking through a pad/tampon in <2 hours, passage of clots ≥quarter-size, and/or PBAC (Pictorial Blood Assessment Chart) score⩾100. ID was defined as ferritin<25 ng/ml, and IDA as hemoglobin (Hgb)<12 g/dl with low iron studies. Depressive symptoms were categorized by PHQ-9 scores as mild (5-9), moderate (10-14), moderately severe (15-19), or severe (⩾20). Chi-squared tests (significance level $p<0.05$) and Pearson's correlation were used to compare ID/IDA with PHQ-9 scores.

Results: Among 125 adolescents with HMB included, the median of averaged menstrual cycle durations was 7 days (interquartile range 6-10), and 39 patients had a bleeding disorder (30.7%). Based on available ferritin and Hgb values, 91/114 patients had ID (79.8%), and 64/123 had IDA (52%). Depressive symptoms were noted in 84 patients (67.2%), which were categorized as mild (N=36; 28.8%), moderate (N=26; 20.8%), moderately severe (N=13; 10.4%) or severe (N=9; 7.2%). Chi-squared analysis showed a significant association between the presence of IDA and depressive symptoms categorized as "moderate" or higher (PHQ-9 score>9), compared to those without IDA ($p=0.004$).

Conclusion: Depressive symptoms, ID, and IDA were highly prevalent in adolescents with HMB in our study, as in previous reports. Furthermore, this study shows a statistically significant association between IDA and depressive symptoms of moderate or higher severity among adolescent patients with HMB. These results highlight the importance of providing routine PHQ-9 screening to adolescent HMB patients with IDA, as both depression and IDA have previously been shown to correlate with impaired

quality of life. As our study is ongoing, future steps include analysis of changes in depressive symptoms with correction of ID/IDA in these patients.

Poster # 053

A STANDARDIZED ANALYSIS OF FATIGUE IN CHILDREN WITH IRON DEFICIENCY AND IRON DEFICIENCY ANEMIA

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Background: Children with iron deficiency (ID) and iron deficiency anemia (IDA) often present with fatigue as a predominant symptom, affecting activities of daily living and translating to a poor quality of life. Early studies were unable to show a clear association between fatigue and ferritin/hemoglobin levels due to lack of proper instrumentation to assess this clinical problem.

Objectives: The aim of this study is to evaluate patient and parental assessment of fatigue for those diagnosed with ID and IDA using a validated fatigue scale.

Design/Method: PedsQLTM Multidimensional fatigue scale was administered to patients > 2 years of age affected with ID/IDA and their parents at St Christopher's hospital for Children in Philadelphia, PA. Lower scores (<50%) on the survey indicated significant fatigue. We performed a retrospective chart review of the participants to obtain cause of ID/IDA, demographics, hemoglobin, red cell indices, iron studies and response to treatment. A total of 72 sets of surveys were analyzed. Correlation and ANOVA analyses were applied.

Results: Results showed patients and parents reported similar fatigue scores as evidenced by the significant moderately positive correlation between the two groups for all fatigue categories, with correlation coefficients ranging between 0.534-0.637 (p-value <0.001). Among all patients, 60% reported total fatigue scores less than 50; 74% reported significant sleep/rest fatigue, 47% reported significant general fatigue, and 45% reported cognitive fatigue. There was no statistically significant difference between fatigue scores in patients with ID and IDA.

Conclusion: Among our population, a significant amount of ID and IDA patients reported high fatigue levels. Fatigue scores did not differ between patients with ID and IDA suggesting that low serum ferritin may be contributing more to fatigue than anemia, as we would expect patients with IDA to have lower scores. Ultimately, we plan to expand our study to a larger sample size and to investigate changes in serum ferritin levels and fatigue scores with ID and IDA populations after completion of iron therapy.

Poster # 054

ETIOLOGIES OF IRON DEFICIENCY ANEMIA IN CHILDREN PRESENTING TO A TERTIARY CARE FACILITY

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Background: Iron deficiency anemia (IDA) is the most common type of anemia worldwide, affecting more than 6 million individuals. In children, IDA can impair psychomotor and cognitive development. Inadequate intake is thought to be the most common cause of iron deficiency anemia, but decreased absorption and blood loss are other possible explanations.

Objectives: To highlight trends and unique findings related to the etiologies of iron deficiency anemia secondary to blood loss in children presenting to a tertiary care facility.

Design/Method: This was a retrospective chart review with 91 subjects. Patients were identified using the ICD 10 code D50.0 (iron deficiency anemia secondary to blood loss). The inclusion criteria for children 6 months to <5 years were ferritin <15 mcg/L and hemoglobin <11 g/dL and for children 5 to 18 years were ferritin <15 mcg/L and hemoglobin <11.5 g/dL. Demographic, baseline and follow up data were collected, and each subject was classified by etiology. Qualitative data were described using frequencies and quantitative data were analyzed using t-tests.

Results: Of the 91 subjects, 76 (83.5%) were female and 15 (16.5%) were male. The frequency of each etiology was heavy menstrual bleeding (HMB) 53 (58.3%) subjects, bleeding disorders 22 (24.2%) subjects, inflammatory bowel disease (IBD) 8 (8.8%) subjects, H. pylori 5 (5.5%) subjects, multifactorial 4 (4.4%) subjects, non-IBD GI bleeding 3 (3.3%) subjects, dietary 2 (2.2%) subjects, and other bleeding 1 (1.1%) subjects. Compared to baseline laboratory values, there was significant improvement with treatment in follow-up laboratory values, including hemoglobin ($p<0.001$), MVC ($p<0.001$), ferritin ($p<0.001$), serum iron ($p=0.005$) and transferrin saturation ($p<0.001$). Patients with HMB with underlying bleeding disorder had statistically inferior improvement in serum iron ($p=0.02$) and transferrin saturation ($p=0.40$). Thirteen percent of the patients with HMB were diagnosed with a bleeding disorder. Thirty three percent of patients had an underlying systemic chronic illness such as IBD or a bleeding disorder.

Conclusion: Pediatric patients presenting to a tertiary care facility with IDA secondary to blood loss receive effective treatment to address the IDA. Approximately a third will have a systemic cause. HMB, bleeding disorders and IBD are the most common underlying etiologies. Bleeding disorders are likely to be under-diagnosed in patients with HMB. Association of HMB and bleeding disorder leads to inferior treatment outcomes of IDA.

Poster # 055

EFFICACY AND SAFETY OF BETI-CEL IN PEDIATRIC PATIENTS WITH TRANSFUSION-DEPENDENT β-THALASSEMIA

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Background: Betibeglogene autotemcel (beti-cel) gene therapy addresses the underlying cause of transfusion-dependent β-thalassemia (TDT) by adding functional copies of a modified version of the β-globin gene to autologous CD34+ hematopoietic stem and progenitor cells (HSPCs) via a third-

generation, self-inactivating lentiviral vector (LVV). Following one-time beti-cel therapy, functional adult hemoglobin (HbA^{T87Q}), is produced in red blood cells.

Objectives: To report long-term outcomes from pediatric patients treated with beti-cel.

Design/Method: Patients with TDT who completed either a phase 1/2 (HGB-204 [NCT01745120]; HGB-205 [NCT02151526]) or phase 3 (HGB-207 [NCT02906202]; HGB-212 [NCT03207009]) beti-cel parent study and subsequently participated in the long-term, 13-year follow-up study LTF-303 (NCT02633943) were included. Efficacy (transfusion independence [TI], defined as a weighted average Hb ≥9 g/dL without packed red blood cell transfusions for ≥12 months) and safety for pediatric patients (<18 years of age at enrollment) are reported through last follow-up.

Results: As of January 30, 2023, 63 patients (pediatric: n=32, median [range] age: 11.5 [4.0-17.0] years; adult: n=31, median [range] age: 21.0 [18.0-35.0] years) had received beti-cel in a phase 1/2 or 3 study and enrolled in LTF-303. Pediatric patients had a median (range) follow-up of 48.2 (23.8-102.2) months, and adult patients had 82.7 (41.5-109.5) months of follow-up. In phase 3 studies, which used the commercial drug product (DP) manufacturing process, 25/27 (92.6%) pediatric and 12/14 (85.7%) adult patients achieved and maintained TI through last follow-up (up to 6 years). Twenty-three of 27 (85.2%) pediatric and 9/14 (64.3%) adult patients required only 1 mobilization cycle to achieve the DP dose. Median percentage of transduced DP cells was comparable between pediatric and adult populations (80% and 78%, respectively), as were month 6 median peripheral blood vector copy number (0.9 c/dg and 1.4 c/dg) and HbA^{T87Q} (8.3 g/dL and 9.4 g/dL).
Overall, 12/63 (19.0%) patients (pediatric: n=6; adult: n=6) experienced ≥1 beti-cel–related adverse event (AE). Beti-cel–related AEs occurring in ≥3 patients included abdominal pain (5/63 [7.9%]; pediatric: n=2) and thrombocytopenia (3/63 [4.8%]; pediatric: n=1). Five patients (pediatric: n=3) experienced serious veno-occlusive liver disease; all 5 received defibrotide and recovered. No malignancies, insertional oncogenesis, or vector-derived replication-competent lentivirus were reported.

Conclusion: Beti-cel is a potentially curative gene therapy for patients with TDT across ages through the achievement of TI and normal or near-normal Hb. These data will inform real-world beti-cel treatment decisions for patients with TDT across age subgroups.

Funding Statement: These studies were funded by bluebird bio, Inc.

Poster # 056

CHILDHOOD AUTOIMMUNE HEMOLYTIC ANEMIA: A SCOPING REVIEW

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Background: Autoimmune hemolytic anemia (AIHA) is a disorder characterized by excessive premature red blood cell breakdown due to the presence of autoantibodies. It is rare in children, with an estimated incidence of 0.2 per one million individuals younger than 20 years. Contemporary approaches to investigation and management are derived from adult guidelines.

Objectives: This scoping review will summarize the current landscape of diagnosis and management of pediatric AIHA to inform future studies aimed at formulating pediatric specific approaches to the investigation and management of this small but complex patient population.

Design/Method: This review searched MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials (CENTRAL) from inception to November 3rd, 2023. All screening and data extraction was done in parallel by two reviewers. Experimental and observational studies reporting on diagnostic criteria, laboratory work up, or treatment/management of AIHA in populations with at least 20% of patients ≤18 years were included. Study characteristics, population characteristics, and study outcomes were extracted and synthesized narratively and descriptively using counts (percentages).

Results: After removing duplicates, 2107 titles and abstracts were screened and 125 studies underwent full-text review. Forty three studies, published between 2003 and 2023, met inclusion criteria and proceeded to data extraction. Forty cohort studies and 3 case-control studies were included. No randomized controlled trials were identified. Diagnostic criteria for AIHA was provided in 31 (72%) studies, with 6 (14%) studies classifying the severity of AIHA. All studies defining AIHA included at least one of: positive direct antibody test, evidence of anemia, and evidence of hemolysis. Twenty-one studies (49%) reported AIHA subtypes within their population.

Patients with Evan's syndrome were included in 27 (63%) studies, and 15 (35%) studies included special populations such as transplant recipients or patients with autoimmune conditions. AIHA treatments in pediatric patients were reported in 40 (93%) studies, with 26 (60%) studies dividing the treatments into first- and second-line therapies. Common first-line therapies included intravenous immunoglobulin (IVIG), steroids, or a combination of these therapies. Common second-line therapies included rituximab, cyclosporine, IVIG, or combinations of these therapies.

Conclusion: Our review identified that most research into pediatric AIHA are single centre, retrospective studies, and case definitions are variable. A standardized definition and severity classification of pediatric AIHA is needed. With increasing availability of novel immuno-therapies it is important to establish a framework for multi-institutional collaboration to conduct prospective studies into this rare disease.

Poster # 057

AUTOIMMUNE HEMOLYTIC ANEMIA IN INFANTS YOUNGER THAN 6 MONTHS OF AGE

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Background: Autoimmune hemolytic anemia (AIHA), characterized by autoantibody-mediated red cell destruction, is rare in children and even less common in infants <6 months old. Given the rarity in infants, there is limited data to guide diagnostic evaluation and management.

Objectives: To describe the clinical characteristics, disease course, and treatment outcomes of infants with AIHA.

Design/Method: Single-center cohort study of patients with AIHA diagnosis at age <6 months between

2012-2022.

Results: Six patients with AIHA were diagnosed at age <6 months over this 10-year period at a large tertiary care center. Median age at diagnosis was 3.5 months (range 1.6-5.5). All had warm AIHA with DAT positive for IgG (6/6) and 2 were positive for C3. Median hemoglobin at diagnosis was 4.4 g/dL (range 3-6.8). Concurrent medical issues included giant cell hepatitis (n=1), iron deficiency anemia (n=1), and immune thrombocytopenia (n=1). None had a history of preceding infection, pre-term birth, or cardiac surgery.
All patients had an immune evaluation which included at least immunoglobulins and lymphocyte subsets. Immunoglobulin tests were normal except for IgA deficiency in one patient. Lymphocyte subsets revealed low CD3+ T cells (n=2), low CD4+ (n=2), normal CD8+ (n=6), and normal or high CD19+ (normal n=5, high n=1). CD3+CD4-CD8- T cells were measured and normal in 5/6 patients. Genetic testing for immune dysregulation was sent in 5/6 patients. Identified genetic findings included trisomy X (n=1), missense variant in DIAPH1 (n=1).
All patients required at least one red cell transfusion. Treatments included: 33% (n=2) corticosteroid monotherapy and 66.7% (n=4) multi-agent pharmacotherapy. Complete response (CR) was seen with corticosteroids in 3/6 (50%) and partial response (PR) in 3/6 (50%). Responses to other agents included rituximab (CR, n=1), sirolimus (CR, n=1; PR, n=1), mycophenolate (NR, n=1), 6-mercaptopurine (CR, n=1), and IVIG (NR, n=1). PJP prophylaxis was prescribed to three receiving multi-agent pharmacotherapy. IgG replacement was required in 33.3% (n=2). Median follow-up was 22.8 months (range 5.8-148.9). All required ongoing pharmacotherapy at 3 months, 66.7% (4/6) at 6 months, 40% (2/5) at 12 months, and 50% (1/2) at 24 months. All patients were alive at most recent follow-up and 33.3% (n=2) remained on treatment.

Conclusion: Warm AIHA presents infrequently in infants <6 months old. In this cohort, an underlying immune disorder was not identified in most patients despite extensive testing. Although many patients required immunosuppressive therapy beyond corticosteroids, there was a high rate of treatment response. Most infants required ongoing pharmacotherapy beyond 6 months from diagnosis.

Poster # 058

GENETIC TESTING FOR INHERITED BONE MARROW FAILURE IN PEDIATRIC PATIENTS WITH SEVERE APLASTIC ANEMIA

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Background: When patients present with severe aplastic anemia (SAA), identifying inherited bone marrow failure syndromes (IBMFS) is critical to inform treatment decisions. Since genetic testing can delay therapy for these severely cytopenic patients, we investigated the incidence of cryptic IBMFS in patients diagnosed with idiopathic SAA following negative comprehensive clinical and laboratory evaluations based on current standards of care.

Objectives: Our study aims to determine the incidence of IBMFS in pediatric patients who meet Camitta

criteria for diagnosis of SAA, and whose laboratory workup, including chromosome breakage testing, physical exam, past medical history and family history are not suggestive of an IBMFS.

Design/Method: The project is a multi-institutional retrospective study of 151 pediatric and young adult patients (age <25 years) presenting with idiopathic SAA between 2004-2021. All patients consented to participate in clinical research studies approved by each local IRB. De-identified clinical data were entered into a REDCap database. We performed exome sequencing of blood or bone marrow samples and sequencing results were filtered to identify variants in 94 genes associated with IBMFS. Variants were then classified based on criteria from the American College of Medical Genetics and Genomics and the Association for Molecular Pathology.

Results: 1020 variants from 151 patients were curated. Most were classified as benign/likely benign (n=958, 93.9%), with an additional 57 (5.6%) variants of uncertain significance and 5 pathogenic/likely pathogenic variants (0.5%).

One patient had two pathogenic variants (PVs) in *FANCC;* however, the zygosity of these variants is still under analysis. The patient underwent hematopoietic stem cell transplant with standard conditioning and no unexpected toxicity, so the diagnosis of Fanconi anemia is unlikely. Two other patients had PVs in IBMFS genes but, in retrospect, had histories suggestive of an IBMFS at the time of diagnosis. One patient had two PVs in *ERCC6L2* (zygosity unknown). She presented with progressive cytopenias over 5 months. Another patient was found to have a missense PV in *SAMD9L*. He had paternal family history of an uncertain neurodegenerative disorder*,* consistent with pancytopenia-ataxia syndrome.

Conclusion: Of 149 patients with SAA and negative clinical evaluation, none had an identifiable IBMFS. Therefore, the benefit of delaying SAA treatment for genetic testing may be low for patients with negative workup/history. On contrast, two patients with concerning history at presentation were found to have possible IBMFS, indicating that genetic testing is indicated for patients with positive findings on standard comprehensive diagnostic workup.

Poster # 059

PERIPHERAL BLOOD AS A SOURCE FOR MONITORING CLONAL HEMATOPOIESIS IN BONE MARROW FAILURE SYNDROMES

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Background: Inherited bone marrow failure syndromes (IBMFS) and acquired aplastic anemia (AA) in childhood are characterized by variable risk of myeloid malignancies which can be driven by pre-existing clonal hematopoiesis. The multitude of clonal genetic alterations with both rescuing and leukemogenic potential prompted the adoption of integrated diagnostic techniques like next-generation sequencing (NGS) and single nucleotide polymorphism (SNP)-array. These are employed for clinical decision-making and monitoring. However, it is unknown if peripheral blood (PB) testing could effectively replace the more invasive bone marrow (BM) sampling.

Objectives: Our aim is to explore the PB source as standard practice for monitoring clonal evolution in IBMFS/AA.

Design/Method: Between May 2019-December 2023 we studied a cohort of 54 IBMFS/AA patients; 42 (77.8%) underwent evaluation at >1 time point with a median follow-up of 12 (range 6-15) months. We examined 36 paired BM/PB samples using NGS, and 33 using SNP-array. Patients' median age was 10 years (IQR 4.5-16 years), with a 0.6 M|F ratio.

Results: The cohort consisted of 9 severe AA, 5 non-severe AA, 1 childhood MDS and 39 IBMFS/MDS predisposition syndromes (10 *ELANE*-associated neutropenia, 10 *SAMD9L*-syndrome, 4 *SAMD9*-syndrome, 4 Shwachman-Diamond syndrome (SDS), 3 *RUNX1*-familial platelet disorder, 2 *GATA2*-deficiency, 2 Fanconi anemia, 1 Diamond-Blackfan anemia, 1 *ERCC6L2*-syndrome, 1 congenital amegakaryocytic thrombocytopenia, 1 leukocyte adhesion deficiency type I). NGS on PB failed in 2 instances due to insufficient DNA. NGS and SNP-array testing was not informative (no lesions identified) in 15/36 and 23/33 of paired-analyzed cases, respectively. In remaining cases with alterations, paired NGS results were concordant (BM=PB) in 88.9% and discordant in 1.8% (BM-/PB+) and 9.3% (BM+/PB-). For cases with BM+/PB- discordance, variant allele frequency (VAF) in BM was ≤4% in all but one case (*BCOR*, 6.5%). Conversely, paired SNP-array results were concordant in 94% and discordant (BM+/PB-) in 6% of cases. There was an overall concordance of VAF% between somatic mutations in BM and PB (R^2 =0.73, p<0.0001). Importantly, longitudinal NGS analysis in PB was able to both detect clinically relevant clone variations (e.g. increase of *TP53*-clone in SDS patient from 16% to 38% within 6-month-period) and verify clone stability over time (e.g. *SAMD9/9L*-syndromes).

Conclusion: Our analysis shows PB testing can effectively monitor clonal alterations in children with IBMFS/AA identified through initial paired BM/PB analysis. Using PB for long-term disease surveillance may reduce reliance on invasive bone marrow biopsies for clinical decision-making.

Poster # 060

MODELING A NOVEL RIBOSOMAL PROTEIN MUTATION IN RPL30 TO PREDICT ITS ROLE IN DIAMOND BLACKFAN ANEMIA

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Background: Diamond Blackfan anemia (DBA) is an inherited bone marrow failure syndrome that is also a ribosomopathy (disease due to ribosome defects). We identified a novel heterozygous variant (c.167+769C>T) in the noncoding region of *RPL30* in a patient diagnosed with DBA. Elucidation of the function of *RPL30* and specifically this noncoding variant with DBA will provide new insight into the pathogenesis of this disease.

Objectives: To create a human cell line model to assess our hypothesis that the transcription and production of ribosomal protein L30 impacts differential gene expression, causes a stressed nucleolar phenotype, and decreases global protein production.

Design/Method: With an established human cell line (hTERT retinal pigment epithelial cells), we applied

CRISPR-Cas9 editing to incorporate the *RPL30* mutation. Since the mutation is noncoding, blocking mutations were avoided and a novel step-wise approach with three RNA guides was employed. With the resultant three homozygous clones of the mutation along with wild type (WT), we performed RNAseq to assess *RPL30* and overall gene expression. We used immunofluorescence to evaluate nucleolar protein organization and assign a normality score (decreased in stress), previously established in our lab. Lastly, to assess any changes in global protein production, we performed an OPP Click-It Assay.

Results: In the three confirmed homozygous clones, RNAseq demonstrated a consistent, alternative splicing pattern with decreased levels of the *RPL30* transcript. Gene expression analysis identified Herpes simplex virus 1 infection as the top inhibited KEGG pathway for all mutants, implicating apoptotic pathways such as p53 (p=10e-16). Upon review of the nucleolar morphology and organization, *RPL30* mutants had an increased normality score compared to WT. Lastly, OPP Click-It Assay revealed global protein translation was unchanged between mutants and wild type.

Conclusion: With a novel CRISPR-modified human cell model of a unique, noncoding *RPL30* mutation, we demonstrated the impact on transcription of the gene as well as differential downstream gene expression. Although we hypothesized this mutation would cause nucleolar stress and a lower normality score, we observed potential upregulation of ribosome biogenesis amplifying the score. Such findings suggest the mutation impacts transcription and L30 but also may trigger a compensatory response in some cell types, leading to inhibited apoptotic pathways and comparable levels of global protein translation. Further study is merited to reveal the role of this mutation in human stem cells and its functional impact on hematopoiesis, which is ultimately observed in the clinical phenotype of this disease.

Poster # 061

A NAPAAC Survey of Practices in Diagnosis and Treatment of Children with Moderate Aplastic Anemia

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Background: Pediatric moderate aplastic anemia (MAA) lacks defined diagnostic criteria or clear standard-of-care for management. Little is known about the natural history of spontaneous recovery versus progression to severe bone marrow failure (BMF), response to conventional immunosuppressive therapy (IST), or evolution to myelodysplasia (MDS).

Objectives: To better understand population characteristics and management practices for children with MAA.

Design/Method: A survey was conducted through the North American Pediatric Aplastic Anemia Consortium (NAPAAC), consisting of 52 centers with experts in BMF across North America. A total of 65 surveys were completed by pediatric hematology-oncology providers (55 attending physicians, 5 nurse practitioners and 5 fellows).

Results: There was marked variability for the definition of MAA. When asked to consider individual

cytopenias as criteria to define MAA, only neutropenia (ANC<1000 cells/ul) was widely considered (79%) while thrombocytopenia (<100K cells/ul), anemia for age, and bone marrow hypocellularity (≤50% cellularity) were considered by less than half (48%) of the responders to be necessary for diagnosis. However, of combined diagnostic criteria, the combination of hypocellular bone marrow plus any two cytopenias was the most common diagnostic definition of MAA supported by 60% of participants.

51% considered targeted next generation sequencing (NGS) and 4% considered whole exome/whole genome sequencing as part of the initial work-up for MAA. Cytogenetics and FISH are obtained more frequently in the initial marrow evaluation (86% and 73%, respectively). The two highest reported indications for treatment were dependence on red blood cell (92%) or platelet (87%) transfusions followed by persistent cytopenias (54%) and cytogenetic abnormalities (53%). Acquired somatic variants triggered treatment in 30% of responses, and infections were a trigger for treatment in 35%. The most common management approaches were observation with transfusions (79%), the use of thrombopoietin receptor agonists (71%) and IST (61%). Progression to severe aplastic anemia (SAA, 97%), myelodysplastic syndrome (MDS, 97%), or refractoriness to IST (61%) were the most common indications for hematopoietic stem cell transplant (HSCT). Availability of a matched sibling donor (MSD, 12%) was an infrequent indication for HSCT in the absence of other reasons.

Conclusion: We observed significant variability regarding the diagnostic criteria and management of children with MAA. Half of practitioners use NGS panels routinely, suggesting a growing awareness to consider germline predisposition at initial diagnosis. Marrow evaluation (cellularity and cytogenetics) highly influence the diagnosis. The heterogeneous survey responses suggest the need to establish guidelines for uniform work-up and treatment, and to facilitate research of this understudied population.

Poster # 062

BENIGN TUMORS AND NON-MELANOMA SKIN CANCERS IN PATIENTS WITH FANCONI ANEMIA

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Background: Fanconi anemia (FA) is an inherited bone marrow failure syndrome characterized by pathogenic variants in the FA DNA repair pathway encompassing 22 genes. Typically diagnosed around age 7, this condition leads to congenital abnormalities and cancer predisposition. Individuals with FA have an elevated risk of developing myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), and solid tumors. Hematopoietic cell transplantation (HCT) is the most effective treatment for FA related bone marrow failure but can increase the risk of cancer development. The most common tumors seen in patients with FA are head and neck squamous cell carcinoma but can also occur in the brain and reproductive system. There have been no previous reports of benign tumor development in patients with FA.

Objectives: Thoroughly characterize patients with FA enrolled in the National Cancer Institute Inherited Bone Marrow Failure Syndrome (IBMFS) Study who have experienced non-melanoma skin cancers and/or benign tumors.

Design/Method: A total of 200 patients diagnosed with FA were enrolled in the Institutional Review

Board approved study "Etiologic investigation of cancer susceptibility in IBMFS: A Natural History Study" **(**NCT00027274). Through medical records review, we identified 30 patients with at least one non-melanoma skin cancer (NMSC), either squamous cell carcinoma (SCC) or basal cell carcinoma (BCC), or benign tumor. The remaining 170 patients comprised the control group. Diagnoses were extracted from pathology reports, physician notes, and personal relation and self-report.

Results: Out of 200 patients, 12 had NMSC, 25 had benign tumors, with an age range of 11-64 and 0-56, respectively. Six patients with NMSC and 11 with benign tumors underwent HCT; Median age at HCT for patients with NMSC was notably higher (30.5 years old (yo)) than benign tumors (9yo) and controls (9.1yo). More women than men had either benign tumor(s) or NMSC(s) compared to controls. The most common genotype observed was *FANCA*, followed by *FANCC* and *FANCI*. Benign tumors occurred in various anatomical locations.

Conclusion: Patients with FA who had NMSCs experienced this cancer at a younger age than the general population. Given this early onset, it is imperative to establish consistent skin cancer monitoring protocols for patients with FA. Among the 25 patients with benign tumors, the distribution spanned diverse anatomical locations, including the central nervous and endocrine systems. Some patients presented with multiple benign tumors and skin cancers, underscoring the need for comprehensive surveillance. This proactive approach is crucial for timely interventions to manage heightened cancer risk in these individuals.

Poster # 063

ROMILOSTIM FOR TREATING CHILDREN WITH SEVERE APLASTIC ANEMIA AND MELODYSPLASTIC SYNDROME

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Background: Thrombopoietin receptor agonists (TPO-RA), eltrombopag and romiplostim, induce trilineage hematopoiesis by binding with TPO receptor C-MPL expressed on hematopoietic stem progenitor cells (HSPCs). These agents have emerged as promising therapeutics for treatment of severe aplastic anemia (SAA) and low-risk myelodysplastic syndrome (MDS). Recently eltrombopag has been approved for children (ages $\geq$ 2 years) with SAA along with standard-of-care immunosuppressive therapy (IST) but emerging data is questioning its efficacy for treating children with SAA. Although romiplostim is more potent that eltrombopag in inducing HSPCs, its safety and efficacy for treating children with SAA/MDS is unknown.

Objectives: Evaluate safety, tolerability and preliminary efficacy of romiplostim (Nplate®), a TPO-RA, with or without standard of care immunosuppressive therapy (±IST) for children (ages $\leq$ 21 years) with newly diagnosed and relapsed/refractory SAA and MDS.

Design/Method: Data were collected from an observational study and a single-arm, open label, interventional pilot study. The primary safety outcome was treatment-related adverse events (AEs). Safety was assessed by occurrence of treatment-related AEs according to NCI CTCAE v5.0, and by parameters specific to this patient population and for intervention including bleeding, clonal evolution,

thrombocytosis, bone marrow fibrosis and elevation of liver enzymes and bilirubin. Efficacy was evaluated by trilineage hematopoietic response with complete hematopoietic response (CHR) defined as improvement in platelets ≥ 100 K/mm^3, hemoglobin ≥ 10 g/dL, and ANC 1.0 K/mm^3. Romiplostim regimen consisted of a 5 mcg/kg/week starting dose, with dose escalation of 2.5 mcg/kg/week (maximum, 20 mcg/kg/dose) until platelet response was observed. This dose was continued up to 52-weeks with response assessment at weeks-12, 24, 52, and 90-days post-therapy

Results: Ten patients [SAA, 9 (IST, 4; without IST, 5); MDS, 1] completed the study [median age, 9.2 years; range, 2.9-21.2]. Median romiplostim dose was 10 mcg/kg/week; range, 5 to 17.5 mcg/kg/week. By week-24, the cumulative incidence of CHR was 70.4% (95% CI, 20.2-92.6%). Seven subjects experienced 21 AEs (Grade 1 to 3), of which 3 were attributed to romiplostim (dyspnea, headache, nausea). All but one tolerated romiplostim. No patient required hosptialization for disease related complications. At a median post-therapy follow-up of 10.9 months (range: 0.7-77.5), no clonal evolution, bone marrow fibrosis or mortality was reported. One subject with partial response relapsed at 27 weeks after initial therapy and responded to second course of romiplostim.

Conclusion: This proof-of-concept study provides data about safety, tolerability and preliminary efficacy of romiplostim (±IST) for treatment of pediatric SAA/MDS. Future studies are needed to clarify our findings.

Poster # 064

ASSESSMENT OF LYMPHOCYTE SUBPOPULATIONS IN BLOOD: RESULTS OF A PHASE 3 TRIAL IN WHIM SYNDROME

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Background: WHIM syndrome is a rare, combined immunodeficiency disease resulting from impaired leukocyte trafficking. Clinical manifestations include neutropenia, lymphopenia, infections, hypogammaglobulinemia, and warts, with up to 88% of people experiencing lymphopenia, affecting both B and T-cell subpopulations.

Objectives: To report results of an investigational analysis evaluating changes in peripheral blood lymphocyte subpopulations, particularly T and B cells, during the randomized placebo-controlled period (RCP) of a global phase 3 trial (NCT03995108) of mavorixafor in WHIM syndrome.

Design/Method: Thirty-one participants aged ≥12 years with WHIM syndrome and absolute neutrophil count (ANC) ≤400 cells/µL were randomized 1:1 to mavorixafor or placebo for 52 weeks. Adults, and adolescents aged 12 to <18 years weighing >50 kg, received oral mavorixafor 400 mg once daily (QD), and adolescents weighing ≤50 kg received oral mavorixafor 200 mg QD. Lymphocyte subpopulations were analyzed at baseline, predose, and 4 hours after dose at 13, 26, 39, and 52 weeks.

Results: At baseline, mean lymphocyte, B-cell, and $CD4^+$ and $CD8^+$ T-cell counts were similar between mavorixafor (485.8, 17.8, 243.0, and 102.6 × 10^6 cells/µL, respectively) and placebo (519.9, 37.7, 246.7, and 110.4 × 10^6 cells/µL, respectively) groups. Participants in mavorixafor group had significantly higher

lymphocyte, B-cell, and $CD4^+$ and $CD8^+$ T-cell counts in blood at each visit 4 hours after last dose (*P*<.003-*P*<.0001 vs placebo). Mean fold increases from baseline were observed with mavorixafor (total lymphocytes, 4.6-; B cells, 26.8-; $CD4^+$ T cells, 5.4-; $CD8^+$ T cells, 4.5-fold increase). Naïve, unswitched memory, and switched memory B-cell subsets increased by mean 42.3-, 16.6-, and 6.4-fold from baseline with mavorixafor, respectively, vs 1.4, 0.9, and 0.3-fold for placebo. Mean fold increases in naïve, effector memory, and central memory subsets were observed for both $CD4^+$ T cells (4.9-, 5.0-, 5.8-fold increase, respectively) and $CD8^+$ T cells (7.4-, 3.7-, 3.8-fold increase, respectively) with mavorixafor vs no change for placebo from baseline. T_H1 ($CXCR3^+$ $CD4^+$) cell counts were significantly higher with mavorixafor vs placebo at Weeks 13 (*P*<.0001), 26 (*P*<.0001), and 39 (*P*=.0024). NK cell levels were similar between groups.

Conclusion: Up to 88% of people with WHIM syndrome experience lymphopenia, including low T- and B-cell counts in blood. Mavorixafor treatment resulted in T- and B-cell counts reaching normal ranges. This, along with previously observed improved ANC, may have contributed to decreased infection rate, severity, and duration reported in mavorixafor-treated participants with WHIM syndrome during the RCP of the phase 3 trial.

Badolato, AAAAI, 2024
Funded by X4 Pharmaceuticals, Inc.

Poster # 065

CXCR4 VARIANT LANDSCAPE IN WHIM SYNDROME: VARIANT INTERPRETATION USING CLINICAL AND FUNCTIONAL DATA

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Background: WHIM syndrome is a rare, combined immunodeficiency disease resulting from impaired leukocyte trafficking, predominantly caused by gain-of-function variants in the C-terminus of C-X-C chemokine receptor 4 (CXCR4). Due to variable clinical presentation, including neutropenia, lymphopenia, infections, hypogammaglobulinemia, and warts, genetic testing for *CXCR4* variants can aid with diagnosis of WHIM syndrome. As of July 2023, 36 *CXCR4* variants in patients with WHIM syndrome were identified via publications, ClinVar, and Invitae/PATH4WARD genetic screening initiative; most were categorized as variants of uncertain significance (VUS) and were not informative for clinical decision-making.

Objectives: To evaluate all known *CXCR4* variants and identify potential disease-causing variants using the Sherloc/ American College of Medical Genetics and the Association for Molecular Pathology (ACMG-AMP) variant classification framework.

Design/Method: Literature, databases (Clinvar, GnomAD), and genetic testing programs (Invitae) were used to collect information on *CXCR4* variants (ie, phenotype, *de novo* occurrence, variant and phenotype segregation within family pedigree, number of independent cases/pedigrees, and allele frequency). *CXCR4* variants identified were tested in a pipeline of *in vitro* assays. CXCR4 internalization response in *CXCR4* variant–expressing cells stimulated with C-X-C chemokine ligand 12 (CXCL12) was

used to assess pathogenicity.

Results: The 36 identified *CXCR4* variants (resulting in 34 distinct protein variants) were interpreted in collaboration with Invitae using Sherloc/refined ACMG-AMP criteria. Absence in general population (GnomAD), segregation with disease, *de novo* occurrence, and reports of multiple unrelated cases were factors that conferred most pathogenic points for *CXCR4* variant classification. *In vitro* functional testing of 32/34 identified protein variants showed that all 32 exhibited substantially impaired CXCR4 receptor internalization across a range of CXCL12 concentrations, in line with previous reports of known pathogenic *CXCR4* variants. By integrating genetic, clinical, and functional data, we reclassified 31 of 36 *CXCR4* variants: 22 from VUS to pathogenic (P), 5 from VUS to likely pathogenic (LP), and 4 from LP to P. The remaining 5 variants retained their P (4) or LP (1) classification, resulting in 36 variants being recognized as LP or P for WHIM syndrome.

Conclusion: Our results show the value of functional *in vitro* testing and detailed variant workup in resolving the pathogenic potential of variants, especially in cases when clinical information is insufficient for confident variant interpretation. These data provide the most comprehensive view of the *CXCR4* variant landscape in WHIM syndrome to date and improve understanding of the genetic etiology of WHIM syndrome.

Nykamp, Genet Med, 2017; Zmajkovicova, IPIC, 2023
Funded by X4 Pharmaceuticals, Inc.

Poster # 066

MAVORIXAFOR IN ADOLESCENTS WITH WHIM SYNDROME: A PRESPECIFIED SUBGROUP ANALYSIS FROM PHASE 3 TRIAL

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Background: Warts, Hypogammaglobulinemia, Infections, and Myelokathexis (WHIM) syndrome is a rare, combined immunodeficiency disease resulting from impaired leukocyte migration, predominantly caused by gain-of-function variants in *CXCR4.* Clinical manifestations, including neutropenia, lymphopenia, infections, hypogammaglobulinemia, and warts, typically manifest in early childhood, yet diagnosis is delayed. Mavorixafor is an investigational, oral CXCR4 antagonist evaluated in a phase 3 trial in patients (aged ≥12 years) with WHIM syndrome (NCT03995108). Results from the previously presented randomized placebo-controlled period (RCP) showed mavorixafor was well tolerated and, compared with placebo, led to sustained increases in absolute neutrophil count (ANC) and absolute lymphocyte count (ALC) as well as reduction in infections.

Objectives: To evaluate efficacy and safety of mavorixafor versus placebo in adolescents (aged 12 to <18 years) with WHIM syndrome enrolled in the RCP of this phase 3 trial.

Design/Method: Eligible participants were randomized 1:1 to mavorixafor or placebo for 52 weeks. Oral mavorixafor dosing was 400 mg once daily (QD) for participants weighing >50 kg and 200 mg QD for participants ≤50 kg. Analysis of the prespecified subgroup of participants included the following

assessments: time (hours) above ANC threshold (≥500/µL) over 24 hours (TAT_{ANC}), TAT_{ALC} over 24 hours (ALC threshold ≥1000/µL), safety, and tolerability.

Results: Of 31 participants who were randomized, 15 were adolescents (mavorixafor, n=7; placebo, n=8). At baseline, all adolescents had neutropenia (median ANC, 125 cells/µL) and lymphopenia (median ALC, 418 cells/µL). At 52 weeks, least squares (LS) mean TAT_{ANC} was 13.05 hours for the mavorixafor group vs 5.12 hours for the placebo group. The LS mean TAT_{ALC} was 13.54 for the mavorixafor group vs 3.14 hours for the placebo group. Reduction in annualized infection rate was observed in the mavorixafor group vs the placebo group. The types of treatment-emergent adverse events (TEAEs) were consistent with the overall study population. No treatment-related serious AEs or treatment-limiting toxicities were observed, and no discontinuations occurred due to TEAEs.

Conclusion: In adolescents, treatment with oral mavorixafor was well tolerated and resulted in increased mean TAT_{ANC} and TAT_{ALC} and reduced infection rate versus placebo. Overall, the efficacy results and safety profile of mavorixafor in adolescents were comparable to that observed in the overall treated population in the phase 3 trial, supporting the potential clinical benefit of mavorixafor in adolescents with WHIM syndrome.

Badolato, *Hemasphere*, 2023
Funded by X4 Pharmaceuticals, Inc.

Poster # 067

OUTCOME OF SIROLIMUS USE IN PEDIATRIC PATIENTS WITH SOLID ORGAN TRANSPLANTS AND IMMUNE CYTOPENIAS

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Background: Solid organ transplantation (SOT) is the first-line treatment for end-stage organ damage in children. To prevent organ rejection, long-term use of immunosuppressant medications is required. Calcineurin inhibitors, such as tacrolimus, are frequently the first-line immunosuppressants used for organ rejection prophylaxis. However, long-term use of immunosuppressants can result in adverse effects including infections and dysregulation of the immune system, potentially resulting in autoimmune cytopenias. Studies of sirolimus, an mTOR inhibitor FDA-approved for organ rejection prophylaxis following renal transplantation, have shown it also exhibits efficacy against autoimmune cytopenias.

Objectives: To review the outcomes of patients with a history of SOT who develop an immune-mediated cytopenia while on calcineurin inhibitor immunosuppressive therapy and are subsequently treated with sirolimus for prevention of organ rejection.

Design/Method: This is a retrospective case series of patients treated at a single tertiary care pediatric hospital between 01/01/2012 and 11/30/2020, with a history of SOT and concomitant immunosuppressive therapy, who developed an autoimmune cytopenia and were subsequently treated with sirolimus. Chart review revealed 548 patients who were prescribed sirolimus, 11 of which met the inclusion criteria and are included in the case series.

Results: Of the 11 patients included, the most common SOT was liver (45.5%) followed by heart (36.4%). The median time from SOT to cytopenia was 31 months, comprised of autoimmune neutropenia (n=8), immune thrombocytopenia (n=4), and autoimmune hemolytic anemia (n=4). Four patients had >1 autoimmune cytopenia. All patients were refractory to initial treatments for the cytopenias, resulting in no or partial response, until transition to sirolimus (median time 43 months after SOT). Three patients were subsequently transitioned from sirolimus to another immunosuppressant, and the remaining eight achieved a complete response. Two patients were maintained on dual therapy of sirolimus with tacrolimus (n=1) or mycophenolate mofetil (n=1). One patient demonstrated rejection of transplanted organ while on sirolimus, and ultimately passed away secondary to multi-organ failure in the setting of infection.

Conclusion: Autoimmune cytopenias are a consequence of immunosuppressive therapy following pediatric SOT and are often refractory to standard therapies. Sirolimus is a potential single or additive agent to address the needs of pediatric patients with the unique combination of SOT and autoimmune cytopenias. Further studies with larger, more diverse sample sizes would be beneficial to continue to explore the utilization of sirolimus in this context.

Poster # 068

IMPROVING LEAD SCREENING RATES IN EARLY CHILDHOOD AT A FQHC: A QUALITY IMPROVEMENT STUDY

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Background: Vulnerable populations in the United States often face multiple barriers to accessing health care, especially for preventative measures such as lead screening. Roughly 50% of all Americans are exposed to lead, particularly in early childhood. While lead screening has been implemented as a standard of care, completion rates have been noted to be less than optimal in Richmond, California.

Objectives: Co-located health care and services have been shown to reduce the disparities and improve patient outcomes. A quality improvement project was undertaken to determine if lead screening rates could be improved with point of care testing. SMART aim was to increase lead testing by at least 30% in early childhood for eligible patients at a federally qualified health center. Key drivers for the project included clinic staff, patients, and local insurance companies.

Design/Method: The quality improvement project utilized a quasi-experimental study in which two Plan-Do-Study-Act cycles were enacted to inform a needs assessment regarding point of care lead testing. Patients were recruited from across a single federally qualified health center with inclusion criteria of 1 to 2 years old and had not completed a blood lead test. Patients were excluded if they have already been screened in the past 6 months or were not able to be contacted. Three hundred fifty patients met criteria in which patients were scheduled for a clinic visit, received a point of care lead blood test. Pre- and post- intervention data were obtained in Tableau and EPIC and analyzed using paired t-tests to determine whether having in-house services increased lead screening rates.

Results: Prior to the quality improvement project, lead screening averaged 40% and afterwards of 80%.

Confidence intervals for pre-intervention35.88-41.78 and post-intervention 78.65-81.35 with a confidence level of 5%. Paired t-test showed statistical significance with the intervention of p = 0.003. Demographic analysis showed a near-equal distribution between Latinx and African American/Black patients.

Conclusion: Lead screening rates improved with point of care testing as social determinants of health often complicate co-located services and external referral processes. The quality improvement process can be useful in identifying whether similar needs are present in other clinic/healthcare settings. Point of care testing can be used to improve screening rates in the primary care setting. Future research can include refining clinic workflows and integrating additional screenings to the well child visit.

Poster # 069

DETERMINING THE FUNCTIONAL ROLES OF GENES ASSOCIATED WITH MULTIPLE BLOOD TRAITS IDENTIFIED BY GWAS

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Background:
Hematopoiesis relies on the proliferation and differentiation of hematopoietic stem and progenitor cells (HSPCs) in the bone marrow. HSPCs are regulated by intrinsic and extrinsic pathways that govern their self-renewal and differentiation. Understanding the regulatory mechanisms of HSPCs is essential to advancing the diagnosis and treatment of hematopoietic diseases.
Genome-Wide Association Studies (GWAS) have revolutionized the study of disease genetics by revealing associations between genetic variants and human traits and diseases. In two large-scale GWAS of hematopoiesis, researchers identified over 5,000 new genetic variants associated with blood cell traits. Our analysis of the identified blood cell traits from these GWAS revealed SNPs that were linked to the abundance of lymphocytes, monocytes, and neutrophils simultaneously. Based on these findings, we formulated the hypothesis that these SNPs and their related genes associated with multiple blood cell traits might play a role in regulating HSPCs.

Objectives: To utilize GWAS to identify genes that regulate HSPCs. To gain insight into novel regulatory functions of candidate genes in hematopoiesis and potential underlying mechanisms.

Design/Method: We analyzed the SNP data from the two large GWAS of blood cell traits. After validating the SNP-gene association, ensuring expression by HSPCs as well as the presence of mouse homologs, five candidate genes fit our selection criteria.

Using CRISPR/Cas9 gene knock-out (KO), we analyzed the functional role of the candidate genes in HSPC regulation by conducting *in vitro* differentiation assays and mouse transplantation.

Results: *In vitro* myeloid differentiation assay shows that KO of *Nlrc5* results in increased production of all myeloid populations.

Mouse transplantation models have been conducted for two candidate genes: *Nlrc5* and *Rest*.

For *Nlrc5,* no difference was found in blood cell count between the KO and control groups. However, the abundance of multipotent progenitor 4 and common lymphoid progenitor, was reduced in the KO group ($P<0.05$).

For *Rest,* increase in B-cell production was observed in the KO group at all time-points post-transplantation with increased abundance of all HSPCs upon evaluation of the bone marrow at 5 months post-transplant ($P <0.01$).

Conclusion: Our study evaluated genes associated with multiple blood cell traits identified by GWAS. Through functional investigation using *in vitro* models with corroboration by HSPC transplantation in mice, we have discovered novel roles of genes *Nlrc5* and *Rest* in lymphoid progenitors and lymphocyte production respectively, which is consistent with their expression levels across various types of HSPCs. Our findings demonstrate an innovative approach to investigating the regulation of hematopoiesis.

Poster # 070

INVESTIGATING MARKERS FOR INTRACRANIAL HEMORRHAGE SEVERITY: INSIGHTS FROM CBC CHANGES AND BEYOND

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Background: While laboratory markers such as white blood cell (WBC) count and neutrophil-lymphocyte ratio (NLR) and their correlation with brain injury severity have been extensively studied in adult populations, there is limited literature on this relationship in pediatric patients.

Objectives: This study explores alternative laboratory markers, including absolute neutrophil count (ANC), and their associations with established indicators of brain injury severity.

Design/Method: A retrospective chart review was conducted at a single tertiary pediatric center. Data collected by the Trauma Surgery team over two years on patients evaluated for trauma included WBC count, hemoglobin, ANC, systolic blood pressure (SBP), Glasgow coma scale (GCS), level of care received, imaging results, and length of stay (LOS). Data analysis involved ANOVA and chi-square where appropriate.

Results: Among the 211 patient charts reviewed, 155 met the criteria for analysis. The majority were male (64.5%) or <12 months old (65.8%). Intracranial hemorrhage (ICH) was diagnosed in 66.5% of patients. Patients with ICH had significantly longer LOS ($M=5.6$, $SD=8.3$) than those without ICH ($M=2.4$, $SD=3.6$), $F(1,153)=357.7$, $p<0.1$. Additionally, patients with ICH presented with significantly lower hemoglobin ($M=11.26$, $SD=2.3$) compared to those without ICH ($M=11.96$, $SD=1.1$), $Fw(1,153)=6.3$, $p<0.05$. Patients >1 year old were more likely to have elevated ANC ($M=7.1$, $SD=4.3$) than those <1 year ($M=4.8$, $SD=4$), $F(1,135)=11$, $p=0.001$. No significant variation in ANC was observed between patients with ICH and those without. Patients older than 1 year had significantly higher hemoglobin ($M= 12.1$, $SD= 1.6$) compared to patients less than 1 year old ($M= 11.2$, $SD= 2.2$), $F(1,153)= 7.4$, $p < 0.01$. No association was found between patients with ICH and SBP at presentation.

Conclusion: While patients with ICH presented with significantly lower hemoglobin, this finding may not be clinically significant. The data did not demonstrate a significant relationship between ANC, WBC count, and blunt head trauma severity in pediatric patients. This inconsistency with current literature warrants further investigation. Future research should focus on assessing modifying factors in isolated ICH in children, particularly in sample groups with greater variability in injury severity.

Sickle Cell Disease (101-160)

Poster # 101

EVALUATION OF RBC MITOCHONDRIAL RETENTION FROM A SICKLE CELL DISEASE PEDIATRIC AND AYA CLINIC

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Background: Sickle cell disease (SCD) is a hemolytic anemia that causes severe pain episodes, multi-organ system failure and affects thousands of individuals worldwide. SCD is caused by a mutation of the β-globin gene which leads to HbS, which polymerizes when deoxygenated. Our laboratory established that peripheral blood from SCD patients contain mature RBCs with mitochondria, which increased formation of reactive oxygen species (ROS) and oxygen consumption. Other investigators have shown that mitochondrial DNA (mtDNA) is associated with neutrophil extracellular entrapment and RBC alloimmunization. Toll-like receptor 9 (TLR9), a marker for cell phagocytosis, has an affinity to fragmented unmethylated mtDNA.

Objectives: To further understand the impact of mitochondrial retention we evaluated RBC mitochondrial retention, ROS, hematologic parameters, and TLR9 RBC presentation in pediatric and young adult SCD.

Design/Method: Blood samples were collected from eligible SCD pediatric patients and adolescent young adults during lab visits. Samples were evaluated by flow cytometry for maturity [transferrin receptor 1 (CD71), which decreases during RBC maturation], mitochondria presence (TMRM), and ROS production (CM-H2DCFDA). A subset was measured for TLR9 RBCs (ODN2006). GraphPad PRISM was used to perform t-test on ANOVA as appropriate.

Results: Recruitment is ongoing with 38 participants currently enrolled (25 HbSS, 5 HbS βthal+ and 8 HbSC). The average mitochondrial retention of CD71 negative RBCs (mature RBCs) was 9.8 ± 5.8(%) in HbSS, 4.6 ± 6.1(%) in HbSC, and 5.28 ± 6.4(%) in HbSβthal+ and are consistent with our previous adult SCD steady-state data. Our analysis showed increased ROS in all RBC with mitochondria compared to those without ($p<0.001$). CD71posRBC with mitochondria had a higher ROS than those without ($p<0.001$), The ROS of mature RBC with mitochondria had a trended higher than those without but was not statistically significant ($p=0.08$). There was a 1 g/dL lower Hb content in patients with the highest mitochondria fraction (>8% positive mature RBCs) compared to those with lower level (<8%) (7.806 ± 0.8 vs 8.733 ± 1.5, $p=0.0562$). We compared mean corpuscular hemoglobin concentration and volume (MCHC/MCV), plasma bilirubin and % CD71 positive RBC. Of these comparisons, only MCV had a significant difference (79.33 ± 9.9 vs 90.13 ± 11.8, $p=0.0294$). Additionally, aberrant surface exposure of

TLR9 increased in RBCs with mitochondria (6% Mito+TLR9+, 1% Mito- TLR9+, p<0.01).

Conclusion: These findings provide further evidence of the significance of mitochondrial retention on RBC viability and may represent a new avenue for therapy development in SCD and others erythropoietic stress disorders.

Poster # 102

UNBIASED ENUMERATION OF MITOCHONDRIA IN RBC OF PEDIATRIC SICKLE PATIENTS

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Background: In Sickle Cell Disease (SCD), we have established that RBCs abnormally retain mitochondria. The role that mitochondria, which are removed in normal RBC, play in SCD pathophysiology had not been considered until this discovery. Functional mitochondria increase reactive oxygen species (ROS) generation and oxygen consumption. Mitochondrial DNA (mtDNA) is associated with neutrophil extracellular entrapment and RBC alloimmunization. Enumeration of the copies number of mtDNA in sickle RBC has been performed by others using nuclear DNA (2n copies per cell) as calibrator reference, which is not a valid methodology for enucleated RBC.

Objectives: To address this challenge, we developed a quantifiable methodology which is not affected by the presence of variable fraction of sickle RBC with variable amount of partially degraded nuclear DNA (nucDNA).

Design/Method: Eligible SCD pediatric patients (aged 2-25) were enrolled (n=40). Real-time PCR standard curve was obtained with mitochondrial human gene mtND1, and total DNA was isolated from cell sorted CD45negGlyApos sickle RBC.

Results: Copy numbers quantification was established for whole blood, plasma and sorted RBCs and can detect 102 to 109 copies (≥1µl plasma, ≥104 RBC). Concentration or dilution are not required to compensate for the wide range of values obtained with clinical samples. Pediatric HbSS have higher mitochondrial content (2-fold) than HbS heterozygote, such as HbSC, HbSE and HbS β-thal+, with an average of ≈20 mitochondria per mitochondria pos RBC and ≈10% mitochondria pos RBC. Plasma was collected a few hours after blood draw to prevent contamination by the released of nuc/mt DNA from blood cells (30-fold mean value difference). We confirmed the presence of cell-free mtDNA associated with RBC. Sickle RBC of patients with higher HbF level, indicative of a lesser erythropoietic stress status, had lower mitochondrial content supporting the hypothesis that the enhanced RBC production in SCD may overwhelm the mitophagy processes resulting in the premature released of immature cells in circulation. However, most patients in the cohort were on hydroxyurea treatment with significant mitochondrial content indicating that additional therapy is necessary to prevent the toxic effects of retained mitochondria in the RBC.

Conclusion: Biomarker of the SCD severity or its progression or, as a metric for therapy is lacking. Flow cytometry and qPCR quantification of sickle RBC retaining mitochondria and copy numbers are cost effective methodologies appropriate for clinical lab analysis. Ongoing investigation of pediatric patients will evaluate its significance as a biomarker in the emerging field of erythrocyte mitochondrial

retention.

Poster # 103

MICROFLUIDIC INSIGHT INTO GENE-EDITED RBCs FOR SICKLE CELL DISEASE

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Background: Gene therapy strategies address, directly or indirectly, the mutated sickle beta-globin gene to prevent the polymerization underlying sickle cell disease (SCD). Strategies include the recently approved electroporation approach, but novel electroporation and virus-free gene editing approaches are in development. Standard DNA sequencing methods quantify the extent to which alleles in the population of SCD Hematopoietic Stem and Progenitor Cells (HSPCs) have been therapeutically edited. However, no available assays measure the percentage of an edited cell product that has gained resistance to the biophysical consequences of SCD such as abnormal RBC adhesion and deformability. have been manufactured. The SCD Biochip is a microfluidic device capable of functionally characterizing several biochemical and biomechanical phenotypes of RBCs namely: adhesion, deformability, optical absorption, and sickling under hypoxic conditions.

Objectives: Application of the SCD-BioChip to study the functional properties RBCs differentiated in-vitro from gene edited HSPCs to assess the biomechanical impact of various gene editing strategies and targets.

Design/Method: We delivered preformed CRISPR Cas9 RNPs targeting the BCL11a enhancer locus (or controls) to commercially obtained healthy donor peripheral blood mobilized (CD34+) HSPCs with the goal of enhancing fetal hemoglobin expression. Edited HSPCs were differentiated into erythroid cells in-vitro using a 3-phase cytokine cocktail system (including IL-3, SCF, and erythropoietin). Flow cytometry of CD71 (transferrin receptor) and CD235a (glycophorin) cell surface markers were used as indicators of RBC maturation over 21 days. Rates of differentiation, and enucleation were compared between control and gene edited samples. Matured and enucleated RBCs were studied for cell adhesion and deformability (surrogate occlusion) using the SCD-Biochip Assay to assess biomechanical consequences of gene editing.

Results: Editing efficiency was estimated as high as 60% via electroporation. The mean cell amplification of CD34+cells reached a 695-fold expansion by Day 16. Differentiation of the immature erythroblasts into mature RBCs continued from day 16 to 21, marked by the progressive loss of CD71 expression; ~50% of CD235a+ cells were enucleated. Using the Occlusion SCD-BioChip, we observed worse deformability for glutaraldehyde crosslinked RBCs (as a surrogate for HbSS RBCs) when compared to control RBCs, and we compared the functional characteristics of in-vitro differentiated RBCs edited at additional loci and via alternative delivery strategies.

Conclusion: We demonstrate the feasibility of adopting a novel microfluidics platform to evaluate some of the biomechanical functions of RBCs derived from CRISPR-edited HSPCs, and we hope to apply these assays as a functional assay (possibly release criteria) in future CRISPR gene editing cures for sickle cell disease.

Poster # 104

AVASCULAR NECROSIS OF THE FEMORAL HEAD IN CHILDREN WITH SICKLE CELL DISEASE WITH HIP PAIN

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Background: Avascular necrosis of the femoral head (ANFH) is the most common and disabling chronic musculoskeletal complication of sickle cell disease (SCD). Its incidence increases with age, and it remains understudied in children and adolescents. As the life expectancy increases for people with SCD, the prevalence of ANFH is anticipated to rise.

Objectives: To determine the prevalence of ANFH in children and adolescents with SCD, and to compare clinical characteristics, laboratory and radiologic findings, and quality of life measures between those with and without ANFH.

Design/Method: This is a retrospective cohort study of children and adolescents with SCD at St. Jude Children's Research Hospital who underwent MRI evaluation for hip pain. Clinical, laboratory, imaging, healthcare utilization, and neuropsychological data of those with and without ANFH were collected through the Sickle Cell Clinical Research and Intervention Program (SCCRIP) between 2001 and 2017. Continuous variables were compared using t-test or Wilcoxon rank-based test and are presented as means or medians. Categorical variables were compared using Pearson's Chi-square test or Fisher's exact test.

Results: Of 743 participants in the SCCRIP study between 2001 and 2017, 68 (9%; age range 0.6–27 years) underwent MRI for evaluation of hip pain. Of these, 34 (50%) were diagnosed with ANFH (prevalence 5%; SS genotype in 65%). Those with ANFH trended older (13.3 vs. 11.3 years, p=0.07) but did not differ in gender (68% vs. 50% males, p=0.14), hemoglobin F (14% vs. 17%, p=0.22), or hydroxyurea use (91% vs. 88%, p=1) as compared to those without ANFH. There were no significant differences in BMI, hemoglobin, calcium, vitamin D, and bone mineral density. The ANFH group trended towards more emergency department visits (23 vs. 21, p=0.49) and inpatient stays (17 vs. 12, p=0.12). On the PedsQL™ SCD Module, the ANFH group scored worse on Pain and Hurt (58.4 vs. 67.9, p=0.07) and Pain Impact (47.3 vs. 62.6, p=0.003). There was no difference in anxiety or depression measured by the Sickle Cell Assessment of Neurological Skills. Core decompression was performed in seven patients (21%) with ANFH (three required subsequent hip arthroplasty within 14 months), and primary hip arthroplasty in five (15%).

Conclusion: Patients with ANFH had significantly impaired quality-of-life by pain, however, minimal population characteristics differences were seen between those with and without ANFH. Studies with a larger sample size are needed to identify clinical risks, biomarkers, and the role of core decompression in delaying hip arthroplasty for ANFH.

Poster # 105

ECONOMIC BURDEN OF SICKLE CELL DISEASE FOR CHILDREN IN THE UNITED STATES WITH COMMERCIAL INSURANCE

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Background: Sickle cell disease (SCD) is a lifelong, inherited blood disorder with complications leading to higher morbidity and mortality. Symptoms typically begin in the first year of life, yet limited information has been reported for pediatric burden of illness.

Objectives: To evaluate healthcare resource use (HCRU) and costs for commercially insured US children with SCD and matched controls without SCD.

Design/Method: Patients and controls (matched 1:1 for age, gender, US region, and race) were retrospectively identified from the IBM® MarketScan® Commercial Database between January-1-2016 and December-31-2020. Eligible patients were <18 years old with ≥3 inpatient or outpatient SCD diagnoses (ICD-10 codes D57.0–D57.219; D57.4–D57.819) during July-1-2016 to December-31-2019 (index-identification period) and enrollment for 6 months pre-index and ≥12 months post-index. HCRU and costs were calculated per-patient per-year (PPPY), costs inflated to 2020 US dollars, and groups compared using ANOVA.

Results: For 1299 patients and 1299 matched controls, mean (SD) age was 10.0 (4.8) years and 51% were female; mean (SD) follow-up was 35.1 (14.3) months for patients and 33.5 (14.4) months for controls. During follow-up, 34.9% of patients with SCD received hydroxyurea, 23.0% ≥1 blood transfusion, and 61.3% an opioid pain medication. The most common acute complication was vaso-occlusive crisis (patients 70.8%; controls 0%) and most common chronic complication was retinopathy (patients 6.5%; controls 0.0%). During 12-months' follow-up, patients with SCD had higher HCRU (all categories $P<0.0001$). For the SCD group versus controls, mean (SD) PPPY number of inpatient hospitalizations was 0.6 (1.1) versus 0.0 (0.2), length of stay 2.4 (7.3) versus 0.1 (0.7) days, outpatient visits 13.5 (14.9) versus 6.0 (10.1), emergency room (ER) visits 1.2 (2.3) versus 0.2 (0.6), and prescriptions 12.8 (14.1) versus 3.8 (7.4). For the SCD cohort, mean (SD) costs PPPY were higher across all HCRU categories, with total costs: $31,445 ($72,213) versus $2844 ($13,411), inpatient costs: $15,195 ($54,222) versus $477 ($8397), outpatient including ER: $12,746 ($24,187) versus $1758 ($4176), and pharmacy: $3504 ($18,546) versus $610 ($4389) (all $P<0.0001$). Total PPPY out-of-pocket (OOP) payments were $2071 ($2487) for patients versus $489 ($861) for controls ($P<0.0001$).

Conclusion: Compared with matched controls, children with SCD had substantially increased HCRU. Payer and OOP costs were higher across all categories, with total costs for the SCD cohort 11-fold those of controls. This study excluded children without commercial insurance, who may have higher burden; however, the results highlight the substantial economic burden of pediatric patients with SCD enrolled in US commercial insurance plans.
Funding: Pfizer.

Poster # 106

MYOCARDIAL FIBROSIS IN SICKLE CELL DISEASE IS ASSOCIATED WITH THE DEGREE OF ANEMIA AND ALBUMINURIA

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Background: Sickle cardiomyopathy manifests as pan-chamber dilation, diastolic dysfunction, diffuse myocardial fibrosis, and delayed repolarization. Cardiovascular magnetic resonance (CMR) is a non-ionizing imaging modality, thus well suited for serial functional assessments and myocardial characterization. Diffuse myocardial fibrosis can be determined by quantifying myocardial extracellular volume (ECV) on CMR. Elevation in ECV has been reported in children with sickle cell disease (SCD). While there is emerging data regarding the effect of disease-modifying therapies (DMT) and curative therapies on reversing myocardial fibrosis, (1,2) the etiopathogenesis of this fibrosis remains elusive.

Objectives: To determine the prevalence of elevated ECV and associated clinical factors in our pediatric population with SCD.

Design/Method: This is a single-center retrospective analysis of CMR evaluations performed from 2020-2023 in children ≤18 years old with SCD. CMR studies were done at the clinician's discretion for the presence of cardiopulmonary symptoms. All individuals were enrolled in the Sickle Cell Clinical Research and Intervention Program (NCT 020098863).(3) Clinical data included laboratory markers of hemolysis, vaso-occlusive events (VOC), and urine albumin-creatinine ratio (UACR). CMR-derived ECV was measured from T1 maps with a modified Look-Locker inversion recovery (MOLLI) sequence in the short axis. Linear regression model was used to determine the association between ECV and hematological markers, VOC, and UACR.

Results: Our study cohort of 41 participants was predominantly male (56%), with Hb SS/β0 thalassemia (85%) and a mean age of 15.5 ±3.5 years. 90% of participants were on DMT (hydroxyurea or monthly transfusions). The mean ECV was elevated at 31± 3.95%, and 63% of participants had ECV ≥ 30%, which is considered abnormal. On univariate analysis, ECV was significantly associated with hydroxyurea treatment, HbSS/Sβ0, lower hemoglobin, higher markers of hemolysis (total bilirubin, lactate dehydrogenase), and higher UACR ($p < 0.05$). Worse anemia and UACR were independently associated with worse ECV on multivariate analysis, where a 1gm/dL decrease in hemoglobin was associated with a 1.2% increase in ECV ($p <0.05$) and a 10mg/g increase in UACR was associated with a 0.3% increase in ECV ($p =0.06$)

Conclusion: The majority of our pediatric cohort had abnormal ECV elevation. This ECV elevation was associated with worse anemia and microalbuminuria, reflecting the pattern of concomitant renal and heart dysfunction in SCD. Prospective studies should evaluate whether maintaining high hemoglobin with DMT or novel therapies can slow the progression of diffuse myocardial fibrosis.

1.*Morin, Blood, 2023*
2. Niss, Blood, 2022
3. Hankins, PediatrIc Blood Cancer 2018

Poster # 107

TRANSCRANIAL DOPPLER SCREENING OF CHILDREN WITH SICKLE CELL DISEASE IN THE HOPE KIDS 2 TRIAL

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Background: Transcranial Doppler (TCD) ultrasound is an effective screening tool for identifying children with sickle cell disease (SCD) who are at high risk of stroke. Implementing TCD screening for the purpose of stroke prevention in resource-constrained settings remains challenging. HOPE Kids 2 (NCT04218084) is an ongoing, phase 3, multicenter, double-blind, placebo-controlled trial of voxelotor in children with SCD and conditional TCD velocities at screening.

Objectives: To describe the findings from successful implementation of a standardized TCD screening protocol that was conducted in a multinational setting.

Design/Method: In HOPE Kids 2, children aged 2 to <15 years with SCD (HbSS/HbSβ^0) were screened after local sonographers were trained and certified on standardized TCD examination protocol and equipment. TCD assessments underwent central quality review and interpretation by 2 independent reviewers. STOP criteria were used to classify stroke risk using time-averaged maximum of the mean velocity (TAMMV): normal, <170 cm/s; conditional, 170 to <200 cm/s; or abnormal, ≥200 cm/s.[1] Baseline characteristics were measured during screening.

Results: Between November 2020 and February 2023, 708 participants consented at 29 sites in Nigeria (n=250), Kenya (n=241), Egypt (n=145), Ghana (n=28), the US (n=17), Italy (n=9), Oman (n=9), Saudi Arabia (n=8), and the UK (n=1). Of these patients, 92.1% (652/708) completed TCD screening examinations (mean [SD] age 7.6 [3.24] years; range 2.0-14.0 years; 50.8% male; 23.0% receiving hydroxyurea). Among TCD screening completers, the mean (SD) TAMMV was 163.0 (31.26) cm/s, and 47.1% (307/652) had conditional TCD at baseline. The main reason for screen failure was index TAMMV outside of conditional range (abnormal, n=39 [6.0%]; normal, n=306 [46.9%]). Elevated TAMMV on screening TCD was more common in younger children (2 to ≤8 years vs >8 to <15 years); patients aged 2 to ≤8 years comprised 66.8% and 82.1% of the conditional and abnormal TCD categories, respectively. Adjudication was required for 39 assessments; 9 assessments were deemed unreadable. Of all patients screened, 36.2% (236/652) fulfilled eligibility criteria for randomization. The mean (SD) hemoglobin level and TAMMV at screening for randomly assigned patients was 7.7 (1.06) g/dL and 182.7 (7.53) cm/s, respectively.

Conclusion: Clinical sites for the HOPE Kids 2 study successfully implemented a standardized, local TCD screening protocol supported by central quality review. For a large interventional trial aimed at reducing the risk of stroke in children with SCD, African and Middle Eastern sites presented relatively few limitations with respect to participant screening.

Funding: Pfizer

1. Adams, *N Engl J Med*, 1998

Poster # 108

TELEHEALTH USE IN CHILDREN WITH SICKLE CELL DISEASE IN TEXAS MEDICAID DURING THE COVID-19 PANDEMIC

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Background: Patients with sickle cell disease (SCD) have suffered from a lack of access to care, which may cause negative health outcomes. During the COVID-19 pandemic, the use of telehealth increased among children with SCD enrolled in Medicaid. However, the factors or outcomes that are associated with the use of telehealth among this population remain unknown.

Objectives: To (1) identify patient characteristics associated with the use of telehealth among children with SCD enrolled in Texas Medicaid and, (2) examine the association between SCD-related telehealth visits and having ≥10 hydroxyurea prescription fills during the first year of the pandemic.

Design/Method: This retrospective study used Texas Medicaid claims data from 03/01/2019 to 03/31/2022. Children aged 1-18 years, had ≥1 inpatient or ≥2 outpatient claims with an SCD diagnosis, had no cancer diagnosis, and were continuously enrolled in Texas Medicaid for the study period were included. For Objective 1, the individual patient's history of telehealth use with any diagnosis during the study period was assessed. For Objective 2, logistic regression analyses were used to examine the association between the main independent variable (history of SCD-related telehealth use during the first year of the pandemic [03/01/2020-02/28/2021]) and the outcome variable (whether or not a patient filled ≥10 hydroxyurea prescriptions during the same period, as an indicator of ≥80% prescription drug coverage) while controlling for sociodemographic (age, gender, living in a city with an SCD clinic) and clinical (the number of SCD-related outpatient visits 1 year before the pandemic [03/01/2019-02/29/2020]) characteristics.

Results: Among 868 patients (mean [SD] age = 10.4 [4.1], 52.0% female) included, 527 (60.7%) had ≥1 telehealth visit during the study period. Patients who had ≥10 SCD-related outpatient visits 1 year before the pandemic were 52.9% more likely to use telehealth compared to those who had 0-4 visits (Odds Ratio [OR]: 1.529, 95% CI: 1.098-2.129, p=0.0120), while controlling for sociodemographic characteristics. During the first year of the pandemic, 366 (42.2%) patients had ≥1 SCD-related telehealth visit, and 112 (12.9%) patients filled ≥10 hydroxyurea prescriptions. After adjustment for covariates including the number of SCD-related outpatient visits before the pandemic, use of SCD-related telehealth visits was associated with a 59.5% greater likelihood of having ≥10 hydroxyurea fills during the first year of the pandemic (OR: 1.595, 95% CI: 1.069-2.379, p<0.0223).

Conclusion: Among children with SCD enrolled in Medicaid, disease severity was related to telehealth use. The use of telehealth for SCD treatment was associated with persistent uptake of hydroxyurea therapy.

Poster # 109

OUTPATIENT COSTS OF YOUNG ADULT PATIENTS WITH SICKLE CELL DISEASE IN RIO DE JANEIRO, BRAZIL

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Background: Brazil has a growing population of young adult patients with sickle cell disease (SCD) with an estimated 100,000 total patients. Use of hydroxyurea (HU) is known to decrease complications in SCD. The overall cost of the drug, as well as the cost and demographics of patients with SCD visiting a large hematology clinic in Rio de Janeiro is not known.

Objectives: This study aimed to determine the landscape of young adult patients visiting the hematology clinic.

Design/Method: A retrospective analysis of patients with SCD seen at the clinic between January 1 and June 30, 2018, was conducted. Patients were stratified by age, gender, genotype, and prescription of HU. The total number of appointments attended and cost per appointment was computed. The cost of medications was then calculated per patient.

Results: A total of 3000 patients with SCD were reviewed. 51.6% were female and mean age was 19.1 (± 14.8). 73% of patients had HbSS. 984 patients (32.8%) were prescribed HU. Out of 14795 appointments, the highest number were made in Hematology (6199, 42%). The highest rates of absenteeism were in patients with HbSS/Sβ^0 (38%), in those aged 19-25 (45%), and in those not taking hydroxyurea (41%). Patients with HbSS had a higher average outpatient visit cost of $45.88 (± $40.01) per person as compared to patients with all other genotypes ($33.10 ± $35.14 per person). The highest costs for all patients were associated with transfusion visits, with an average of $390.43 (± $299.02) per patient. Compared to those patients not on HU, patients on HU had a significantly higher ($p<0.01$) cost for all types of visits, excluding dressing changes.

Conclusion: At a clinic in a middle-income country, patients with HbSS/Sβ^0 genotypes had notably higher treatment costs. This is consistent with the fact that these patients have a more severe form of disease and require more interventions. A low number of overall patients were prescribed hydroxyurea, and the highest rates of absenteeism were noted in young adult patients and those not on hydroxyurea, highlighting a vulnerable population. Patients receiving hydroxyurea had overall higher costs. This is likely because these patients have a more severe disease course and require more medical services. In future studies, we hope to demonstrate that these same young patients have lower overall costs for inpatient and emergency visits, which would provide a net cost-saving with hydroxyurea treatment and benefit the hospital system and patient population. Supported by a grant from Agios.

Poster # 110

RETROSPECTIVE ANALYSIS OF INDIVIDUALS WITH SICKLE CELL DISEASE AND VENOUS THROMBOEMBOLISM

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Background: Sickle cell disease (SCD) predisposes patients to venous thromboembolism (VTE) as it causes chronic inflammation and vasculopathy. Observational studies have shown a 25% increased risk of VTE in SCD with a mean age of first VTE event of 30 years, compared to 65 years in the general population. However, risk factors for VTE in SCD are not clearly defined, leaving minimal data to guide prevention strategies in these patients.

Objectives: The objective was to retrospectively analyze the risk factors associated with VTEs in SCD patients followed at our lifelong sickle cell center at University of California, San Francisco Oakland. We hypothesized that central venous catheters (CVCs) are a significant risk factor.

Design/Method: After IRB approval, we extracted 70 unique SCD patients who developed a VTE between May 30, 2013, to May 30, 2023. We assessed their VTE type, patient clinical and laboratory data, and other known VTE risk factors. We documented recurrence rates of VTE in addition to bleeding events, if available, in this cohort. Descriptive statistics were used to summarize the data. Wilcoxon rank sum test and Chi-squared test were used to compare the continuous and categorical variables between the two groups, respectively.

Results: The 70 patients in our cohort were predominantly hemoglobin SS genotype (n= 53, 76%). First VTE events during our study period were mostly deep venous thrombosis (DVT) (n=43, 63%) and pulmonary embolism (n=23, 33%).
Forty-three (61%) patients with VTE events during our review period were first time VTE event while twenty-four (34%) patients had a VTE event prior to our review period and were having a recurrent event during our study period. The median age at the time of our cohort was 32 years (range 17-65). Forty-three (61%) of the patients had a CVC in place at the time of VTE diagnosis. The age of the patient at the time of VTE was lower in patients with CVC compared to patients without a CVC ($p<0.05$). Rate of bleeding complications in our cohort was 8.5%.

Conclusion: VTEs in SCD are predominantly DVTs and PEs with a median age of first VTE of about 30 years which is significantly lower than the general population. CVCs are associated with VTEs in SCD. In addition, recurrence rates of VTEs are very high in SCD individuals. Further prospective studies are needed to validate our findings and create strategies to minimize VTE rates.

Poster # 111

PREVALANCE AND SIGNIFICANCE OF PANCREATIC IRON IN TRANFUSION DEPENDENT SICKLE CELL DISEASE

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Background: Chronically transfused patients such as sickle cell disease (SCD) and beta thalassemia major (TM) develop iron overload. Extrahepatic iron deposition occurs when transfusional iron loading rate exceeds iron utilization, saturating transferrin binding capacity and creating non-transferrin bound iron

species. Pancreatic iron (PI) deposition and glucose dysregulation in adolescents that progress with age has been described in TM, but less is known in SCD.

Objectives: To determine the prevalence and significance of PI in transfusion dependent SCD. To compare the oral glucose tolerance tests (OGTT) and abdominal MRI measurements in chronically transfused SCD and TM.

Design/Method: 28 SCD and 40 TM patients underwent research MRI's (CCI#014-0034) at 1.5T and 3.0T for cross validation of liver and pancreas R2* values between 2014-2017. Ferritin, OGTT, fasting glucose and insulin levels, height, and weight were collected during the MRI study visit; 1 SCD and 13 TM patients refused OGTT.

Results: The TM group averaged 8 years older (17 vs 25 years) and 8 years longer transfusion exposure (11 vs 19 years) but were balanced for gender and BMI. The SCD patients had greater ferritin (4842 ng/dL vs 2231 ng/dL, p=0.0036) and LIC (18.8 vs 12.3, p=0.09) but had lower PI burden (pancreatic R2* >100 Hz, 22% vs 53%. P =0.047). Impaired fasting glucose (IFG) (2 vs 19,p=0.27) and impaired glucose tolerance (IGT) (1 vs 11,p=0.019) were less common in SCD compared with TM patients. Two SCD patients with IFG had pancreas R2* > 100 Hz, suggesting that this MRI surrogate of risk is likely relevant for SCD. One SCD patient with IGT did not have PI, but was obese, implying that traditional risk factors also play a role in glucose dysregulation. We could not match the age and transfusion duration between the two cohorts. Thus, the absence of significant glucose dysregulation in this relatively young SCD cohort does not guarantee protection in middle age and beyond.

Conclusion: We demonstrate a low burden of glucose dysregulation in this cohort of adolescents and young adults with SCD compared with TM. Adult hematology practitioners should retain an index of suspicion for their SCD patients having decades of transfusion exposure and evidence of PI deposition.

Poster # 112

PREVALENCE OF NEUROPATHIC PAIN IN ADOLESCENTS WITH SICKLE CELL DISEASE AND RELATED RISK FACTORS

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Background: Neuropathic pain (NP) is underrecognized and undertreated in patients with sickle cell disease (SCD) and is associated with decreased patient-reported quality of life. Older age, female sex, frequent acute care visits for pain, and hydroxyurea therapy have been shown to be associated with increased risk of NP in SCD. The prevalence of NP in adolescent patients with SCD and associated risk factors, as well as the interaction of these risk factors on the risk of NP, remain unknown.

Objectives: We sought to characterize the prevalence of NP in adolescents with SCD who have at least one risk factor for NP and determine the relative impact of these risk factors.

Design/Method: From April 2022 to June 2023, patients ages 14-18 years with SCD and at least one risk factor for NP (female sex, ≥3 acute care visits for pain in the preceding 12 months, hydroxyurea therapy)

completed the painDETECT questionnaire at a routine outpatient visit. painDETECT results characterized likelihood of NP as unlikely, possible, or likely. Results were analyzed by total number of risk factors present and by individual risk factors or combinations of risk factors. Comparisons were made using Fisher's exact test, paired t-test, or Kruskal-Wallis test, as appropriate.

Results: A total of 101 patients completed the painDETECT questionnaire. Sixty-four patients (63.4%) were female and median age was 16.1 years (range 14.0-18.6). Seventy-one patients (70.3%) were prescribed hydroxyurea and 14 (13.9%) had ≥3 acute care visits for pain in the preceding 12 months. painDETECT scores indicated that NP was unlikely for 81 patients (80.2%), possible for 16 patients (15.8%), and likely for 4 patients (4.0%). No individual risk factor was independently associated with an increased risk of NP. Patients with all 3 risk factors were significantly more likely than patients with 2 or 1 risk factor to have scores indicating that NP was likely (17% vs. 5.4% vs. 1.7%) or possible (50% vs. 8.1% vs. 17%) (p=0.017). There was no significant difference when comparing painDETECT scores of patients with 1 risk factor to those with 2 risk factors.

Conclusion: Individual risk factors did not correlate with a higher risk of NP in adolescents with SCD, but the combination of female sex, increased frequency of acute care visits for pain, and hydroxyurea therapy was associated with a higher risk of NP in this population. Routine screening and evaluation of patients with SCD at risk of NP may improve the detection and treatment of NP.

Poster # 113

MONITORING OF PHARMACOLOGIC THROMBOPROPHYLAXIS IN HOSPITALIZED PATIENTS WITH SICKLE CELL DISEASE

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Background: Sickle cell disease (SCD) has been well-recognized as a hypercoagulable state in adult literature with growing evidence suggesting similar phenomenon in children and adolescents. There is currently limited data to guide venous thromboprophylaxis in adolescents and young adults with SCD.

Objectives: To describe effective and safe dosing strategies for venous thromboprophylaxis in hospitalized adolescents and young adults with sickle cell disease.

Design/Method: Retrospective chart review identified patients with SCD hospitalized over a 6-month period. Prophylactic anticoagulation and monitoring was per institutional guidelines. Demographic data collected included admission labs, venous thromboembolism (VTE) risk factors, low molecular weight heparin (LMWH) dose, anti-Xa concentrations, bleeding symptoms, development of thrombosis within 30 days of admission.

Results: The study population consisted of 41 patients with 70 total admissions, divided into an older cohort (age >16 and weight >50kg) of 31 patients with 56 admissions and a younger cohort (age <16 and weight <50kg) of 10 patients with 14 admissions. Average number of VTE risk factors per patient per admission was 2.7±1.36 and average length of stay was 6.4±4.94 day. The older cohort was considered for adult dosing (enoxaparin 40mg daily) and the younger cohort for pediatric dosing (enoxaparin 0.5mg/kg BID, maximum 40mg BID).

In the older cohort 36/56 (64.3%) were started on LMWH, 18/56 (32.1%) were not started, and 12/56 (21.4%) refused prophylaxis. Of those started on anticoagulation for the first time (16 patients), anti-Xa concentrations were obtained for 68.8% (11/16) with a mean 0.27±0.09 IU/mL. In the younger cohort 2/14 (14.3%) admissions started LMWH, 4/14 (28.6%) were not started, and 8/14 (57.1%) refused prophylaxis. Of those started on anticoagulation (2 patients), anti-Xa concentrations were obtained for 100% (2/2) with a mean 0.38±0.13 IU/mL.
Within both cohorts 38 patients were started on LMWH (36 older, 2 younger), and in 25/38 (65.8%) instances they received concomitant NSAIDs. One patient developed bleeding symptoms and prophylaxis was discontinued. No thrombi occurred in either group within 30 days of admission.

Conclusion: Our study describes the ability of standard adult dosing to achieve appropriate anti-Xa levels in hospitalized adolescents and young adults with SCD as low as age 16. Further investigation is warranted regarding standardized indications to initiate prophylaxis and dosing in patients younger than 16.

Poster # 114

SAFETY AND EFFICACY OF DEFIBROTIDE IN SICKLE CELL DISEASE-RELATED ACUTE CHEST SYNDROME

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Background: Acute Chest Syndrome (ACS) stands as a predominant cause of morbidity and mortality in Sickle Cell Disease (SCD) patients, with adults facing a fourfold higher mortality rate than children. Endothelial dysfunction emerges as a pivotal contributor to ACS in SCD, an aspect not effectively targeted by current therapeutic approaches addressing infection, inflammation, and alveolar hypoxia. Defibrotide, a polydisperse mixture derived from porcine intestinal mucosa, exhibits promise in safeguarding endothelial function, particularly in small vessels.

Objectives: To determine the safety and efficacy of defibrotide in the treatment of patients with SCD-associated ACS.

Design/Method: Patients with SCD- (Homozygous Hemoglobin S disease, Hemoglobin SC Disease or Hemoglobin S$\beta^{0/+}$Thalassemia) associated ACS 2 to 40 years of age were enrolled. Defibrotide was administered at 6.25 mg/kg IV Q6H (total daily dose 25 mg/kg/day) within 24 hours of consent and continued for 7 days or until the patient was discharged from hospital (IND 127812) (NCT 03805581). Standard care, including antibiotics, analgesics, oxygen, and transfusions, was concurrently administered. Comprehensive assessments, encompassing blood tests, imaging, and plasma biomarker analysis, were conducted at baseline, day 7, and day 30.

Results: Twenty patients, with a median age of 9.5 years and diverse SCD types, participated. The median defibrotide dose was 18.5 mg/kg per day, with an average hospital stay of 6.1 days. No serious adverse events related to defibrotide were reported, with only two patients experiencing mild epistaxis. Pulmonary infiltrate was observed in 18 out of 20 participants. Thirteen patients had fever as a presenting symptom, nine patients required O_2supplementation, and thirteen patients were treated

with blood transfusions with a median of 1.9 units transfused per patient. Fibrinolytic activity, measured by tissue plasminogen activator and prostaglandin plasma concentrations positively correlated with total defibrotide doses in patients at day 7 of treatment ($p < 0.01$, $p < 0.05$ respectively). There was a reduction in inflammation by day 7 of defibrotide treatment, marked by a reduction in neutrophils and interleukin-6 concentrations ($p < 0.05$ each).

Conclusion: Defibrotide demonstrated to be safe and tolerable in patients with SCD-associated ACS and appears to reduce coagulation risk and inflammation. Future endeavors should involve randomized multi-center trials to ascertain the efficacy of defibrotide in the context of SCD-associated ACS.

Jazz Pharmaceuticals provided financial support and the defibrotide used in this study.

Poster # 115

SICKLE CELL DISEASE RELATED VASCULOPATHIES AND EARLY EVALUATION IN A PEDIATRIC POPULATION

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Background: Recently, we studied vaso-occlusive crises in our pediatric sickle cell disease (SCD) population. Vasculopathy in SCD deserves distinct exploration. Per predominantly adult literature, cardiovascular pathologies are up to 10-fold more prevalent in patients with SCD versus the general population.

Objectives: Here, we aim to retrospectively evaluate vasculopathies and surrogate markers in pediatric SCD.

Design/Method: An IRB-approved review was conducted to study the surrogate parameters of pediatric SCD-associated vasculopathy in relation to patients' age, SCD genotype, and fetal hemoglobin (HbF) percentages. We analyzed tricuspid valve jet velocity (TRJV) data from echocardiograms, trans-cranial doppler (TCD) velocities, and urine microalbumin/creatinine ratios (UM/Cr). Retinographies and overt vasculopathies were presented descriptively.

Results: There were 20 females and 20 males (average age 8.3 years, range 2.3-19), with beta-globin genotypes of HbSS/Sβ^0 (70%), HbSC (22.5%), and HbSβ^+ (7.5%). The mean (±SD) HbF percentage was 17.4±12.7% (30% higher in <10 versus ≥10 y/o, and 3 times higher in SS/Sβ^0 versus SC/Sβ^+). Sixty-five % of patients were on hydroxyurea, and half of those were also on L-glutamine. Thirty-six patients had TCDs obtained within 1.4±0.9 years (HbF, UM/Cr, and brain natriuretic peptide (BNP) within ≤12 months). TCD velocities were low-normal. Bilateral MCA and PCA velocities were significantly higher for HbSS/Sβ^0 versus HbSC/Sβ^+ groups (respectively, 96 vs 86 cm/sec, p=0.03; and 50 vs 41 cm/sec, p<0.001). Echocardiograms were done for 28 patients; however, TRJV was measurable in only 19 (Mean±SD: 2.46±0.19 m/s; for SS patients <10 y/o vs. ≥10 y/o, 2.43 vs 2.49 m/s, p=0.6). Nine patients had TRJV ≥2.5-2.8 m/s, but BNP levels ≤80 pg/ml. UM/Cr ratios were 9-fold higher in SS/Sβ^0 versus SC/Sβ^+ groups. There was one case of moyamoya, two silent infarcts, two cases of persistent macroalbuminuria, and one instance of severe hematuria/renal papillary necrosis. Most patients ≥9 y/o had retinographies without any SCD-related changes. Overall, there was no correlation among TCD(MCA), TRJV, and UM/Cr

values in 17 patients, suggesting that in this population, pathologies of cerebral, cardiopulmonary, renal, and retinal vascular beds may evolve relatively independently. However, patients with higher TRJV and/or overt vasculopathy (n=14) were older than ones without (12.5±4.7 versus 6.1±3.1 y/o, p<0.001)) and had lower HbF (11.4±7.6 versus 20.6±13.8%, p=0.026).

Conclusion: Overt vasculopathies are less frequent in this pediatric SCD population than adults. However, age-dependent trends and surrogate markers are suggestive of early origination of SCD vasculopathies in youth, justifying intense screening to actively detect and prevent progression of SCD vasculopathy with disease modifying agents and supportive measures.

Poster # 116

TELEHEALTH USE AMONG CHILDREN WITH SICKLE CELL DISEASE BEFORE AND DURING COVID-19 IN THE U.S.

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Background: Limited access to care for patients with sickle cell disease (SCD) is associated with lower quality of care and poor health outcomes. During the COVID-19 pandemic, telehealth has grown significantly, improving access to care for many conditions. The adoption of telehealth among commercially-insured children with SCD is unknown.

Objectives: To (1) examine telehealth use among commercially-insured U.S. children with SCD before and during the COVID-19 pandemic; and (2) identify patient characteristics associated with telehealth use.

Design/Method: This retrospective study analyzed commercial insurance claims data from Merative™ MarketScan® Research Databases from 1/1/2019 to 12/31/2021. Individuals aged 1 to 18 years with ≥3 SCD diagnoses and no cancer diagnosis, who were enrolled ≥11 months each year were included. For Objective 1, monthly telehealth and in-person outpatient visits were counted. For Objective 2, descriptive analyses and logistic regression were used to determine the association between patient characteristics (age, gender, geographic region, rural vs. urban status, and the number of SCD-related outpatient visits 1-year prior [03/2019-02/2020]) and the use of telehealth visits during the first year of the pandemic (03/2020-02/2021).

Results: Among 547 SCD patients (mean [SD] age = 9.9 [4.6], 48.6% female) included, 31.8% used ≥1 telehealth visit during the pandemic. Before the shutdowns in 03/2020, monthly telehealth visits averaged 0.1 [SD=0.4] out of 611.9 [SD=38.5] outpatient visits (0.02%). In the first year of the pandemic, the mean monthly telehealth visits increased to 25.8 [SD=10.5] among 469.5 [SD=54.2] outpatient visits (5.5%), and peaked in 05/2020 (49/354; 13.8%). Telehealth visits decreased slightly to 24.5 [SD=4.0] per month (4.0%) while outpatient visits increased to 609.1 [SD=30.0] per month after the first year. Living in a rural area is associated with a 70.8% lower likelihood of using telehealth (compared to urban; OR: 0.292, 95% CI: 0.099-0.862, p=0.0259), after controlling for other covariates. A higher likelihood of using telehealth was associated with living in the West or Northeast (compared to the South; odds ratio [OR]=2.707, 95% CI: 1.181-6.206, p=0.0186; OR=1.775, 95% CI: 1.030-3.057, p=0.0386, respectively); and having 5-7 or 8-12 outpatient visits 1 year prior to the pandemic (compared to 0-4 visits; OR=1.811, 95%

CI: 1.086-3.021, p=0.0228; OR=1.862, 95% CI: 1.069-3.245, p=0.0282, respectively).

Conclusion: Telehealth use among children with SCD rapidly increased after the COVID-19 shutdown in March 2020 but decreased afterwards. More severely affected patients are more likely to use telehealth, and children living in the South and rural areas may have issues accessing telehealth.

Poster # 117

OSTEOPATHIC TREATMENT, A NOVEL ADJUNCT IN SICKLE CELL CARE: INTERIM SAFETY AND FEASIBILITY ANALYSIS

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Background: Children and adolescent young adults (CAYAs) with sickle cell disease (SCD) suffer from severe SCD-related pain and treatment-related side effects that result in hospitalization and diminish healthcare-related quality of life. With substantial morbidity conferred by SCD-related pain, improved supportive therapies are needed. Osteopathic medical treatment (OMT) utilizes manual techniques to diagnose and treat body dysfunctions and has the potential to be a valuable non-pharmacologic addition to multimodal pain management. To date, no studies have investigated OMT as adjunctive therapy in the care of CAYAs with SCD.

Objectives: To investigate the safety and feasibility of OMT in CAYAs with SCD.

Design/Method: Prospective, single institution, observational study evaluating CAYAs with SCD aged 3-26 years hospitalized at Riley Hospital for Children. Interim analysis included data obtained between December 2022-July 2023. Approval was obtained from the Indiana University Institutional Review Board. Patients who reported pain were offered OMT. Verbal informed consent/assent were obtained. OMT was provided by trained osteopathic medical students under the supervision of a board-certified osteopathic physician. Safety was assessed by adverse event grading, and pain was assessed with validated pain FACES scores immediately pre- and post-OMT. Feasibility endpoints were calculated as the percentage of OMT encounters offered and completed without interruption to standard inpatient care. Data were summarized using descriptive statistics.

Results: At interim analysis, 8 patients received OMT, with 32 separate OMT encounters over the study period. Across the 32 OMT encounters, 60 unique areas of pain were reported and treated. The majority of patients were male (n=5, 62.5%) with median age of 17.5 years at the time of OMT (range 6.8-23.5 years). One hundred percent of OMT encounters offered were completed without interruption to standard inpatient care. There were no reported adverse events within 24 hours of OMT. Further, there were no FACES scores that correlated with worsening pain. Median FACES scores immediately pre- and post-OMT were 9 and 7.5, respectively. FACES scores immediately post-OMT were decreased (n=22, 68.8%) or unchanged (n=10, 31.3%) in all encounters.

Conclusion: OMT for hospitalized CAYAs with SCD is safe and feasible at this interim analysis. Further, there were no worsening of FACES pain scores, and the majority of patients had a decrease in pain following OMT. These findings support continued investigation into the potential efficacy of

incorporating OMT into the multimodal management of CAYAs with SCD with continued prospective studies in this vulnerable patient population.

Poster # 118

Sickle cell EHR population management approach for high-quality care delivery: genotype testing

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Background: We instituted sickle cell disease clinical care guidelines for stroke risk screening, disease-modifying therapies (DMTs) and transfusion therapy in the late 1990's. This generated the design of care protocols requiring accurate identification of those with SS/SB0thal for stroke prevention screening and appropriate DMT discussions to deliver evidence-based care. However, tracking was cumbersome as we used paper and Excel files.

Objectives: We aimed to perform molecular testing for disease and red cell antigen (RCA) genotypes, then use these results within an electronic population management model to identify selected patient subpopulations for appropriate screening and red cell alloimmunization prevention protocols.

Design/Method: In 2016, the Comprehensive Sickle Cell Center (CSCC) at Children's Hospital of Philadelphia (CHOP) developed and implemented an electronic health record (EHR)-based system, the SCD patient registry and proactive care outreach tools, to facilitate processes for timely service delivery. We focused on stroke screening, hydroxyurea therapy initiation and monitoring, and red cell alloimmunization prevention. Between January 2015 and December 2023, approximately 1400 patients with SCD were tracked across two CHOP outpatient clinics. EHR-based ordersets and new workflows allowed the nursing team to proactively manage necessary testing for patients.

Results: Prior to implementation of the EHR-based tools and new workflows in October 2016, on average 61% of eligible patients had received alpha and beta globin molecular testing, 24% had received a blood bank order for C-, E-, K-matched red cell units, and 78% had received RCA testing. As of December 2023, on average alpha and beta globin molecular testing increased to 77%, receipt of the specialized blood bank order increased to 99%, and completion of RCA testing increased to 96%.

The increase in appropriate testing described above supported a sustained increase in ensuring initiation of annual TCD ultrasounds by age 3. In 2015, only 55% of eligible patients completed a TCD by age 3, but in years 2017-2023, that number increased to 98%.

Conclusion: This implementation of an SCD EHR-based population health registry tool, built to organize and facilitate the completion of molecular diagnostic and other testing, improved our ability to accurately provide genetic counseling, disease-modifying therapies, stroke risk screening, and appropriate selection of red cell units when transfusion is needed. Accurate SCD genotype data allows for more tailored identification of subpopulations to screen for disease complications, promote research project participation, and track care protocols to prevent red cell alloimmunization.

Poster # 119

CONSENSUS WORKGROUP TO ENHANCE ASSESSMENT OF DEVELOPMENT AND COGNITION IN SICKLE CELL DISEASE

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Background: Developmental delay/cognitive deficits are common among children and adults with sickle cell disease (SCD). In 2020, the American Society of Hematology published evidence-based clinical guidelines, including recommendations to implement signaling questions regarding early childhood development as well as screening and evaluation under specific circumstances.

Objectives: To provide more consensus-based guidance for assessing development and cognition for individuals with SCD across the lifespan.

Design/Method: The National Alliance of Sickle Cell Centers (NASCC) convened a consensus workgroup of experts in neuropsychology, psychology, hematology, occupational therapy, and neurodevelopmental pediatrics. The goal of the panel was to outline specific clinical practices to meet current guidelines and expand on recommendations for enhanced care. Members of the panel represented regions from across the U.S., pediatric, adult and lifespan care, and they had either published or led clinical programming for assessing development and cognition in SCD. The group met face-to-face for two days at the larger NASCC consensus meeting and then in monthly video conferences. Members reviewed published studies that included assessment of children and/or adults with SCD. Protocols were sought from in and outside of NASCC-affiliated institutions for assessing cognition in patients with SCD. Sub-groups formed to focus on early childhood, school-age, and adulthood as well as specific indications for more extensive evaluation.

Results: Upon review of literature and based on panel expertise, clinical practices were outlined to meet current guideline standards and additional recommendations were made for enhanced care: (A) Across ages, education to patients and families about effects of SCD on development and cognition should accompany signaling questions. (B) For young children, guidance was provided for ensuring AAP-recommended universal developmental and social-emotional screening are completed. (C) For school-age children and adults, screening evaluations were recommended at key transition timepoints. Goals for screenings include patient/caregiver and medical provider understanding of patient functioning, referral for early intervention services, cognitive assessment, therapy services, and/or community, school, and vocational supports. (D) Through consensus, a list of indicators was developed that would supersede screening in favor of comprehensive neuropsychological evaluation.

Conclusion: The panel outlined specific clinical practices for SCD centers to either meet existing standards or provide enhanced care through additional recommendations. Several options exist for each age group, and clinicians will need to determine which approach are feasible within their setting. Collaboration across NASCC and other Sickle Cell Disease Specialty Care Centers will be important to advance our understanding and improve habilitation for this population.

Poster # 120

Evaluating GFR Calculations in Pediatric Patients with Sickle Cell Disease: A Comparative Study

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Background: Sickle cell disease (SCD) is an inherited disorder where abnormal hemoglobin causes red blood cells to become sickled and dense, leading to ongoing hemolysis and vaso-occlusion. Chronic organ damage, ischemia, and renal complications that often start in the first decade of life.
It is well known that GFR has been an unreliable marker of kidney function in pediatric SCD due to hyperfiltration. We aimed to compare the new 2021 GFR calculations – one includes cystatin C (GFRCysCr) and one only Cr (GFRCr) – with markers of kidney function in pediatric patients with SCD. We hypothesized there would be a find difference between GFR calculations when compared to markers of kidney function and erythropoietin (EPO) in pediatric patients with SCD and that the relationship will be more significant in the younger age group due to hyperfiltration.

Objectives: Evaluation of both 2021 GFR calculations in patients with SCD and their relation to markers of kidney damage and erythropoietin

Design/Method: Data gathered through retrospective chart review of pediatric patients with SCD seen at St. Christopher's Hospital in Philadelphia. Data collected from appointments between 3/1/21 and 8/15/21. Data was excluded for patients who had ever undergone EPO treatment, those with underlying kidney disease, or if laboratory tests were conducted during disease exacerbation.

Results: 137 patients included in analysis, ages 1-28. Genotypes included SS(60%), SB+(9%), SBO(7%), and SC(24%). Patients were split into two groups: <12 years old and ≥ 12 years old. Nonparametric correlation was used to compare each GFR calculation with EPO. Pearson's correlation was used to compare each GFR calculation with urine protein, Cr, and cystatin C. In both groups <12 y/o and ≥ 12 y/o there was a statistically significant relationship between EPO, Cystatin C, and Cr with both GFRCysCr and GFRCr.
Urine protein had no statistically significant correlation to either GFR calculation in either group. Patients taking hydroxyurea had statistically significantly higher EPO in both groups vs those who did not. GFR was significantly lower in the older age group. GFRCysCr relationships were more statistically significant in <12 y/o group than in the group ≥ 12 y/o.

Conclusion: Both GFR calculations showed statistically significant relationships with markers of kidney function in both groups. The relationship between GFRCysCr and markers of kidney function were more significant in the <12y/o age group, possibly due to cystatin C not as affected by hyperfiltration. Further studies necessary to evaluate utility of GFRCysCr in younger patients with SCD.

Poster # 121

IMPROVING CARE FOR PATIENTS WITH SICKLE CELL DISEASE THROUGH A MEDICAL HOME MODEL IN HEMATOLOGY

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Background: Persons with sickle cell disease (SCD) historically have significant barriers to high quality care whether through poor access to care, fractured care, or lack of a "medical home". In SCD programs, identifying patients in care and tracking quality metrics in patients with SCD presents a significant challenge. Especially in programs with multiple Hematology providers, continuity of care can be difficult to achieve. Poor continuity of care may have adverse effects on patient outcomes. Improving patient care requires improvements in healthcare utilization, screenings, and use of preventive treatments.

Objectives: To increase the portion of children with SCD who complete an annual comprehensive visit with a primary Hematologist and nurse champion by 30% by end of 2022.

Design/Method: Using the electronic medical record, patient lists were extracted based on ICD 10 codes for SCD. The lists were culled by age (to remove adult patients) and by date of last visit. Active patients were defined as those having been seen in the Hematology program in the prior 3 years. Manual data validation was performed on a subset of patients. The complete patient list was divided among all SCD providers in the Hematology program in relative portion to the clinical effort of the provider. Successive PDSA cycles were designed to identify a primary Hematologist and nurse coordinator for each patient. The primary team responsibilities were carefully defined to set consistent and achievable goals for the role. Hematology physicians, advanced practice providers, and nurse coordinators were asked to assign themselves using tools in the electronic medical record to patient charts. Provider assignment were made based upon prior relationships with a given patient, the last provider seen by the patient, family preference and/or provider preference. Clinic schedulers were asked to preferentially schedule patients with their assigned provider to improve continuity of care.

Results: The portion of patients with an assigned Hematologist increased from 16% to 85% over 18 months. The portion of patients with an assigned nurse coordinator increased from 8% to 92% over 18 months. Assessments of frequency of visits with the primary team are ongoing. Parallel quality improvement efforts leveraged the primary team assignments to specifically target opportunities for improvement.

Conclusion: Using a medical home model with a primary Hematology team assigned to each patient facilitated targeted improvements in quality metrics and improved continuity of care. Further optimization of the model will lead to improved outcomes for children with SCD.

Poster # 122

MANDATED ADMISSION FOR FEBRILE INFANTS WITH SICKLE CELL DISEASE?: SINGLE CENTER RETROSPECTIVE REVIEW

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Background: Children with sickle cell disease (SCD) are at increased risk of invasive bacterial infections. It is recommended that children with SCD present for medical evaluation with every fever. Criteria for admission varies widely, with some institutions mandating hospitalization for all febrile patients with SCD under 12 months of age. There is a paucity of data regarding the relative risk of invasive bacterial infection among pediatric age groups in the era of pneumococcal vaccination and routine use of hydroxyurea.

Objectives: As an institution with no guideline mandating admission of febrile patients with SCD <12 months of age, we aimed to determine the rates of admission, readmission, and invasive infection as a means of establishing the relative safety of discharging well appearing infants with SCD presenting with fever.

Design/Method: We conducted a retrospective review of the St. Jude Children's Hospital Sickle Cell Clinical Research and Intervention Program (SCCRIP) database to identify fever evaluations (discharge diagnosis of fever or recorded temperature ≥38.0°C) to the outpatient clinic, acute care clinic, or associated outside emergency departments. Discharge diagnoses, hospital admission, and return for reevaluation within 7 days was analyzed from January 1, 2011, to December 31, 2021. Age subgroups were defined as: infants <12 months, preschool 12-60 months, school aged >60 months.

Results: Of 832 patients with 4733 episodes of fever, hospital admission at initial presentation was low, with infants(26.0%, 150/577) slightly lower than preschool (20.0%, 351/1751, *p*=<.01), but similar to school aged (25.1%, 377/1502, *p*=0.7) children with SCD. There was no significant difference between infants and older children in the rate of 7-day-return for reevaluation (11.4% vs.9.8%, *p*=1.6), or readmission within 7 days of initial presentation (48.1% vs. 45.2% of return visits, *p*=0.2). Viral illness was the leading diagnosis in all subgroups (16.8% overall). Infants were more likely to be diagnosed with soft tissue infection or urinary tract infection, and school aged children were more likely to have ACS and osteomyelitis than the other subgroups. There was no significant difference between the rate of bacteremia amongst infants (0.3%, n=2), preschool (0.8%, n=17), and school aged children (0.6%, n=12)(*p*=0.165).

Conclusion: Although risk of invasive pneumococcal infection has been a major driver of management for febrile infants with SCD, no difference can be seen regarding the rates of bacteremia in infants versus older children. The risk of other serious comorbidities of SCD may be significantly lower in infants as compared to 1-5-year-old, and older patients.

Poster # 123

EXPLORING THE EXPERIENCES OF PEDIATRIC PATIENTS WITH SICKLE CELL DISEASE AND THEIR FAMILIES

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Background: Sickle Cell Disease (SCD) is a lifelong genetic disorder of red blood cells, which causes abnormal hemoglobin shape often resulting in pain crises and other serious health complications. Several surveys have shown that patients with SCD experience discrimination and lower levels of

satisfaction in healthcare settings. There has been little research done to explore the satisfaction of pediatric patients with SCD in inpatient and outpatient settings.

Objectives: This qualitative project aimed to explore further specific, actionable areas of dissatisfaction and any areas of increased satisfaction among pediatric patients with SCD and their families.

Design/Method: Semi-structured interviews were conducted with pediatric patients with SCD and/or their guardians at one academic institution. Any patient with SCD eight years of age or older was eligible to participate in an interview, and parents of a child with SCD of any age were also eligible. Interviews were audio-recorded and took place in clinic. Recordings were transcribed verbatim and were qualitatively coded using standard multi-level semantic analysis. Fourty-one percent of the interviews were independently double-coded, and discrepancies were resolved by consensus. Final codes were analyzed, and major themes were identified.

Results: Eighteen pediatric patients with SCD and/or their families were asked to participate in the study. Seventeen (94%) agreed for a total of twenty-six participants (seventeen guardians, nine patients). Nine family interviews were conducted, and another eight were conducted with parents only because the patients were younger than eight. Fifteen families identified as African American, one identified as Hispanic, and one identified as African. Patients and their families described five main areas leading to dissatisfaction in the healthcare setting: (1) Long wait times; (2) Neglect for SCD protocols within emergency departments; (3) Biases against patients with sickle cell disease; (4) Frustration with procedures, specifically with blood draws; (5) Lack of empathy and compassionate listening among healthcare providers. Positive experiences were almost all due to aspects of strong patient-provider relationships. Outside of the healthcare setting, patients and their families emphasized the need for improved education and awareness of SCD within the community.

Conclusion: Exploring perspectives from these pediatric families provided insight into specific areas of dissatisfaction among patients with SCD. This research offers actionable items that healthcare providers can apply to improve the healthcare experiences and everyday lives of children with SCD. Additional efforts should be directed towards addressing social determinants of health and systemic racism to further improve healthcare experiences of patients with SCD.

Poster # 124

QUALITY IMPROVEMENT: IMPLEMENTING OUTPATIENT PAIN ACTION PLANS FOR PATIENTS WITH SICKLE CELL DISEASE

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Background: The ASPHO "Position Paper on Transition of Patients with Sickle Cell Disease (SCD) from Pediatric to Adult Healthcare" and the American Society of Hematology (ASH) best practice guidelines recommend that individuals with SCD have individualized outpatient pain plans for home management of vaso-occlusive crises (VOC). We used Quality Improvement (QI) methodology to adapt an electronic health record (EHR)-enabled asthma action plan into a Pain Action Plan (PAP), aiming for easier implementation and sustainability.

Objectives: Global Aim: Improve pain management and quality of life of children with SCD by implementing patient- and family-centered PAPs.

Smart Aim: Within 9 months (January-September 2023), ≥50% of patients with SCD seen during their annual comprehensive clinic visit will receive a PAP.

Design/Method: Our QI team met with the SCD team to discuss barriers and facilitators to implementation of PAPs. Meetings with clinical informatics, pulmonology, and hematology teams informed our QI tools (process mapping, key driver and Ishikawa diagrams). The PAPs were modeled with green, yellow, and red zones to indicate different levels of pain management and included pain medication dosages and supportive care measures for each zone based on discussion between the SCD team and patients and caregivers. Families received printed color copies of their PAP. Each comprehensive clinic session constituted a Plan-Do-Study-Act (PDSA) cycle. Our outcome measure was the percentage of patients who received a PAP at their SCD comprehensive clinic visit.

Results: There have been 10 comprehensive clinic sessions (PDSA cycles) including 35 patients from May-September 2023 and 92% of eligible patients (33/35) received their PAP. Of patients who did not receive a PAP, one left clinic before the PAP was delivered, and the other spoke and read Haitian Creole. Families indicated that the PAP was a valuable tool to have at home during VOC. Of 14 evaluable patients, 5 had VOC and 3 (60%) used their PAP at home. Providers reported that the new EHR-enabled PAP is easy to use and facilitates efficient communication during comprehensive clinic visits.

Conclusion: Our inter-professional approach and leveraging and adapting existing tools in the EHR led to successful implementation of the PAP at SCD comprehensive visits. To further increase the percentage of patients with PAPs, we will link PAP use to medication reconciliation and expansion into all visit types for patients with SCD. Our strategy may be adapted by other comprehensive SCD teams to ensure implementation of best practice guidelines to improve quality of care for individuals with SCD.

Poster # 125

IMPROVING INPATIENT MANAGEMENT OF VASO-OCCLUSIVE EPISODES IN CHILDREN WITH SICKLE CELL:
QI Project

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Background: Vaso-occlusive episode (VOE) is the most common reason for hospitalization in children and adults with sickle cell disease. The negative impacts of frequent VOE hospitalization in the SCD population include emotional distress, poor school performance, diminished quality of life, and negatively impacting healthcare costs analysis. Reducing hospital length of stay (LOS) involves adopting an early, aggressive pain management approach along with mutli-disciplinary support from complementary non-pharmacological methods like music and physical therapy.

Objectives: To implement a QI model focused on a comprehensive approach to VOE inpatient management including pharmacological, and non-pharmacological interventions aimed to decrease

hospital length of stay by 20% as well as to decrease the 30-day readmission rate for VOE by 30% in 1 year-period.

Design/Method: We are conducting a prospective QI project using the plan-do-study-act (PDSA) method. Our target population is children and young adults aged 0–21 years old with SCD admitted to our hospital for VOE. Institutional approval for QI determination was obtained. Our team includes pediatric hematology providers, nurse representatives, pharmacist, physical therapist, child life specialist, and social worker. We identified key drivers as follows: 1)an updated inpatient pain plan based on patient's risk stratification; individualized inpatient pain plan for high-risk patients and standardized inpatient pain plan for non-high-risk patients 2)Incorporating into an agile clinical pathway, and 3)providing non-pharmacological interventions during admission including daily routine, physical therapy massage and music therapies, and child life activities. We started implementing this project in a stepwise approach in June 2023. Our interventions so far included obtaining patient consent, nursing education, resident education, and launching Agile clinical pathway.

Results: Patients have been willing to participate in this project. Thus far we have 100 patients consented. We noticed that all the multidisciplinary teams embracing the launch and adopting the change. Total number of admissions for VOE was 34 between August and November 2023. We have seen a drop in LOS from the pre-intervention average length of stay was 6.16 days vs post-intervention 5.04 days. An estimated 30 day readmission rate for the pre-intervention period was 52.67% which dropped to 23.52% post-intervention.

Conclusion: Improving inpatient pain management for SCD through implementing a comprehensive approach is effective in terms of decreasing LOS. Longer-term follow-up is needed to ensure sustainability and longer-term impact on quality of patient care and reduction in healthcare costs.

Poster # 126

DEFINING THE PSYCHOSOCIAL CARE LANDSCAPE IN SICKLE CELL DISEASE

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Background: As more patients with sickle cell disease (SCD) live longer, the need for complementary psychosocial staff and services to address the psychological, emotional, and social tolls of this chronic and pain-riddled condition has also expanded. Evidence based medical guidelines exist yet none for psychosocial care. Despite the abundant literature attesting to the psychosocial toll of SCD on patients and their caregivers, little is known about the true infrastructure that exists to address these complex issues.

Objectives: Through the distribution of a nationwide comprehensive survey to psychosocial support team members, this project seeks to establish a baseline understanding of what psychosocial roles, training, and services currently exist in the Sickle Cell Disease Treatment Center Community, particularly among the National Alliance of Sickle Cell Centers (NASCC) designated sites.

Design/Method: A mixed methods cross-sectional survey design captured quantitative and qualitative data from English-speaking psychosocial providers at National Alliance of Sickle Cell Centers (NASCC). Fifty-six questions were designed to gauge psychosocial infrastructures and roles via these topics: job responsibilities, demographics, work experience, caseload number, high-risk patient percentage, sickle cell care embeddedness, licensure, center types, NASCC affiliation awareness, work priorities, sickle cell training, role funding, compensation structure, billing practice, supervisory arrangement, barriers to care, and ideas for advancing care access.

Results: Eighty seven psychosocial providers responded at the time of abstract submission, most being social workers (31.6%), licensed clinical social workers (16.5%), and psychologists (16.5%). All regions were represented with 30.8% from the Southeast. Thirty-nine percent worked in SCD for 0-2 years, 6% over 21 years, with 29.5% working only with pediatric patients, and 20.5% only with adults. Thirty two percent of providers work only in SCD, with 52.6% being part-time. Thirty one percent were unsatisfied with psychosocial supports at their center. In terms of a major barrier to care, 41.9% cited lack of staff, 47.5% checked lack of funding, 29.5% checked lack of time for care. Qualitative responses echoed the dire need for more staff, protected time, and funding as consistent themes.

Conclusion: Insights from varied psychosocial disciplines helped clarify existent supportive services across "comprehensive" centers. These results indicate that the demand of SCD's layered psychosocial challenges far outweigh the supply of embedded providers able to appropriately address these complex issues. This snapshot of today's psychosocial care landscape in SCD lays a foundation for next steps toward sickle cell-specific psychosocial guidelines and evidence based advocacy to expand psychosocial teams and their bandwidth to provide quality comprehensive care.

Poster # 127

MORBIDITY PATTERN AND IMPACT OF HYDROXYUREA THERAPY AMONG SICKLE CELL PATIENTS OF CHHATTISGARH INDIA

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Background: Sickle Cell Disease (SCD) is characterized by a single-point mutation in the beta-globin gene. Clinical symptoms are brought by RBC breakdown and blood vessel occlusion. Along with other manifestations, patients need to handle pain crises. There are many genetic variations seen between the patient's genotype and phenotype. Enormous variation is observed in morbidity pattern and clinical characteristics too. Current study is aimed to document morbidity pattern and impact of Hydroxyurea therapy of sickle cell patients in the Sickle Cell Institute Raipur's Outpatient Department patients.

Objectives: 1. To know the morbidity pattern of Sickle cell Disease Pt in Sickle Cell Institute of Chhattisgarh, Raipur.
2. To ascertain the impact of Hydroxy Urea therapy of Sickle cell Disease Pt in Sickle Cell Institute of Chhattisgarh, Raipur.

Design/Method: 65 patients, including adults and children above six years, were included in this study. After the acquisition of informed consent, relevant data collection was done by a predesigned pretested questionnaire. The appropriate statistical exercise was used for interpretation of results and inferences.

Results: Out of all 65 included in the study, acute febrile illness 54 (83%) and 53 (81.5%) reported pain crisis as the most common morbidity among them. Followed by 55.4% (36) jaundice, 33 (50.8%) patients had difficulty breathing. Joint pain was most commonly seen at knee joint (76.9%) as preferred location. Other complaints are Hand Foot Syndrome (24.6%), Epistaxis (27.7%), Acute Chest Syndrome (14, 21.5%) and Vaso-occlusive crisis (72.4%), difficulty in walking (60.0%) and eyesight (35.4%), Leg ulcers (9.2%) and Dactylitis (3.1%). Out of all 44.46% (29) had an awareness of SCD. Hydroxyurea therapy was highly significant in improving the patient's clinical picture and also lowering the frequency of hospitalization & requirement for blood transfusion (P <0.01).

Conclusion: Febrile illness and pain crisis is the most common morbidity among study participants along with low level of knowledge among them. Hydroxyurea therapy was quite effective as disease-modifying agent, especially for reducing the frequency of blood transfusion and lowering hospitalization rates among them

Poster # 128

Increased Hydroxyurea Adherence for Pediatric Patients with Sickle Cell at US Military Hospitals

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Background: Sickle Cell Anemia (SCA) causes significant acute, chronic complications, and premature mortality. The foundational treatment for SCA is hydroxyurea (HU) which reduces acute and chronic complications. Suboptimal HU adherence increases the burden of SCA complications for patients. Military service member's children who have SCA have access to either military or civilian pediatric hematology care at no or low cost.

Objectives: Our objective was to identify factors associated with HU adherence among pediatric, adolescent, and young adult (AYA) patients with SCA in the United States Military Health System (MHS).

Design/Method: Our cross-sectional study included 206 pediatric and (AYA) patients with SCA in the MHS who were prescribed HU in the last 12 months. We analysed factors association with adherence by unadjusted and adjusted logistic regression. Patient's adherence was categorized dichotomously according to the American Society of Hematology quality metric goal for HU adherence. Adherence was defined as having HU dispensed for at least 300 days of the last year.

Results: The adherent group, 26% of the study population, had a younger mean age in years, 11.7 versus 14.9 (p = 0.0003). The adherent group was more likely to receive hematology care in the MHS than in a civilian system, 39.3% adherent versus 19.3% (p = 0.0003). Logistic regression analysis of HU adherence, adjusted for age and gender demonstrated the patients receiving pediatric hematology care at a military healthcare facility had 2.96 (1.47-5.99, 95% CI) the odds of adherence compared to patients receiving pediatric hematology care at civilian healthcare facilities. The monthly base pay of the patient's sponsor, a strong indicator of socioeconomic status, was not associated with HU adherence odds ratio 1.00 (0.99-1.01, 95% CI).

Conclusion: Among Pediatric and AYA patients with SCA in the MHS, HU adherence appears equitable

throughout socioeconomic status (SES) when using sponsor monthly base pay as surrogate measure. The MHS is a single payer system without co-pays for care or prescriptions. Low to zero out of pocket cost for military or civilian pediatric hematology care likely contributes to this indication equity of HU adherence across SES for the patients in this study.
Hematology care at military facilities associated with increased HU adherence may also be explained by the removing the barrier of complexity. HU prescriptions in the MHS are filled at the same location as care. Prescriptions ordered by civilian providers to retail pharmacies are usually not at the location of care, increasing complexity.

Poster # 129

Extent and determinants of nutritional challenges and morbidity among sickle cell children

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Background: Sickle cell disease (SCD), a common single gene disorders, is a global public health priority. Growth of affected children is reduced. Role of nutrition is now said to be linked with the severity of the disease. Dietary supplementation for treating SCD is considered for these patients. Hence, this study was conducted with an objective to ascertain extent and determinants of nutritional challenges among SCD patient registered in Chhattisgarh.

Objectives: To assess the nutritional profile and ascertain the clinical determinants among children of Sickle cell Disease in Sickle Cell Institute of Chhattisgarh, Raipur.

Design/Method: Medical records of 671 SCD children ws ere reviewed, registered at sickle cell institute Chhattisgarh, Raipur. Appropriate statistical exercises were used for interpretation of results.

Results: Out of all 671 children included in the study, 380 (56.6%) were males, 72.11 were belongs to Other Backwards Class (OBC) while 6.11% were Schedule tribe. Among all underweight, stunting and wasting were 58%, 37.7% and 38.9% respectively. 16% children had chronic malnutrition and of them significantly high proportion had Hb < 10 mg/dl (P < 0.01). Chronic malnutrition was significantly higher (39.81%) among O +Ve blood group in comparison to other blood groups. Older children (11-18 Yrs) were significantly more (62.04%) in comparison to younger children (1-10Yrs) (P <0.01). More of all older children (64%) needed hospital care (P < 0.01). Study reveals Majority (73.92%) were diagnosed SCD beyond 5 Yrs of age. At time of diagnosis most common symptoms were generalized bodyache and Vaso Occlusive Crisis (28.17%) followed by Icterus (27.72%), needs hospitalization (26.83%), Bone and joint pain (2.53%) and Asymptomatic (14.7%) too. More than one fourth (26.68%) sought care in hospital before diagnosis either for blood transfusion (BT) or for after an episodes of Vaso-Occlusive Crisis (VOC). Pt with Hb level > 10mg and Hb F > 20% were significantly lesser risk of hospitalization.

Conclusion: Significant proportion of SCD children had chronic malnutrition. Older children with identified blood group, underweight and low Hemoglobin (<10mg/dl) and Low Hb F were at increased risk of hospital admission. Hospital admission is an opportunity for nutritional intervention and can be used as adjunct treatment in SCD children.

Poster # 130

LONG-TERM SAFETY OF DEFERIPRONE IN PEDIATRIC PATIENTS WITH SICKLE CELL DISEASE FROM A US REGISTRY

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Background: Patients with sickle cell disease (SCD) often require iron chelation therapy to reduce transfusional iron overload and minimize organ dysfunction. Deferiprone (DFP) is an oral iron chelator for transfusional iron overload in patients with thalassemia, SCD, or other anemias. Long-term safety data among pediatric patients with SCD treated with DFP in real-world clinical settings are limited.

Objectives: To evaluate long-term safety profile of DFP in pediatric patients with SCD from a US patient registry over ~10 years.

Design/Method: Data were obtained from pediatric patients receiving DFP in the Ferriprox® Total Care Registry between December 5, 2011, and August 31, 2020. The registry was designed to collect all information related to neutropenia and any adverse event (AE) that were fatal or led to hospitalization. All episodes of neutropenia were classified as serious adverse events, irrespective of their rates or clinical significance. Following enrollment, information on AEs, including severity, duration, and potential relationship to DFP, was collected.

Results: This analysis included 130 pediatric patients; 50 children (3–12 years; 48% male; mean exposure, 2.6 [range 0.1–8.5] years) and 80 adolescents (13–17 years; 39% male; mean exposure, 2.1 [range 0.1–8.5] years).
At the cutoff date, 46 patients (35%) were receiving DFP, 79 (61%) had been discharged from the registry (29 [22%] at physician's direction, 22 [17%] switched to deferasirox, 8 [6%] due to AEs), and 5 (4%) had not yet initiated treatment. Two (1.5%) deaths (myocardial infarction and congestive cardiomyopathy in 1 patient; hemophagocytic lymphohistiocytosis and hepatospenomegaly in 1 patient) occurred, both unrelated to DFP.
Overall, 26 (52%) children reported 132 AEs and 45 (56%) adolescents reported 118 AEs. In both age groups, the most common AEs included increased liver enzymes (22 events, 2 serious), sickle cell crisis (20 events, all serious), and pyrexia (18 events, 9 serious). Of the 250 AEs, 107 were deemed DFP-related (57 events in 16 children; 50 events in 28 adolescents), with abdominal discomfort being the most common DFP-related AE. One (0.8%) adolescent patient reported neutropenia (neutrophil count: 0.5–1.5×10^9/L), which was considered serious and related to DFP.

Conclusion: The safety profile of DFP was similar in young children (3–12 years old) and adolescents (13–17 years old) with SCD. DFP was well tolerated in pediatric patients with SCD, no new safety concerns were identified, and only one adolescent patient reported neutropenia. These findings are consistent with clinical trials and the known safety profile of DFP in thalassemia.

Poster # 131

OPTIMIZING AT-HOME ACUTE PAIN MANAGEMENT IN PEDIATRIC SICKLE CELL DISEASE: A QI PROJECT

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Background: Pain from acute vaso-occlusive crises (VOC) causes high rates of healthcare utilization in children with sickle cell disease (SCD). Patients' caregivers are responsible for first-line intervention when pain initially presents. Caregiver stress is related to worse pain and higher healthcare utilization. In our institutional practice, we noted the majority of patients did not have optimal at-home pain management prior to presenting for acute care to either our day-hospital or emergency room.

Objectives: Our global aim is to improve caregiver confidence in managing acute sickle cell pain episodes in the home setting and decrease healthcare utilization. Our smart aim is to provide personalized pain management plans to sickle cell patients in order to decrease acute healthcare utilization by 15% from a baseline of 21 visits in 9 months by one year from implementation.

Design/Method: We reviewed visits to our day-hospital or emergency room for simple VOC between January 1, 2023 and September 1, 2023 to establish a baseline, excluding encounters when other confounding diagnoses were also present, such as fever or other SCD complications. Using Plan-Do-Study-Act (PDSA) quality improvement methodology, we identified areas of potential intervention. Our primary intervention is the introduction of an individualized "Sickle Cell Action Pain Plan" for every patient with SCD. We performed a pre-implementation survey assessing caregiver confidence in managing their child's pain crises at home, and plan to perform a post-implementation survey.

Results: For our baseline data, we reviewed 21 patient encounters for VOC acute care. Of these, 2 took no medications at all prior to presentation for acute care, and 6 (29%) took the recommended combination of non-opioid and opioid medications. Eight encounters (38%) resulted in escalation to admission for pain control. Of 24 caregiver pre-implementation surveys, 54% of caregivers strongly agreed that they felt satisfied or confident in their ability to manage their child's pain at home. Only 62% of caregivers strongly agreed that it was easy to decide when to give their child pain medication.

Conclusion: At our institution, we have an ongoing need to optimize VOC pain management by caregivers at home. Through implementation of individualized pain plans, we hope to improve caregiver confidence and self-efficacy, and ultimately decrease acute healthcare utilization.

Poster # 132

TRABECULAR BONE SCORE IS ASSOCIATED WITH FRAGILITY FRACTURE IN THALASSEMIA AND SICKLE CELL DISEASE

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Background: Low bone mass has been described in over 50% of patients with thalassemia (Thal) and sickle cell disease (SCD), and though DXA is part of routine clinical practice, it has limitations with fracture prediction. Trabecular bone score (TBS), a textural analysis of bone quality assessed from a spine DXA scan, is highly predictive of fracture in individuals without hemoglobinopathies. Fracture risk

is poorly characterized in Thal and SCD.

Objectives: To evaluate the prevalence of abnormal bone quality from lumbar spine DXA and its relationship to fracture in patients with Thal and SCD

Design/Method: A retrospective chart review was conducted in patients with Thal or SCD > 11 years who had at least one spine bone mineral density (BMD) scan performed on Hologic DXA scanner in the past 13 years. The most recent scan was reanalyzed for bone quality using TBS Insight (Medimaps v 3.0.2, Geneva) and abnormal bone quality defined as TBS <1.20. Fracture prevalence was determined by patient report at time of DXA. Results were compared with data obtained from healthy controls.

Results: Data from 372 individuals with mean (SD) 27±13 years of age were abstracted including 57% female and 38% under 21 years. There were 136 patients with Thal, 169 with SCD, and 67 controls. Thal had greater deficits in spine BMD Z-score (-2.2±1.2), compared with SCD (-1.4±1.5, p<0.01) and control (-0.1±0.8, p<0.01) groups. There was also a higher prevalence of abnormal TBS in Thal (24.6%) compared with 7.8% in SCD. TBS was positively correlated with BMD (r=0.6) and negatively with age (r=-0.3). Low TBS strongly associated with hypogonadism (p<0.001) and hypogonadism was more common in Thal vs SCD (27% vs. 1%). After controlling for age and hypogonadism, low TBS was more likely found in patients with Thal (p=0.013). Of interest, there was no difference in overall fracture prevalence between Thal and SCD, averaging 26%. Although low TBS was not related to overall fracture prevalence, it was highly predictive of fragility type fracture, regardless of diagnosis (RR: 8.9, p=0.013).

Conclusion: These data support the relationship between reduced bone mass and bone quality in adolescent and adult patients with hemoglobinopathies. TBS may be a valuable tool in differentiating risk of fragility fractures particularly in patients where vertebral abnormalities complicate accurate spine assessment by DXA alone. There is a need to develop models that include both BMD and TBS for prediction of absolute fracture risk in hemoglobinopathies.

Poster # 133

RECOMMENDATIONS FOR STRUCTURAL BARRIERS FACING FAMILIES OF CHILDREN LIVING WITH SICKLE CELL DISEASE

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Background: Families of children living with sickle cell disease (SCD) are subjected to disease stigma and racial bias in healthcare settings. These experiences can lead to challenging interactions with providers and mistrust of the healthcare system, thereby impacting delivery of holistic care (HC) for individuals with SCD.

Objectives: This study aims to identify recommendations to be implemented by healthcare providers and organizations to address structural barriers facing families of children living with SCD.

Design/Method: Two pediatric hematology clinics in New England implemented a social-care-screening-system to address families' unmet basic needs. Providers participated in qualitative interviews (3, 9, and

18-months) post-implementation to assess provider perspectives on implementation using the integrated Promoting Action on Research Implementation in Health Services (iPARIHS) framework informing the interview guide and coding. This study focuses on themes that arose that could address the structural barriers to HC to families of children living with SCD.

Results: Twenty-three participants (5 nurses and physicians; 4 nurse practitioners and social workers; 2 psychologists and medical assistants; 1 research assistant) completed 29 interviews (12/2020-11/2022). Ninety % were female and 61% were aged 35-54 years old. Three organizational-level themes emerged as recommendations to address structural barriers. First, organizations should hire staff from the same backgrounds/communities and elicit their perspectives to enhance the experiences between staff and families. Second, organizations should provide resources to address unmet needs outside the clinic settings, such as inpatient wards. Third, organizations should advocate for comparable (per-patient/family) funding for SCD as for oncology. In addition, four provider/clinic level themes arose. First, positive communal gatekeeping (self and team accountability) should occur through recurring provider education and sustainable internal programs to address bias toward people living with SCD across medical settings. Second, providers should consider the political structural climate when building rapport and offering resources for unmet needs. Third, clinic providers ought to display sensitivity for families, as many fear for their immigration status and experience shame when asked about their unmet needs. Finally, clinics should remain abreast of potential familial resource stressors that occur, such as COVID-19.

Conclusion: These findings provide recommendations for organizations and hematology clinics to help address structural barriers that may hinder HC for families of children living with SCD. Future research is needed to identify which recommendations are most impactful on care delivery and feasible to implement.

Poster # 134

EVALUATION OF A CLINICAL PATHWAY FOR SICKLE CELL PAIN MANAGEMENT IN A PEDIATRIC EMERGENCY DEPARTMENT

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Background: In children with sickle cell disease (SCD), vaso-occlusive episodes (VOE) are the leading cause of emergency department (ED) presentation. Inconsistent pain management strategies can result in inadequately treated pain and increased admissions. Rapid assessment and administration of analgesia are critical for effective pain control.

Objectives: The NHLBI recommends administration of analgesia within thirty minutes of triage or one hour of ED registration. Through implementation of a standardized clinical pathway, this quality improvement project seeks to improve timeliness to achieving optimal pain control in pediatric patients presenting for VOE management.

Design/Method: A clinical pathway and order panel was published into the EMR for use by Pediatric Emergency Medicine (PEM) providers in the Children's Hospital ED. The pathway encouraged use of

intranasal fentanyl as first-line therapy. Retrospective data was collected with the following inclusion criteria: existing diagnosis of SCD, age 6 months to 18 years, and diagnosis code for sickle cell pain. Data sets were comprised of 5 patients per month for 6 months pre-implementation and 15 months post-implementation.
Outcome measures include time to first pain medication in minutes, percentage of patients who received pain medication within one hour from time of registration, and percentage of patients who received their first medication intranasally. Process measures include time to IV access in minutes, and percentage of PEM providers who referenced the pathway.

Results: Following implementation, patients receiving their first pain medication within the first hour following registration remained approximately 40% (p0.07). However, patients receiving their first pain medication within thirty minutes of triage improved from 17% to 21% (p0.101). Use of intranasal pain medication as first-line therapy increased from 3% to 41%.
All providers who responded to a post-implementation survey reported referencing the clinical guidelines when caring for patients presenting with VOE. Choice of first-line pain medication was most frequently reported as a benefit of the clinical guidelines. A barrier to use of the clinical pathway was hesitation from patients and their families on the use of intranasal fentanyl.

Conclusion: Our standardized clinical pathway demonstrated improvement in the timeliness of ED pain management and increased the use of intranasal pain medication as first-line treatment. The primary barrier to utilization of the clinical pathway was patient or parental refusal, therefore, educational interventions were implemented. We created informational handouts to distribute to patients with SCD in the hematology clinic to further discussion on the benefits of intranasal fentanyl in this context. We also provided educational lectures to PEM providers.

Poster # 135

AUDIT ON IN-HOSPITAL ANALGESIC ADMINISTRATION IN CHILDREN WITH SICKLE CELL DISEASE IN GHANA

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Background: Acute pain episodes are a recognised and frequent complication of sickle cell disease (SCD), often resulting in hospital admissions. Appropriate pain management improves the quality of life, reduces hospital stay and improves outcomes. About 16,000 children are born in Ghana with SCD each year and is the one of the top 3 causes of morbidity in Korle Bu Teaching Hospital, the largest tertiary referral hospital.

Objectives: To audit the in-hospital analgesic administration practices in the management of children with SCD.

Design/Method: Retrospective review of electronic health records of children with sickle cell disease admitted to the general Paediatric wards of the Department of Child Health, Korle Bu Teaching Hospital, Accra, Ghana from September to November 2023.

Results: Out of 216 children admitted during the study period, 43 (20.4%) had SCD; 79% with HbSS and

12% HbSC. Ages ranged from 1yr to 18yrs (average: 8.1 years (SD 4.6)). Males accounted for 72%. Average length of hospital stay was 12 days. All but 2 patient received analgesics during admission. The most common indication was vaso-occlusive pain episode (68.3%). Pain was graded in only 7 patients prior to commencement of first analgesic with 6 graded using the numerical pain scale, and the other, FLACC scale. All 7 children were aged ≥8 years. Scores ranged from 4/10 to 10/10.
All 41 patients received Paracetamol as the first-line analgesic. Dosing was inadequate in 3/41 patients; 2 of these patients had their doses reviewed within 72 hours of admission. Six-hourly dosing regimen was most commonly used. The other analgesics used were NSAIDs: Ibuprofen (32/41; 78%), Naproxen (1/41), and the opioid Morphine (23/41; 56%). Ibuprofen was started as second-line for persistent or increasing pain in 5/32 patients (16%) and Morphine in 10/23 (43%). The average duration on analgesics was 10.4 days (SD 9.6 days), ranging from 3 to 57 days. Nine (9) patients were discharged home on analgesics on account of incomplete pain resolution. One patient with migraine headaches received Sumatriptan as an adjuvant analgesic.

Conclusion: SCD accounts for a high proportion of inpatient admissions. There is a need for objective pain assessment and development of guidelines to guide analgesic choice in patients with SCD presenting with acute and chronic pain complications.

Poster # 136

PHYSICAL THERAPY USE AND HOSPITALIZATION OUTCOMES FOR CHILDREN WITH SICKLE CELL DISEASE IN CRISIS

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Background: Children with sickle cell disease (SCD) experience recurrent hospitalizations due to painful vaso-occlusive crises (VOC) that reduce quality of life and functional independence. In addition to physical therapy's (PT) essential role in preventing deconditioning and promoting rehabilitation in patients with acute and chronic health conditions, the American Society of Hematology's guidelines on SCD state that an interdisciplinary approach to pain management, which includes PT, is optimal. However, PT utilization among hospitalized children with VOC in the real-world setting is unknown.

Objectives: Examine PT use among children with SCD hospitalized with VOC and explore associations between PT use and hospitalization outcomes.

Design/Method: A retrospective, multi-center cohort study was conducted using data from the Pediatric Health Information Systems. Patients aged 3-21 years with SCD who were hospitalized for 3-10 days and who had a co-existent diagnosis for VOC between 1/2015-9/2023 were included to isolate admissions that included acute management of VOC. Diagnostic codes identified patients with SCD and VOC, and billing codes identified encounters with PT use. Descriptive statistics summarized patient demographics. Nonparametric tests were used to assess associations between PT use, location, and outcomes (e.g., length of stay, days receiving opioids, intensive care unit (ICU) admissions).

Results: Of 26,967 admissions involving 6,982 unique patients with SCD (50.2% male; median age 15.9 years (IQR: 11.2-18.7); 90.1% non-Hispanic black; and 72.1% Hemoglobin SS), 46.7% included PT for ≥1 day. PT began most commonly one day after admission (38%). Significant geographic variation in PT use

was observed (Midwest: 58.1%, South 52.2%, West 31.4%, and Northeast 17.7%; p<.0001). Admissions with PT were longer (median 5 days vs. 4 days; p<.0001), more likely to include ICU admission (5.2% vs. 3.0%; p<.0001), more likely to include an acute chest syndrome diagnosis (4.7% vs 3.4%; p<.0001) and had a longer median duration of opioid use (6 days vs. 5 days; p<.0001) compared to those that did not.

Conclusion: Aligning with evidence supporting early mobilization for hospitalized children, this study demonstrates almost half of admissions of children with SCD and VOC receive PT, though significant geographic variability exists. While PT improves hospitalization outcomes in other chronically ill pediatric populations, we found that hospitalization outcomes appeared worse for those with SCD who were using PT. Further exploration is needed to determine if this may be due to increased use among more complex patients, or if the optimal dosage of PT for these children is being achieved.

Poster # 137

EVALUATING MENTAL HEALTH AND RATES OF HOSPITALIZATION IN ADOLESCENTS WITH SICKLE CELL DISEASE

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Background: Sickle cell disease (SCD) causes complications like pain episodes, acute chest events, and stroke. There is extensive damage that occurs in the brain, resulting in silent cerebral infarcts (SCI) during critical developmental stages. Routine depression screening is integral for adolescents with SCD as those with depression and anxiety may experience heightened neurocognitive abnormalities leading to increased vaso-occlusive crises (VOC's). Facing physical, social, and mental challenges during adolescence, these individuals may endure more complications and hospitalizations without appropriate intervention. This study seeks to explore the relationship between mental health, as assessed by the Patient Health Questionnaire-9 for Adolescents (PHQ-9A), and the frequency of hospitalizations for VOC's in adolescents with SCD.

Objectives: This study aims to (1) explore the association between PHQ9-A scores and VOC-related hospitalizations and (2) identify other demographic factors influencing hospitalization rates.

Design/Method: Adolescents (age > 12years) with SCD at St. Christopher's Hospital for Children will be included. Chart reviews will precede PHQ-9A administration, covering hospitalization data six months prior to and post-survey. Surveys will be administered via secure channels, including phone, email, or in-person. We hypothesize a significant association between mental health and VOC-related hospitalizations.

Results: The analysis of 51 patient charts revealed no statistically significant correlations between PHQ9-A scores with number of hospitalizations, length of stay, baseline hemoglobins or type of sickle cell disease. The analysis did reveal 39 patients with PHQ9-A scores over 4, indicating there is a level of depression, whether it be mild, moderate or severe.

Conclusion: This study addresses a critical gap in understanding the interplay between mental health and hospitalization rates in adolescents with SCD. By using the PHQ-9A, tailored for adolescents, we aim to contribute insights into the mental health aspects of SCD. Anticipated outcomes may inform targeted

interventions, improving mental well-being and potentially reducing hospitalizations in this population. Findings could have broader implications for integrated care strategies, emphasizing the importance of mental health screening and intervention in the comprehensive care of adolescents with chronic illnesses.

Poster # 138

ADDRESSING EMOTIONAL HEALTH IN CHILDREN WITH SICKLE CELL DISEASE: A QI INITIATIVE AT UNC

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Background: Youth with chronic conditions often experience higher rates of depression and anxiety with resultant functional impairments compared to healthy peers. If mental health is not adequately addressed, these functional impairments may persist into adulthood and negatively impact medical outcomes. Notably, the sickle cell disease (SCD) population experiences elevated rates of anxiety and depression[1] . Children with SCD and comorbid mental health problems may experience increased pain, higher hospitalization rates, and longer lengths of stay[2]. Many children with SCD receive most of their care from their subspeciality provider. Thus, incorporating mental health screening into routine subspecialty care can help improve quality of care and outcomes.

Objectives: The primary objective is that by March of 2024, 80% of youth who are followed at the University of North Carolina (UNC) Comprehensive Sickle Cell Clinic will have their emotional health needs assessed and documented at each visit.

Design/Method: The Roadmap Project is a multi-center quality improvement (QI) initiative supported by the American Board of Pediatrics to address the mental health needs of children with chronic conditions. QI Methodology, including rapid Plan-Do-Study-Act (PDSA) cycles, was used to test multiple process changes to improve depression and anxiety screening in the Comprehensive Sickle Cell Clinic at UNC. This QI project focused on children 12 years of age and older with SCD. The first 10 clinical encounters of eligible patients were reviewed each month to determine if mental health was discussed and documented in the EMR.

Results: Data has been collected from June to December 2023. At baseline, 40% of children had documented mental health screening. After the first rapid PDSA cycle, screening rate increased to 60%. After the second and third PDSA cycles, screening has increased to 70%.

Conclusion: Due to the high prevalence of anxiety and depression in children with SCD and its association with negative health outcomes, it is extremely important to address emotional health and implement screening into routine clinical practice. With the knowledge and support from the Roadmap Collaborative, our team has improved assessing and discussing mental health in children with SCD followed at the Comprehensive Sickle Cell Clinic at UNC.

References

1. Espinoza-Gutarra *Blood* ,2022
2. Panepinto JA. *Pediatr Blood Cancer*, 2013

Poster # 139

INFECTIOUS CAUSES OF ACUTE CHEST SYNDROME IN PEDIATRIC PATIENTS A SINGLE-CENTER RETROSPECTIVE STUDY

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Background: Acute chest syndrome (ACS) is a common sickle cell disease (SCD) complication. Infectious pathogens are the most common cause of ACS. Our knowledge about the causes of ACS is mainly based on a study by The National Acute Chest Syndrome Study published in 2000. This study was conducted prior to the implementation of routine conjugate Pneumococcal and Influenza vaccinations. Data regarding the incidence of these pathogens is now outdated. A molecular diagnostic method, The BioFire® FilmArray® Respiratory 2 (RP2) Panel (RVP) was implemented in 2017 at our institution.

Objectives: In this study, we aim to revisit the infectious pathogens responsible for ACS in children with SCD and identify admission variables associated with prolonged hospital stay.

Design/Method: We conducted a single-center retrospective study. Records of children ≤ 21 years of age with sickle cell disease were reviewed. Nighty-five episodes of ACS who were admitted to our institution from January 2013 to March 2021 were identified. Episodes were split into two cohorts, pre-RVP, and RVP. The infectious causes of ACS were compared among cohorts. A multivariate logistic regression model was used to identify variables associated with hospital stay.

Results: Among 95 episodes, 38 (40%) were admitted with a diagnosis other than ACS and developed ACS during their hospital stay. Within the RVP-cohort (n=45) an infectious etiology was identified in 42% (19/45) of episodes vs 6% (3/50) in the pre-RVP cohort. In the RVP-cohort, more than one pathogen was identified on RVP in 13% (6/45) of episodes. The two most commonly identified pathogens were Rhino/Enterovirus and Influenza virus, both found in 11% (5/45) of episodes. Atypical bacteria comprised 4% (2/45) of episodes. Variables significantly associated with prolonged hospital stay (>5 days) were age, (OR 1.14, 95% CI: 1.01-1.30, p= 0.04) and the admission diagnosis of VOC (OR 9.42, 95% CI: 2.14-42.43, p= 0.003).

Conclusion: The pathogens identified via RVP in our single-center study differed from previously reported results. Atypical bacteria for which part of ACS treatment is geared towards do not appear as prevalent (4%), as in prior studies (13-18%); including a retrospective study conducted at our institution. A weakness of our study lies in is its limited sample size and single-center nature.
We found that age and the admission diagnosis of VOC were correlated with prolonged hospital stay. The former confirms a previously described association. Patients admitted with VOC who later developed ACS experienced an extended hospital stay, likely due to these consecutive events.

Poster # 140

HEALTH OUTCOMES IN PATIENTS WITH SICKLE CELL DISEASE WITH COVID-19 INFECTION IN NEWARK, NJ

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Background: The COVID-19 pandemic has caused immense loss of life, but also has devastating implications for patients with comorbidities like sickle cell disease (SCD). In patient populations such as these, the literature has shown multiple varying effects on systemic outcomes, such as as adverse liver and kidney function, thromboses, acute chest syndrome, splenic sequestration, hemolytic crises, increased pain crises, or spontaneous recovery without significant adverse effects noted.

Objectives: In our study, we aimed to assess health outcomes in patients with SCD with COVID-19 infection throughout the pandemic in an urban patient population.

Design/Method: We performed a retrospective chart review examining patients with SCD at the Children's Hospital of New Jersey at Newark Beth Israel Medical Center in Newark, NJ who had evidence of COVID-19 infection by PCR between April 2020 and December 2022. Our objective was to study their clinical course, outcomes and prognosis.

Results: We analyzed data for 94 patients. Of these, 51.1% were males and 48.9% were females. More than half of all patients were adolescents or young adults, and 22.3% were children (aged 5-13 years old) and the remainder were infants (13.8%) and toddlers (11.7%). The genotypes included HbSS or HbS-BetaThal-zero (84.0%), HbSC (9.6%), HbS-BetaThal-plus (4.3%). We observed that 81.9% of patients had Medicaid, 10.6% had private insurance, 3.2% had a combination of private and public insurance, and 4.3% were uninsured. Sixty-two percent of patients were hospitalized with an average length of stay of 5.8 days. Forty-five percent presented with fever as an initial complaint commonly in the emergency room. Among all patients, 42.6% had URI symptoms and 56.4% had painful vaso-occlusive episodes (VOEs). Sixty-six percent of patients received IV antibiotics and only 14.9% received COVID-targeted treatment. Out of patients receiving COVID treatment, 9.6% received Remdesivir, 7.4% received steroids with or without remdesivir, 3.2% received hydroxychloroquine, and 1.1% received bamlanivimab. As for the complications experienced, 11.7% experienced respiratory distress requiring supplemental oxygenation and almost 80% of patients did not experience any major complications, while a smaller percentage experienced complications that included respiratory failure (4 patients), UTI (1 patient), hydrocele (1 patient), and blood infections (2 patients).

Conclusion: Our data suggests that patients with SCD and COVID-19 did not have significant respiratory complications, but we observed an increase in VOE rates in these patients. Our data also suggests that most patients recovered spontaneously without the use of COVID-19 directed therapy. However, further examination of the long-term effects in these patients is warranted.

Poster # 141

IMPLEMENTATION OF PROMIS QUESTIONNAIRE IN SICKLE CELL DISEASE CLINIC

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Background: The National Institute of Health (NIH) highlights mental and physical health as equally important components of overall health. This is particularly salient for pediatric patients with sickle cell disease (SCD), given the likelihood of disease-specific complications, increased rates of mental health disorders, and social disadvantages. Given the nature of SCD, recommendations for this population include targeted evaluation of biopsychosocial factors and comprehensive intervention to treat pain associated with SCD. Further, routine screening may help to support early identification of and intervention for youth with SCD who are at risk for developing more complicated disease course.

Objectives: 1) Implement routine screening within a pediatric SCD clinic to identify biopsychosocial risk factors within this clinic's population
2) Explore the utility of the screening process to facilitate referrals to supportive services and other sub-specialties.

Design/Method: Cross-sectional patient-reported outcomes were evaluated. Eligible patients 8-17 years or older with a diagnosis of sickle cell disease (subtypes SS, SC, SB+, SB0) completed the PROMIS Pediatric Profile-25 at routine clinic visits. The measure assesses the following domains over the previous 7 days: mobility/physical functioning, anxiety, depression, fatigue, peer relationships, pain interference, and pain intensity. Basic demographic data, such as age, race, disease type, pertinent comorbid health issues, and health care utilization were gathered through retrospective chart review from electronic medical records.

Results: Data obtained from forty-four pediatric patients were used in this preliminary analysis. Sixty-one percent of patients were female (61.4%), all identified as African American, and most patients were SS (63.6%) or SC (20.5%) genotypes. Patients are complex, with 54.5% of the sample having one or more comorbid condition (i.e., asthma, obstructive sleep apnea) and 38.6% having one or more psychiatric diagnosis (i.e., depression, neurodevelopmental disorder). Descriptive analyses of PROMIS screener domain t-scores show clinically significant impairment for some patients in mobility/physical functioning (11.4%), anxiety (6.9%), depressive symptoms (11.5%), fatigue (11.5%), peer relationships (6.9%), and pain interference (13.8%). While only eight patients received a referral to another sub-specialty, thirty-nine patients had a consult with Psychology during their clinic visit. Upon completion of data collection and chart review, independent sample t-tests and chi square tests of independence will be conducted to further explore biopsychosocial variables and the utility of this screener for identifying patients who would benefit from additional services.

Conclusion: This project shows the feasibility of implementing a routine screener for SCD patients and only serves to highlight the importance of biopsychosocial approach to the care of these patients.

Poster # 142

IDENTIFYING PATIENT AND FAMILY KNOWLEDGE GAPS ABOUT HSCT AS A TREATMENT FOR SICKLE CELL DISEASE

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Background: Sickle cell disease (SCD) is the most common inherited hemoglobinopathy worldwide, occurring in approximately 1 in 400 black Americans. With a human leukocyte antigen (HLA) matched

sibling donor, a hematopoietic stem cell transplant (HSCT) can be curative, with low mortality risk. While HSCT has been shown to be curative, only 1,200 transplants have been reported since 1984. Younger recipients have less complications, including both acute and chronic graft versus host disease, making it advisable to identify candidates in early childhood.

Objectives: Utilizing the parental population at a sickle cell center at an urban tertiary care center in the Midwest, our aim was to identify gaps of knowledge about HSCT and potential candidates for HLA testing.

Design/Method: Surveys were conducted by parents or guardians at their child's annual comprehensive sickle cell clinic appointments. After informed consent was obtained, subjects were educated about HSCT risks and benefits before completing a nine-question survey, using a Likert scale to determine knowledge of HSCT and willingness to participate in HLA testing. Data were analyzed descriptively.

Results: Eighty-six parents/guardians completed the survey. The median patient was 10 years of age (1-21 years). Most caregivers (88%) were aware that HSCT was a curative option for SCD. However, significant gaps in both the subjects' understanding of HSCT and willingness to consider HSCT therapy for their children were identified. Fifty-nine percent knew that the ideal donor for HSCT is a full sibling, without SCD, who is a "tissue HLA match." A minority (26%) of parent/guardians were aware that the test for an HLA match can be a painless cheek swab of patient and full siblings, at no cost to the family. Half (51%) of parents/guardians expressed interest in obtaining cheek swab tests from potential sibling donors. Despite apparent knowledge gaps, 81% of parents/guardians noted that if a potential sibling donor were available, they would like to learn more about HSCT as an option for their child.

Conclusion: Our results reveal that guardians of patients treated at our hematology clinic are aware that HSCT is a curative therapy for SCD. However, we found additional education is required to increase subjects' understanding of the simple, painless process of identifying potential sibling-donors via cheek swab. Our data suggests that an educational strategy may increase the willingness of families to consider cheek swab testing, and therefore identify potential matched sibling donors.

Poster # 143

Sickle Cell Vitamin D: Friend or Foe?

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Background: Sickle cell disease (SCD) is an autosomal recessive disease caused by a mutation in the beta-globin subunit of hemoglobin, causing sickled Red blood cells (RBCs). SCD is characterized by hemolytic anemia, increased susceptibility to infections, auto-splenectomy, and progressive multi-organ failure; sickle cell crises (SCC) have become the leading cause of significant morbidity and healthcare utilization for patients. Individuals with SCD have a high prevalence of Vitamin D (VitD) deficiency, with estimates ranging from 56.4% to 96.4%. Blood transfusions, vaccines, antibiotics, pain relievers, and hydroxyurea are all designed to prevent and decrease SCC. The only potential cure is bone marrow transplant. Although the role of VitD is not fully understood, VitD could be a cheaper, safer, easier alternative therapy.

Objectives: The goal of this retrospective study was to investigate if VitD supplementation lowers SCC, decreases the number of ED visits, reduces complications, and improves quality of life

Design/Method: Patients with SCD were identified using electronic health records under the Cooper Hospital Pediatric Hematology Department. The number of SCC, ED visits, and/or hospitalizations between January 2018 and May 2023 were tracked. Their routine labs for CBC with differential, reticulocyte count, iron profile, LDH, uric acid, CMP, Hg variant, and VitD were evaluated for each year. Spearman Rho Correlation was used to compare the VitD levels for each year to the other laboratory values within the same respective years. P<=0.05 was the significance level. SPSS 2 was used for analysis.

Results: There were 60 subjects included in our data. The average age was 11 years of age (+/- 5.2 years). In 2018, Vitamin D had a moderately negative correlation with Retic Count (R=-0.44, p=0.034) and a moderately positive relationship with the number of hospitalizations (R=0.436, p=0.042). In 2020, Vitamin D was found to have a moderately negative relationship with Uric Acid (R=-0.491, p=0.015) and in 2022 there was a moderately positive relationship with hemoglobin levels (R=0.480, p=0.001).

Conclusion: VitD has potential correlational effects on parameters that affect the progression of SCD patients. As anemia in SCD is indicative of symptoms, VitD has the potential to be a major factor in the treatment of SCD. Though the study was limited due to its retrospective nature and nonadherence, it is representative of 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 # 144

FACTORS AFFECTING HYDROXYUREA ADHERENCE AMONG CHILDREN WITH SICKLE CELL DISEASE

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Background: Sickle cell disease (SCD) is an inherited hemoglobin disorder with potential severe consequences if left untreated. Hydroxyurea (HU) has emerged as a therapeutic approach to elevate fetal hemoglobin (HbF) levels, aiming to alleviate complications and acute care needs. Monitoring medication adherence remains challenging, particularly among individuals with SCD, especially those enrolled in Medicaid, where the influencing factors are not fully understood.
There is limited evidence regarding the efficacy of hydroxyurea in patients enrolled in Medicaid. This underscores the need for a more in-depth examination of adherence patterns and treatment outcomes within this specific population to enhance our understanding and guide targeted interventions.

Objectives: Our goal was to assess HU adherence and its effectiveness in treating children enrolled in Medicaid. We aimed to explore relationships between dosage, formulation, adherence biomarkers, acute care utilization, and demographics, hypothesizing that younger patients using the liquid formulation would exhibit adherence biomarkers and encounter reduced acute care utilization.

Design/Method: Conducting a retrospective chart review at St. Christopher’s Hospital for Children in

Philadelphia from September 2022, we collected demographics, hospitalizations, ED and office visits, dosage and formulation, and recent biomarkers for those with HbSS and SB0. Data analysis employed Pearson correlation tests.

Results: Our study involved 94 patients, 83 covered by public insurance, with an average age of 12.8 years. Analysis revealed a negative correlation between Hb levels and HU dose (r=-0.405, p=0.01) for all patients. No significant correlations emerged between HbF and HU dose, ED visits, or hospitalizations. Subgroup analysis showed that the 37 patients using the liquid form at an average age of 7.1 exhibited positive correlations between HbF and office visits (r=0.362, p=0.03) and a negative correlation between Hb and HU dose (r=-0.405, p=0.01). The liquid formulation was notably associated with fewer ED visits (r=-0.518, p=0.001) and hospitalizations (r=-0.526, p=0.001). Conversely, the 57 patients using the pill formulation at an average age of 16.3 displayed a negative correlation between Hb and HU dose (r=-0.513, p=0.001). However, no significant correlations were evident between HU dose or HbF and acute care utilization metrics. Moreover, no discernible associations were found between HbF or HU dose and ED visits, hospitalizations, or office visits for those using the pill formulation.

Conclusion: The liquid formulation of hydroxyurea demonstrated enhanced adherence and reduced acute care utilization compared to the pill formulation. Contributing factors likely include patient age, parental involvement in care, home delivery of medication, and regular follow-up.

Poster # 145

MULTIFOCAL OSTEOMYELITIS & SPINAL EPIDURAL ABSCESS DUE TO BACTEROIDES CACCAE IN SICKLE CELL DISEASE

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Background: Children with sickle cell disease (**SCD**) are prone to severe infections due to impaired immunity and vaso-occlusive crises. Osteomyelitis is a serious complication of SCD most often caused by *Salmonella* sp. or *Staphylococcus aureus*. Anaerobic pathogens such as *Bacteroides fragilis* are rarely reported, occurring because of gut mucosal ischemia, and bacterial translocation/colonization within infarcted bone marrow. We report the first case of an SCD child with multifocal osteomyelitis and L5-S1 spinal epidural abscess due to *Bacteroides caccae*.

Objectives: To describe the clinical course and outcome of a child with SCD with multifocal *B. caccae* osteomyelitis and spinal epidural abscess.

Design/Method: Case report

Results: An autistic 6-year-old male with SCD (Hemoglobin SS), on penicillin prophylaxis and hydroxyurea, presented with 3 weeks of intermittent high-grade fevers, requiring two prior hospitalizations with negative blood cultures and normal chest radiograph (**CXR**). Procalcitonin was elevated (12.64 ng/ml). Patient presented for 3rd admission with fever (105° F) and headache radiating to neck/upper back. Laboratory evaluation revealed Hb 6.5 g/dl, reticulocyte count 5.4%, and markedly elevated inflammatory markers (CRP >190 mg/l, procalcitonin 32.26 ng/ml); cerebrospinal fluid with 9 nucleated cells/ml. CXR revealed left lower lobe opacity. Due to concerns of aseptic meningitis and

acute chest syndrome, Vancomycin, Ceftriaxone, and Azithromycin were initiated.
Subsequently, patient developed severe bilateral thigh/back pain with decreased ambulation. MRI with contrast revealed extensive spinal/pelvic/bilateral femoral infarcts, L5/S1 epidural/paraspinal collection concerning for phlegmon and left femoral subperiosteal fluid collection. A PETCT and MRI revealed bilateral humeral osteomyelitis. Aspiration, debridement of left distal femur subperiosteal abscess, and bone biopsy of femur and L5 vertebrae aspirate (with grossly purulent drainage) were obtained. *B. caccae* was isolated from blood culture, epidural fluid PCR and blood Karius testing. *A*ntibiotics were changed to Meropenem (HD #6-19), and once fever resolved, to oral Metronidazole (HD #19). Analgesic and transfusion support were provided. The patient was hospitalized for 7 weeks due to prolonged fever, deconditioning and reduced musculoskeletal strength/mobility. The anticipated duration of antibiotic therapy is approximately 1 year.

Conclusion: Anaerobic osteomyelitis in SCD is rare, with few cases reported due to *B. fragilis*. We report the first case of multifocal osteomyelitis complicated by L5-S1 spinal epidural abscess due to *B. caccae* in a child with SCD. Accurate diagnosis required a high index of suspicion, employing optimal testing methodologies, and successful isolation of anaerobic organism with precise specimen collection and handling. A combination of medical, orthopedic, and interventional therapeutic measures was required for final improved outcome.

Poster # 146

ECULIZUMAB FOR MANAGEMENT OF HYPERHEMOLYSIS SYNDROME IN PEDIATRIC PATIENTS WITH SICKLE CELL DISEASE

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Background: Sickle cell disease (SCD) is an inherited red blood cell (RBC) disorder for which chronic hemolytic anemia and vascular occlusion are hallmarks of disease. Blood transfusions are critical for both supportive and preventative management of SCD complications despite increasing use of hydroxyurea. Hyperhemolysis syndrome (HHS), a sub-type of delayed hemolytic transfusion reactions, is characterized by hemolysis of transfused RBCs in addition to the recipient's own RBCs. Standard management includes IVIG, corticosteroids, and avoidance of further transfusions. Not all patients respond to first-line agents. Dysregulation of complement activation has been described as a contributor in the pathophysiology of HHS. Eculizumab, a C5 terminal complement inhibitor, has been proposed in management of HHS. The utility of eculizumab for HHS management in the pediatric SCD population remains unknown.

Objectives: To describe our experience with eculizumab for pediatric HHS.

Design/Method: Case series

Results: Two patients received eculizumab for management of HHS.

Case 1: A 9-year-old male with SCD and asthma was admitted for acute chest syndrome (ACS). He received a transfusion for hemoglobin (Hgb) of 5.3. He returned five days later due to persistent extremity pain and dark-appearing urine. His work-up was notable for Hgb of 4.2, elevated LDH,

decreased haptoglobin, and elevated unconjugated bilirubin. DAT and alloantibodies were not identified. He received IVIG, erythropoietin, and pulse dose methylprednisolone without improvement. He received eculizumab on day of admission (DOA) 4 due to Hgb of 2.4. Prior to treatment, patient had elevated levels of soluble complement 5b-9 (sC5b-9 = 567, normal < 244 ng/ml) and normal total complement (CH50) levels. He had subsequent improvement in Hgb was discharged on DOA 9 with Hgb of 5.1.

Case 2: An 18-year-old female with SCD, asthma, and obstructive sleep apnea was admitted for ACS and received a transfusion for Hgb of 7.2. She returned one day later with bilateral lower extremity pain and fatigue. Repeat lab work demonstrated Hgb of 3.4, elevated LDH, decreased haptoglobin, and elevated unconjugated bilirubin. DAT was negative. A new anti-Jkb alloantibody was identified. She received IVIG, rituximab, and pulse dose methylprednisolone without improvement. Patient received 2 doses of eculizumab on DOA 4 and 10. CH50 levels were low following treatment (CH50 = 29, reference 101-300 CH50 units), consistent with effective eculizumab dosing. Hgb level eventually improved and was discharged on DOA 17 with Hgb of 5.7.

Conclusion: Eculizumab should be considered in the setting of refractory life-threatening pediatric HHS.

Poster # 147

SUCCESSFUL USE OF PLASMAPHERESIS IN PEDIATRIC PATIENT WITH SICKLE CELL DISEASE & MULTIORGAN FAILURE

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Background: Multiorgan dysfunction syndrome (MODS) is defined as acute dysfunction of two or more organ systems. Adults with sickle cell disease (SCD) can develop this life-threatening complication, particularly during vaso-occlusive crisis (VOC) and/or acute chest syndrome (ACS). MODS is thought to be mediated by diffuse sickling and inflammation secondary to free heme release and nitric oxide depletion. While rare among pediatrics, there is evidence among the adult population to suggest that plasma exchange is beneficial for treating patients with MODS and SCD refractory to red cell exchange, although the exact mechanism is not entirely understood.

Objectives: This case report documents the first case of MODS in a pediatric patient with SCD that was successfully treated with plasma exchange.

Design/Method: Case report developed from patient's electronic medical record and review of current literature.

Results: An 8-year-old female with SCD (Hemoglobin SC) and type 1 diabetes mellitus initially presented in severe diabetic ketoacidosis (DKA) (pH of 6.84, HCO3 <5, and lactate 9.1) with altered mental status and hypotension requiring vasopressors. During management of DKA, she developed acute hypoxic respiratory failure requiring intubation and ventilation due to acute chest syndrome, acute liver failure, neurologic deficits (right sided hemiplegia) and acute renal failure requiring dialysis. The brain MRI showed cytotoxic edema with bilateral watershed infarcts without arteriopathy on vessel imaging. Her

laboratory results were consistent with significant hemolysis, and she was diagnosed with MODS (acute kidney failure, acute liver failure, and acute hypoxic respiratory failure) in the setting of SCD. Despite multiple red cell exchange transfusions, her organ failure did not improve. She underwent five days of plasma exchange with improvement in her overall clinical course and hemolytic parameters.

Conclusion: Case series showed that adult patients with SCD and MODS refractory to red cell exchange benefited from plasma exchange with a decrease in mortality. This report documents the first pediatric case of SCD associated MODS successfully treated with plasma exchange, consistent with management documented in adult literature. While the exact mechanism is unknown, plasma exchange is thought to increase proteins, such as hemopexin and haptoglobin, that bind to free heme3. It is also believed to remove adhesion molecules, oxygen radicals, cytokines, and chemokines that may further worsen inflammation and vaso-occlusion. Further studies with larger patient populations would be needed to further investigate the validity of this treatment method for pediatric patients with SCD presenting with MODS.

Poster # 148

RARE COMPLICATION OF ORBITAL BONE INFARCTION AND HEMATOMA IN A CHILD WITH SICKLE CELL DISEASE

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Background: Patients with Sickle cell disease (SCD) experience serious complications due to vaso-occlusive crises. We report a child with SCD with an unusual presentation of bilateral orbital infarction/hematoma mimicking pre-septal cellulitis.

Objectives: To describe a challenging, unusual case of orbital/sphenoid bone infarction/hematoma in a child with SCD

Design/Method: Case Report

Results: A 5-year-old girl with SCD (Hemoglobin SS), on penicillin/hydroxyurea, was admitted with sudden onset fever, diffuse periorbital swelling, and abdominal pain. Examination revealed bilateral non-tender eyelids swelling without discharge, and proptosis. Labs showed leukocytosis (24.3 x $10^3/mm^3$), thrombocytopenia, elevated CRP/procalcitonin, and hemoglobin 6.3 g/dL requiring transfusion, elevated PT (17.7 seconds) & PTT (83.4 seconds) in the absence of bleeding, not corrected by mixing studies and a positive lupus anticoagulant. Due to concern for sepsis/orbital cellulitis, she was started on ceftriaxone and vancomycin; azithromycin was added for concern of acute chest syndrome on chest X-ray. Urine exam showed positive nitrites and grew Staphylococcus aureus; antibiotics were switched to TMP-SMX. Patient's fever subsided; however periorbital edema persisted. Ophthalmological exam was negative for preseptal/orbital cellulitis. MRI orbits showed T2 hyperintense non-enhancing extraconal masses in the dorsolateral aspect of both orbits, marked displacement of the intra-orbital contents with proptosis of the right lobe and areas of heterogeneous abnormal enhancement of bilateral sphenoid bones indicating bone infarctions with secondary orbital hematoma formation without signs of infection. She received intravenous methyl prednisone with subsequent significant improvement in periorbital swelling.

Conclusion: SCD-related orbital bone infarction is a rare complication posing a risk of missed diagnosis, treatment delays, and superadded osteomyelitis. Our case illustrates the importance of considering rare complications especially when the presentation is atypical as in our patient with painless, bilateral periorbital swelling as opposed to painful, unilateral swelling previously reported in the literature which could be mistaken for infection. The presence of orbital hematoma also warrants ruling out coagulopathy. Role of steroids has been controversial; our case had remarkable improvement with steroids which could be considered in severe cases to expedite recovery. Ophthalmology evaluation/follow-up is critical due to risk of vision loss as reported previously given the location of infarction/hematoma; it was prevented possibly by early intervention (transfusion, steroids) in our case. Additionally, MRI evaluation is important to differentiate orbital bone infarction from osteomyelitis in the presence of fevers. This case emphasizes having a high index of suspicion to expedite evaluation for atypical SCD complications, namely orbital infarction/hematoma, to avoid delay in diagnosis and treatment and prevent adverse consequences.

Poster # 149

SUBGALEAL HEMORRHAGE SECONDARY TO A VASO-OCCLUSIVE CRISIS IN A SICKLE CELL DISEASE PATIENT

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Background: Sickle cell disease is a red blood cell disorder that affects hemoglobin, the protein that carries oxygen throughout the body. Instead of the red blood cells being disc-shaped, the red blood cells become “sickle” shaped and can’t flow easily throughout the body. A vaso-occlusive crisis is a complication of sickle disease and it occurs when there is ischemia to body tissues or organs.

Objectives: We report a case of an 18 year-old African American male with a history of sickle cell disease who developed a subgaleal hemorrhage secondary to a vaso-occlusive crisis.

Design/Method: Literature and chart review.

Results: An 18 year-old African American male, with a history of sickle cell disease, initially presented to the emergency department due to back pain as well as pain in his bilateral upper and lower extremities. Chest XRAY was obtained and was significant for a left lower lobe opacity. Patient was admitted for treatment of vaso-occlusive crisis and acute chest syndrome. Prior to discharge, pain had improved and patient had completed a 10 day course of antibiotics.
Patient returned to the emergency department six days after discharge due to headache and forehead swelling. Patient denied trauma or injury. Vitals were within normal limits. Scalp swelling was fluctuant and tender. Laboratories revealed a WBC 7.8 K/uL, RBC 2.89 M/uL, Hgb 8.5 gm/dL, Hct 27.4%, platelet 285 K/uL, PT 15.1 seconds, PTT 20.3 seconds, INR 1.23. Hgb S% 49.8%. Head/brain CT without contrast was significant for marked subgaleal edema and acute hemorrhage along the bilateral frontoparietal convexity, more pronounced on the left. There was no acute intracranial hemorrhage, midline shift, or mass effect. Over the course of his five-day hospitalization, patient was managed conservatively with analgesic medication and kept under close observation. Prior to discharge, swelling and pain had significantly improved. Two weeks later, patient followed-up with his hematologist and swelling had

completely resolved.

Conclusion: Spontaneous subgaleal hemorrhage is very rare in sickle cell disease patients and therefore there is no clear explanation regarding its pathophysiology. The most common explanation is that it is a result of cortical bone disruption secondary to bone infarction in the seting of a vaso-occlusive crisis. It usually resolves spontaneously with conservative management. This should be considered as part of the differential for sickle cell disease patients who present with acute headache.

Poster # 150

CASE REPORT: SUDDEN DEATH CAUSED BY PLASTIC BRONCHITIS IN A CHILD WITH ACUTE CHEST SYNDROME

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Background: Plastic bronchitis is a rare and poorly described complication of sickle cell disease and acute chest syndrome. It is defined as the formation of casts made of various materials, which obstruct lung bronchi. Plastic bronchitis has been diagnosed in several disease states including asthma, cystic fibrosis, and congenital heart disease following Fontan procedure.

Objectives: To describe a case of a 5-year-old male with Sickle Cell SS Disease, admitted for pain crisis and Acute Chest Syndrome, which rapidly progressed to cardiovascular decompensation and death secondary to diffuse lung infiltration and obstruction due to plastic bronchitis.

Design/Method: Single case report

Results: A 5-year-old male with Sickle Cell SS Disease and moderate persistent asthma was admitted to the pediatric ward for generalized abdominal pain and extremity pain consistent with vaso-occlusive pain crisis. Subsequently, the patient developed a fever associated with respiratory distress and pain at his port-a-cath site. He was started on broad-spectrum antibiotics for Acute Chest Syndrome, given a new lung infiltrate in the right lower lobe on chest x-ray, and possible central line-associated bloodstream infection (CLABSI). He was initiated on high-flow nasal cannula (HFNC) and transferred to the pediatric intensive care unit. His respiratory status stabilized on HFNC with moderate supplemental oxygen and intermittent albuterol; however, he continued to have persistent tachycardia, tachypnea, and worsening lung infiltrates on repeat chest x-ray. Several hours later, he went into sudden cardiac arrest with asystole. Despite immediate CPR, intubation, and resuscitative measures, the patient expired. The autopsy revealed plastic bronchitis with fibrinous casts with 95% airway occlusion from the carina to the bronchioles in both lung fields.

Conclusion: Plastic bronchitis, a rare complication, can progress to rapid deterioration and death in pediatric patients with acute chest syndrome and sickle cell disease. The presentation of plastic bronchitis in sickle cell disease is unique compared to other underlying disease states. Clinicians should be on high alert for signs and symptoms indicating this potential complication, especially worsening chest radiographs in a patient with acute chest syndrome.

Poster # 151

VENOUS AND WATERSHED CEREBRAL INFARCTIONS DUE TO SINO-VENOUS THROMBOSIS IN SICKLE CELL DISEASE

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Background: CNS complications are amongst the most common and devastating sequelae of sickle cell disease (SCD). Cerebral Sino-Venous Thrombosis (CSVT) is a rare, but serious neurological complication associated with hypercoagulability. Patients with SCD have a prothrombotic state due to increased thrombin generation, tissue factor expression, and enhanced platelet activation.

Objectives: We present a case series comparing the cerebral infarct symptoms, location, and management in two adolescents with SCD and CSVT.

Design/Method: Retrospective chart review was performed on two patients treated at St. Louis Children's Hospital

Results: Patient A, a 12-year-old female with HbSS, presented with headaches and first lifetime seizure. She had a normal screening Transcranial Doppler (TCD) 8 months prior and prior MRI finding of two punctate silent infarcts. The family declined disease-modifying therapy. At presentation, she had right hemiparesis and NIHSS score 14. Brain CT showed left cortical vein thrombosis with patchy left parietal lobe intraparenchymal hemorrhage and vasogenic edema. MRI Brain showed diffusion restriction, consistent with acute infarction. MRV demonstrated nonocclusive left transverse and sigmoid sinus thrombosis. She underwent erythrocytapheresis to achieve HbS <30%. CSVT was suspected to precipitate infarction due to venous congestion with hemorrhagic conversion. She was anticoagulated with unfractionated heparin and later converted to rivaroxaban. Due to alloimmunization, she could not continue chronic transfusion therapy.
Patient B, a 17-year-old male with HbS b^+ thalassemia on hydroxyurea, presented with right hemiparesis (NIHSS 7) following a weeklong headache. History included straight sinus thrombosis 9 years prior (resolved after enoxaparin), silent cerebral infarcts (SCIs), and nondiagnostic TCDs due to skull thickness. MRI Brain showed acute infarcts in the left internal border zone with left thalamus and basal ganglia edema, plus acute thrombosis of the vein of Galen, straight sinus, and left internal cerebral vein. Infarction distribution was consistent with both watershed infarction, potentially from hypoperfusion, and venous hypertension. He underwent erythrocytapheresis to achieve Hb S <30% and anticoagulation with enoxaparin. He continued chronic transfusion therapy.

Conclusion: Symptoms of CSVT often mimic other disease processes; however, headaches are the most common presenting symptom as observed in both patients. Following CSVT, venous infarctions are common, but watershed distribution strokes (patient B) are uncommon. The presence of SCI predicts future arterial/watershed infarcts but not venous infarct risk. The ASH 2020 guidelines recommend annual TCD screening for patients with SCD; however, TCDs lack sensitivity in screening for CSVT risk. Additional investigation is needed to identify CSVT risk factors in people with SCD.

Poster # 152

HYPERHEMOLYSIS SYNDROME IN AN ADOLESCENT WITH SICKLE CELL DISEASE: A CASE REPORT & LITERATURE REVIEW

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Background: Worsening anemia in the setting of various sickle cell disease sequelae is often treated with packed red blood cell (pRBC) transfusion. Hyperhemolysis syndrome (HHS) is a rare and life-threatening complication of transfusion. HHS is the destruction of host RBC and transfused RBC in the absence of red cell antibodies. This is evidenced by declining hemoglobin (Hb) and reticulocyte counts following transfusion, with negative antibody testing. The pathophysiology of HHS continues to be investigated. Proposed mechanisms include bystander hemolysis, erythropoiesis suppression, and macrophage mediated destruction. Hyperhemolysis is typically treated with IVIG and steroids. Goals of treatment include improving Hb and reticulocyte count.

Objectives: Describe a case of a 15 year old male with sickle cell SS disease with acute chest syndrome (ACS) complicated by hyperhemolysis syndrome.

Design/Method: Single case report and literature review

Results: 15 year old male with sickle cell disease type SS and history of delayed transfusion reactions who initially presented with right sided chest pain and shortness of breath. Patient found to have acute hypoxic respiratory failure with new infiltrates on chest x-ray consistent with right sided pneumonia progressing to ACS requiring increasing respiratory support and antibiotics. Patient noted to have significant anemia, requiring pRBC transfusions. After PRBC transfusion, he experienced worsening clinical status with increasing oxygen requirements, anemia, reticulocytopenia, thrombocytopenia, and leukocytosis with negative Direct Coombs test, raising concern for acute HHS. Patient demonstrated cyclical pattern of significant anemia necessitating transfusions with expected increase in hemoglobin followed by significant thrombocytopenia, reticulocytopenia, and anemia within 48-72 hours of transfusion. Given history of transfusion reactions and suspected HHS, patient was initiated on IV glucocorticoids with demonstrated resolution of anemia, thrombocytopenia, and reticulocytopenia.

Conclusion: While the exact underlying cause of this patient's hyperhemolysis remains unknown, he responded immediately to the administration of IV steroids. Both steroids and IVIG together are standard treatment, however this case supports that IV steroids alone are sufficient to treat HHS. IV steroids are more cost effective than IVIG. Furthermore, there is evidence of IVIG induced hemolytic anemia, which would exacerbate the underlying pathologic process in HHS. Being familiar with the presentation of HHS is important to be able to recognize the condition and provide timely treatment.

Poster # 153

BILATERAL AVASCULAR NECROSIS OF THE FEMORAL HEAD IN A FOUR-YEAR-OLD CHILD WITH SICKLE CELL DISEASE

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Background: Avascular necrosis (AVN) of the femoral head is a progressive, potentially disabling chronic complication in patients with sickle cell disease (SCD). Its prevalence increases with age and is reported to be 11% in individuals under 21 years. It is rare in children under five years.

Objectives: To highlight that AVN can occur in younger pediatric patients with SCD presenting with hip pain and to improve early diagnosis and treatment.

Design/Method: Clinical and imaging data were obtained through a retrospective chart review. Laboratory data were obtained from the Sickle Cell Clinical Research and Intervention Program (SCCRIP) database.

Results: A four-year-old male African American patient with SCD (HbSS) presented to the St. Jude Children's Research Hospital sickle cell clinic in 2016 complaining of bilateral hip pain. On physical exam, the patient had bilateral hip pain on external rotation, left hip pain on internal rotation, and points of tenderness over the left iliac crest. Significant medical history included multiple episodes of acute chest syndrome, vaso-occlusive crises, vitamin D deficiency, bilateral pes planus, and mild developmental dysplasia of the hips. There was no history of trauma, autoimmune disease, or steroid use. The patient was on hydroxyurea (30 mg/kg). Pertinent laboratory markers were baseline hemoglobin 9 g/dL, hemoglobin F 21.5%, calcium 9.6 mg/dL, and vitamin D 18-25 ng/mL. The patient was referred for imaging to rule out AVN. A hip radiograph showed osteonecrosis of bilateral capital femoral epiphyses with flattening of lateral aspects. A follow-up MRI showed changes consistent with bilateral osteonecrosis, confirming the diagnosis of AVN (Arlet and Ficat stage II on the right and stage III on the left). There were no other findings to suggest AVN of other etiologies, such as Legg-Calve-Perthes disease or trauma. The patient was managed conservatively, with analgesics as needed and regular follow-ups. Follow-up hip radiographs at ages seven and eight years old showed improvement in the left femoral head and no progression on the right. The patient is currently 12 years old, followed up regularly, maintained on pain medication as needed and hydroxyurea, and his condition has not clinically worsened.

Conclusion: Despite being rare in patients with SCD under five, AVN should be considered as one of the differentials in children with SCD presenting with hip pain. Early diagnosis allows for prompt intervention and the creation of a long-term management plan. Further research on pathophysiology, prevalence, and management of AVN in young pediatric patients with SCD is needed.

Poster # 154

POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME IN A PATIENT WITH SICKLE CELL ANEMIA

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Background: Posterior reversible encephalopathy syndrome (PRES) is a transient and reversible neurological disorder. It is characterized by radiological findings of vasogenic edema predominantly within the posterior occipital and parietal lobes of the brain causing neurological symptoms like headache, seizures, and altered mental status. PRES is commonly known to present in the setting of hypertensive crises, renal failure, and use of cytotoxic drugs. However, the etiology behind the pathophysiology has yet to be clearly identified though hypotheses thus far, have proposed involvement of cerebral vasoconstriction causing brain infarcts, impaired cerebral autoregulation leading to compromise of the blood-brain barrier, and endothelial dysfunction yielding fluid and protein transudation in the brain. Specifically, in sickle cell anemia (SCA), vaso-occlusive crises are inflammatory processes that lead to endothelial dysfunction. Therefore, patient's with SCA may have an increased risk of developing PRES.

Objectives: To present a unique case of a young male with SCA who developed PRES associated with hypertension and clinical seizures.

Design/Method: Case study

Results: An 8-year-old male with SCA presented with severe abdominal and back pain. He was admitted for the management of vaso-occlusive crisis requiring scheduled opioid medication which was escalated to a patient controlled analgesic pump due to the persistence of severe pain. On the sixth day of hospitalization, the patient reported transient severe headaches and also found with hypertension and transient bradycardia, though his work up at that time was inconclusive. On the eighth day of hospitalization, the patient developed a severe headache, followed by acute mental deterioration with seizure-like activity. A CT brain was obtained which revealed a subarachnoid hemorrhage (SAH). He was transferred to the Pediatric Intensive Care Unit for higher level of care. The initial and repeat CT angiograms were negative for brain aneurysms, arteriovenous malformations, or fistulas as possible cause of SAH. However, the patient continued with headaches, clinical seizures, and persistent hypertension. Due to suspicion for PRES, the patient underwent an MRI brain, of which, the findings strongly correlated with PRES.

Conclusion: Our patient clinically and radiologically exhibited PRES in the setting of vaso-occlusive crisis. On his MRI brain, the patient clearly displayed one of the predominant characterizations of PRES, in this case, symmetric parieto-occipital white matter edema. Although PRES is rarely reported in patients with SCA, impaired cerebrovascular function can be seen in the pathophysiology of SCA, thus it is important to maintain a high level of suspicion to achieve diagnosis.

Poster # 155

TELEHEALTH AND TRANSITION: IMPLEMENTATION OF TRANSITION TOOLS IN PATIENTS WITH SICKLE CELL DISEASE

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Background: Sickle cell disease (SCD) is a chronic anemia and vasculopathy. There is increased morbidity and mortality during transition from pediatric to adult care, due in part to inconsistent transition preparation as well as socioeconomic and geographic challenges in accessing SCD-focused healthcare.

Validated SCD-focused transition tools have been developed to address these barriers. However, accessible testing, standardized processes, and routine tracking are deficient, reducing the impact of these tools.

Objectives: We tested the feasibility and patient acceptability of telehealth-applied assessment tools by comparing scores from a provider-facing survey tool, the TRxANSITION Index (TI), and a patient-facing self-assessment tool, the TIP-RFT. We also assessed self-efficacy using the SCD Self Efficacy Scale (SE).

Design/Method: Of eligible pediatric patients 15-21 years old with SCD, 21 gave informed consent. The TI, TIP-RFT, and SE were administered in-person and via telehealth, followed by a feedback survey. In-person and telehealth measures were compared with paired sample T-test and using linear regression.

Results: Transition survey data were collected from 18 participants. There was no significant difference in scores for in-person vs telehealth, with mean TI scores 7.2 vs 7.5 ($p>0.9$), and mean TIP-RFT scores 67 vs 69 ($p=0.9$) for in-person vs telehealth respectively. Comparing TIP-RFT to the TI administered in-person, participants scored 37% higher on the TIP-RFT than the TI ($p=0.026$, 95% CI 5%-70%). The TIP-RFT and TI were associated with SE via telehealth ($p=0.013$ and $p=0.009$ respectively) but for in-person visits only the TIP-RFT was associated with SE ($p=0.033$).

On the feedback survey from 12 participants, 4 found it difficult to get to clinic visits in person and 8 would choose to incorporate telehealth visits into their transition preparation. Although only 3 participants found the TI slightly stressful vs 1 for the TIP-RFT, 6 felt the TI was more stressful than the TIP due to the length and lack of confidence in their answers.

Conclusion: Our results suggest that administering transition tools via telehealth is as effective as is in-person. Based on patient feedback, incorporation of telehealth visits could facilitate access to transition evaluation and preparation for patients with SCD. The lower scores on the TI may indicate it is a more sensitive tool that could provide a more accurate skill assessment due to the objectivity of the survey, which could prove valuable in the development of an individualized transition plan. However, further studies are needed to determine the optimal implementation of these measures and their impact on long-term transition outcomes.

Poster # 156

UTILITY OF FRENCH TRAQ IN PREDICTING TRANSFER SUCCESS OF YOUTHS WITH SICKLE CELL DISEASE IN QUEBEC

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Background:
Adolescents and young adults (AYA) with Sickle Cell Disease (SCD) experience more medical complications, acute care utilization and hospitalizations between ages 18 and 30. Programs aiming to prepare, transfer and integrate emerging adults in healthcare need objective measures to identify AYA

at higher risk of transition challenges. The Transition Readiness Assessment Questionnaire (TRAQ) is a validated disease neutral, self-administered questionnaire.

Objectives: This quantitative exploratory study aimed to measure the association between transition readiness, measured by the TRAQ, and *transfer* success, defined by transfer latency lesser than 6 months. Secondary objectives aimed to determine the association between TRAQ scores and *transition* success, defined by health care engagement and utilization.

Design/Method: A retrospective chart review of AYA with SCD who transferred from a pediatric to an adult hematology clinic in tertiary care centers in Quebec, Canada, was conducted. Total and domain-specific scores for TRAQ answered by AYA between ages 16 and 18 were calculated. Information regarding transfer, follow-up visits and communications with clinic nurse was collected. The observation period was between two years prior to transfer and September, 2023.

Results: Amongst 39 patients, 29 completed at least one TRAQ between ages 16 and 18. Ten AYA were excluded: 3/39 had completed their first TRAQ at age 19 or older, 5/29 never presented to an adult appointment and 2/39 questionnaires were unavailable. Median age at transfer was 18.1 years [17.2-19.0] and 15/29 participants were male. Median overall TRAQ score was 3.5 [2.6-4.6]. The domain with the highest median score was "Talking with providers" (5.0), while the lowest was "Tracking health issues" (3.0). 23/29 AYA had a successful transfer, while 6/29 transferred after 6 months; median TRAQ scores were 3.3 [2.8-4.6] and 3.8 [2.6-4.4], and mean ages at TRAQ completion were 17.9 and 18.0, respectively. AYA in the upper quartiles initiated more communications with the clinic nurse compared to those in the lower quartiles (52% vs. 39%). Proportion of attendance to adult clinic appointments in upper and lower quartiles were 79% and 74%, respectively.

Conclusion: In this first analysis of the French TRAQ in AYA with SCD, overall TRAQ scores did not differ between those with successful and delayed transfer. However, AYA with higher TRAQ scores seem to have better health care engagement. Individualising transition processes by using objective measures to identify gaps and guide interventions may improve successful transitions for AYA with SCD.

Poster # 157

HRQOL AMONG PATIENTS WITH SICKLE CELL DISEASE DURING TRANSITION FROM PEDIATRIC TO ADULT CARE.

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Background: Sickle Cell Disease (SCD) is associated with painful vaso-occlusion episodes (VOE), chronic pain, and organ damage. Painful VOE and chronic pain can hinder daily activities affecting Quality of Life (QoL). The transition period of SCD patients from pediatric to adult care is often marked by frequent hospitalizations, complications, and higher mortality.

Objectives: Our study evaluated patient-reported QoL outcomes in patients with SCD during the transition period.

Design/Method: This is a descriptive study of SCD patients receiving medical care in Newark NJ.

Informed consent was obtained from patients or legal guardians. Patients filled out a questionnaire using seven domains from the Adult Sickle Cell Quality of Life Measurement (ASCQ-Me): pain episodes and impact, medical history, sleep impact, social functioning, stiffness, and emotional impacts. Eligible patients were aged 16-25 years presenting to pediatric or adult hematology clinics from December 2021 to April 2023.

Results: Seventy-six individuals were enrolled, most were 16-21 years old with homozygous SCD. Pain episodes: 10-18% of 16-20-year-olds reported pain attacks compared to 43-100% of 21-25-year-olds. 25-50% of 22-25-year-olds were unable to do daily tasks or relied on family compared to 40-83% of 16-21-year-olds. Pain impact: 50-100% of 22-24 year-olds struggled due to pain, while younger patients were unaffected. 25-60% of 20-25 year-olds were occasionally, rarely, or never pain-free. Sleep impact: 29-60% of 20-25-year-olds did not get enough sleep, and 20-60% of all ages stayed up most of the night. Medical history: 17-36% of 16-20 year-olds and 40-100% of 21-25 year-olds used daily pain medicine. Sickle cell complications affected 8-40% of patients in all age groups. Social functioning: 25-60% of 20-25-year-olds reported their health impacted social life. 16-17-year-olds (21%) and 20-22-year-olds (25-60%) reported that their family felt that they were a burden. No significant findings were noted in stiffness impact. Emotional impact: 25-83% of all patients were often sad (70% of 16-year-olds and 83% of 21-year-olds). Nine % (19-year-olds) to 83% (21-year-olds) were depressed and 21-year-olds seemed most affected by the emotional impact of their disease.

Conclusion: Our cross-sectional study revealed a significant impact of SCD on HRQoL during the transition to adulthood. Therefore, screening for mental health in patients aged 16-25 years is crucial, offering support to those at risk. Disease-modifying therapy adherence should be emphasized. Limitations of our study include a small sample size in the older age group. Further studies could assess age and genotype-stratified HRQoL outcomes for 16-25-year-old SCD patients and potential measures for improvements.

Poster # 158

FROM PEDIATRIC TO ADULT CARE: PERSPECTIVES OF ADOLESCENTS WITH SICKLE CELL DISEASE AND THEIR PARENTS

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Background: Sickle cell disease (SCD) is a progressive, life-limiting disease hallmarked by sudden onset of significant pain. Beginning in childhood, effective disease management is critical to minimizing serious complications and mitigating heightened morbidity and mortality risks associated with transition from pediatric to adult care. During adolescence, disease management responsibilities often shift from parents to patients to foster development of self-management skills. Yet, the transition to adult SCD care often coincides with adolescents' *ongoing* development of self-management skills, resulting in insufficient mastery and preparedness.

Objectives: The current qualitative study examines adolescents' (ages 13-17) and their parents' perspectives about transitioning from pediatric to adult SCD care.

Design/Method: Adolescent patients with SCD (N= 21) and their parents (N=18) were recruited from

four New England outpatient pediatric hematology clinics. Participants completed individual semi-structured qualitative interviews exploring when/how disease management responsibilities shift from parents to patients during adolescence and considerations/concerns regarding transitioning from pediatric to adult care. Data were collected until thematic saturation was reached. Data were transcribed verbatim, cleaned, systematically coded via NVivo and analyzed using applied thematic analysis. This study was funded by National Heart, Lung, and Blood Institute.

Results: Adolescents identified as Black/African American or Afro-Latino and (100%) and primarily male (61.9%). Parents were primarily mothers (82%), publicly insured (52%) and identified as Black/African American (94%). Both adolescents and parents described concerns regarding transitioning from pediatric to adult SCD care. Parents chiefly reported concerns about their adolescent's under-preparedness for self-management upon entering adulthood, and their own unavailability to offer necessary and timely support. Parents also cited anxiety regarding the process surrounding their child transitioning to adult SCD care. Adolescents reported fears of having insufficient disease knowledge for effective self-management. Additionally, adolescents attributed experienced barriers during self-manage attempts to their age (e.g., being disregarded by medical providers during hospitalization). To promote transition preparedness, participants recommended increasing (1) opportunities for adolescents to further their disease knowledge and develop self-management skills across care settings and (2) increasing parent-focused supports to facilitate shifting disease management responsibilities to adolescents.

Conclusion: Understanding adolescents' and parents' concerns related to transitioning from pediatric to adult SCD care is critical to identifying ways to mitigate morbidity and mortality during this vulnerable period. Primary reported concerns and subsequent recommendations pertained to addressing perceived insufficient preparedness for transitioning to adult care. Findings suggest modifying current transition approaches may ensure earlier and more robust preparedness for adolescents with SCD *and* their parents when transitioning from pediatric to adult care.

Poster # 159

PERSPECTIVES ON HEALTHCARE TRANSITION OF YOUTH AND CAREGIVERS AFFECTED BY SICKLE CELL DISEASE

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Background: Healthcare transition (HCT) is documented to have profound social, emotional, and medical impacts on youth affected by Sickle Cell Disease (SCD). Prior studies show that youth with SCD are uniquely vulnerable to disparate health outcomes related to inconsistent data collection practices, regional knowledge deficits, and systemic racism throughout their HCT journey. Existing literature predominantly centers provider perspectives, not lived experiences of individuals navigating SCD. Research illuminating patient and caregiver perspectives on HCT specifically from regions with low disease prevalence can support the delivery of more equitable, comprehensive, and integrative healthcare.

Objectives: This interview study provides insight into the experiences of youths and caregivers

throughout the HCT from a small SCD center in a geographic region with a low prevalence of SCD. Findings from this analysis can contribute to future efforts to define best practices for healthcare delivery on both the pediatric and adult care sides along the HCT continuum in all geographic regions.

Design/Method: Eligible participants include 16-26-year-old English-speaking youths with SCD and their caregivers. The research interviewer conducted one-on-one semi-structured interviews, asking youths and their caregivers about factors that helped or hindered the HCT experience. Drawing from an intersectional framework, interview questions were designed to reflect the documented structural forces that shape the lived experiences of youths with SCD and their caregivers. Interviews were transcribed, coded, and analyzed using inductive thematic analysis.

Results: Eleven interviews, consisting of 5 caregivers and 6 youths (ages 17-25) were conducted between May 11, 2023 and July 13, 2023. Several themes emerged from the interviews. Both youths and caregivers consistently relied on the pediatric team for health information and facilitating transfer to adult care. Rapport established with the medical team had a profound impact on the perception of quality care. Lastly, participants' responses situated their experiences beyond a medical context, deepening our understanding of development, readiness, engagement, and autonomy relating to their HCT experience.

Conclusion: This study contributes to future efforts to define best practices for HCT in both pediatric and adult care settings. Interview findings demonstrate the importance of comprehensive HCT that prioritizes planning and care coordination, effective communication strategies, and developmentally and culturally appropriate care delivery. Consideration must be taken for the individual, regional, and structural SCD knowledge base. Further qualitative research efforts to improve HCT should evaluate how intersectional factors affecting the lived experiences of youths with SCD impact quality of life, health outcomes, and the education of regional providers and community members.

Poster # 160

GENETIC KNOWLEDGE AMONG ADOLESCENT PATIENTS AND PARENTS OF CHILDREN WITH SICKLE CELL DISEASE

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Background: Genetic therapies for sickle cell disease (SCD) are in the clinical trial pipeline or have recently been approved. Although potentially curative, these interventions are complex and associated with serious risks. Knowledge and attitudes about genetic therapies may influence patient and parent decision-making, but baseline genetic knowledge among these stakeholders is unknown.

Objectives: To assess familiarity with both basic and SCD specific genetic concepts among pediatric SCD families.

Design/Method: Patients with SCD at least 13 years of age and caregivers of children with SCD were approached during clinic encounters and asked to complete an 11-item true-false genetic knowledge survey (i.e. genes are made of DNA) as part of a larger survey surrounding knowledge, attitudes, and

beliefs about genetic testing and clinical research. Health literacy was assessed using the single-item literacy screen (SILS) and numeracy measured by the 3-item subjective numeracy scale (SNS-3). Generalized estimating equations were used to compare survey results between patients and caregivers and to correlate genetic knowledge surveys with health literacy.

Results: Of 299 survey respondents, 99% identified as Black with Hb SS the most common genotype followed by Hb SC (61% and 30%, respectively). The mean age of adolescent respondents was 15.89 years. Health literacy was higher among parental caregivers than adolescents (SILS mean 4.56 versus 3.94, p <.0001) as were numeracy skills (SNS-3 mean 10.54 versus 9.46, p =.0001)

The mean percent of correct responses on the genetic knowledge survey was 71% (IQR 64%-82%) with a positive association between health literacy and overall genetic knowledge score (p= 0.01). Adolescents were significantly less likely than caregivers to understand that genes are part of chromosomes (p <.0001) or that healthy parents can have a child with an inherited disease (p= 0.021), but more likely to understand that a person born with SCD must have at least one parent with the sickle gene (p= 0.0011). Only 32% of respondents understand that the gene mutation for sickle cell is in all cells (i.e. germline) as most (86%) believe the mutation is only in the blood cells.

Conclusion: Parents of children with SCD and adolescent patients are familiar with basic genetic concepts but are less familiar with principles of inheritance and the presence of the SCD gene mutation in all cells. Communication around genetic therapies should highlight that the intervention targets blood-producing cells and reinforce that the mutation is present in all cells, including reproductive cells, and that subsequent offspring can inherit the SCD mutation.

Hemostasis/Thrombosis (201-228)

Poster # 201

PROPHYLACTIC FVIII INFUSIONS MAY BE UNNECESSARY IN TOLERIZED HEMOPHILIA A PATIENTS ON EMICIZUMAB

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Background: Hemophilia A is a hereditary bleeding disorder causing low factor VIII (FVIII) activity, leading to bleeding-related morbidity. Emicizumab prophylaxis is preferred due to its ease of self-administration, long half-life, and low annual bleeding rate (ABR), independent of tolerization to alloantibodies against FVIII (inhibitors). Emicizumab use in previously untreated patients and patients with <20 exposures to FVIII is poorly understood due to a lack of long-term experience and understanding of the impact on inhibitor development. Further investigation is needed to assess the risk of inhibitor recurrence in patients with previous inhibitors and the concomitant use of emicizumab.

Objectives: We examined inhibitor incidence and recurrence amidst emicizumab prophylaxis.

Design/Method: We performed a single-center retrospective analysis of patients with Hemophilia A on emicizumab prophylaxis. We collected demographics, inhibitor status at the time of transition to emicizumab and in the follow-up period, bleeding events after transition, and number of FVIII exposures

pre- and post-transition. Inhibitor recurrence was defined as laboratory evidence of inhibitor and/or unexplained breakthrough bleeding events despite on-demand FVIII infusions.

Results: We reviewed 36 patients. Median age was 15.3 years (range 1.2 – 82). Median follow-up on emicizumab was 3.5 years (range 0.5 - 5). Two patients had < 20 FVIII exposures pre-emicizumab; one had inhibitor pre-emicizumab. Fifteen patients (45%) were diagnosed with inhibitor pre-emicizumab. Of these, 8 patients (53%) were tolerized pre-emicizumab, and 7 patients (47%) were not. Median peak inhibitor titer was 4.2 Bethesda units (range 0.7 – 281). Post-emicizumab, no tolerized patients had inhibitor recurrence, and 1 non-tolerized patient's inhibitor became undetectable after 4 years of emicizumab therapy. Mean ABR was 0.33 events/year for tolerized patients (median 0, range 0 – 3); 0.17 events/year for non-tolerized patients (median 0, range 0 – 1); and 0.60 events/year for patients with no history of inhibitor (median 0, range 0 - 4). Mean FVIII exposures annually was 0.09 for tolerized patients (median 0, range 0 – 1); 0.07 for non-tolerized patients (median 0, range 0 – 1); and 1.2 for patients with no history of inhibitor (median 0, range 0 – 20).

Conclusion: In our cohort, no tolerized patient on emicizumab had a recurrence of inhibitor, despite infrequent exposure to FVIII. One patient had inhibitor resolution on emicizumab without tolerization. This adds to data on emicizumab safety and its impact on the natural history of FVIII inhibitors. Our study suggests continuing post-ITI prophylactic FVIII infusions in tolerized patients on emicizumab may not be necessary.

Poster # 202

GENETIC TESTING UPTAKE FOR PEDIATRIC PATIENTS AT RISK TO BE HEMOPHILIA CARRIERS

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Background: Female hemophilia carriers can be symptomatic with bleeding even with a normal factor level. Targeted genetic testing is the most reliable method for diagnosis and is considered standard of care for all females at-risk to be carriers, although offering testing to asymptomatic pediatric patients prior to childbearing age is not a universal practice.

Objectives: Our objectives were to describe (1) the percent of female children at-risk to be carriers who complete genetic testing after it was discussed at a comprehensive clinic visit with genetic counseling, (2) characteristics of caregivers consenting to genetic testing, and (3) reasons provided by caregivers or providers for not pursuing genetic testing.

Design/Method: Clinical and laboratory data were obtained retrospectively from electronic medical records for all patients with a diagnosis of hemophilia A or B and their female siblings under 18 years at the time of a genetic counseling visit at Seattle Children's Hospital between June 2019 and June 2023. All maternal female siblings were considered at-risk to be carriers unless their mother had genetic testing showing she did not carry the familial variant. Data obtained included caregiver demographics, insurance authorization for genetic testing, completion of testing, factor activity levels, and hemophilia severity in male family members.

Results: Sixty-four unique children representing 55 families were identified. Thirty-two (50%) had male

family members with severe hemophilia. Fourteen (21.9%) were found to be hemophilia carriers, with median factor level of 46%. The mother was the sole caregiver at the visit for 67% (43/64) of patients. Twenty-seven percent (17/64) of patients had prior genetic testing at a median age of 5 years, all of whom had a factor level. Of those who had not yet had genetic testing, factor level was obtained for 36%, insurance authorization was initiated for 49%, and genetic testing was completed for 28%. Most common reasons for not initiating authorization were the familial variant was not known (58%), and family declined testing (21%). Insurance denied testing for 3 patients. Caregivers declined testing due to respect for the child's autonomy, financial reasons, or belief that hemophilia carriers cannot be symptomatic.

Conclusion: Pediatric hematology providers are in a unique position to identify hemophilia carriers through targeted genetic testing. A shared decision-making model that includes education about bleeding risk in carriers, and addressing family concerns about autonomy and cost, is essential. Improving diagnosis of potential hemophilia carriers includes increasing the availability of a familial variant through proband testing at diagnosis.

Poster # 203

NOT A-NOUGH BUZZ ABOUT IT: HEPATITIS A&B ANTIBODY STATUS IN BLEEDING DISORDERS (SINGLE CENTER)

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Background: Hepatitis A (HAV) and Hepatitis B (HBV) are commonly vaccinated, preventable viral infections in the United States. Antibodies to confirm immunity after vaccination are not routinely checked in healthy patients, but are recommended for special populations, such as those with immunodeficiency or other high-risk disorders, with guidance for re-immunization if needed. MASAC of the National Bleeding Disorders Foundation (NBDF) recommends evaluation of immunity to HAV and HBV in persons with bleeding disorders (PWBD, including Hemophilia A (HA), Hemophilia B (HB), Von Willebrand Disease (VWD)). However, the CDC has recently changed recommendations to no longer include PWBD as a high risk population for these recommendations. This has led to a disconnect between primary care physicians and hematologists in the care of this patient population. In this study we assessed the HAV/HBV antibody status in PWBD at our center.

Objectives: Determine the immunity to HAV and HBV in PWBD at our center and evaluate the relationship, if any, with age, race, and bleeding disorder type.

Design/Method: A descriptive, cross-sectional study was performed including 115 patients, age 6 to 37 years, all previously vaccinated for HAV and HBV. Data on age, race, gender, HAV IgG antibody (Ab), HBV Surface Ab (HBV sAb), and bleeding disorder type were obtained from 5/28/2020 – 3/2/2023.

Results: Mean age was 16.3 ± 5.1 years; 91 (79.1%) were male; 59 (51.3%) had HA, 11 (9.6%) HB, 36 (31.3%) VWD, 9 (7.8%) other. Race: 81 (70.4%) Caucasian, 19 (16.5%) African American, 6 (5.2%) Asian, and 9 (7.8%) Other/Undefined. HAV IgG (n=113) was positive in 101 (89.3%) PWBD (HA 91%, HB 91%, VWD 89%). HBV sAb (n=115) detected in 54% PWBD (HA 61%, HB 82%, VWD 33%). A significant difference was shown with negative HBV sAb based on bleeding disorder type ($p = 0.012$), but not with

HAV Ab (p = 0.667). There was no difference in HAV or HBV antibody status for age (HAV p = 0.128) and (HBV p = 0.139). Numbers were too small to differentiate for gender or race.

Conclusion: Many of our PWBD are not immune to HBV despite vaccination. Given that PWBD remain at risk for infection, screening for HAV and HBV immunity status may be beneficial to guide reimmunization practice. Further evaluation in this population is needed.

Poster # 204

JOINT ANGLES AND FORCES DURING SIMULATED SPORTS ACTIVITIES IN PERSONS WITH HEMOPHILIA VS CONTROLS

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Background: Although prophylaxis decreases bleeding and joint damage in persons with hemophilia (PwH), musculoskeletal bleeding still occurs. We hypothesize that bleeding occurs despite prophylaxis because of movement patterns that increase injury risk. The POBBOY study (Prevention of Bleeding with Biomechanics and Optimization of prophYlaxis) measures forces and angles during simulated sports activities in a motion lab to understand how movement patterns relate to past joint damage and subsequent bleeding.

Objectives: The objective of this analysis is to compare angles and forces during simulated sports activities in controls vs PwH with more joint damage.

Design/Method: The Hemophilia Joint Health Score (HJHS), a validated physical exam score of swelling, range of motion, pain, crepitus, and strength, was used to measure joint damage in the ankles and knees (higher worse). Participants performed walking, bilateral deceleration, drop jump with counterjump, and squatting tasks, while forces and angles were measured using force plates and reflective markers taped to bony landmarks and tracked using motion capture cameras. For this analysis, participants with summed HJHS lower extremity (LE) scores >85th percentile for the study population were compared to age-matched controls. Data from PwH worse legs and control non-dominant legs were compared using t-tests.

Results: Data from 11 PwH (age 13-42; average total LE-HJHS 21) were compared to data from 11 age-matched controls (age 13-41; LE-HJHS 3.7). Units of measurement expressed as mean±stdev: force (times body weight), angle (degrees), moment (Nm/kg), distance (m), squat depth (%leg length).

In walking, PwH had similar vertical force during weight acceptance but lower vertical force during push-off vs controls (1.06±0.06,1.12±0.06,p=0.04) in barefoot but not shod walking, with no differences in speed or step length between hemophilia and controls.

In squatting, PwH had less deep squats than controls (43±0.1%,56 ±0.1%,p=0.01), with lower ankle dorsiflexion (20±10,31±7,p=0.01) and lower knee flexion (97±21,122±12,p<0.001) angles. The knee extension internal moment, which reflects torque demand on quadriceps, was lower in PwH than controls (0.9±0.6,1.4±0.4,p=0.03).

In drop jump, counterjump height (0.17±0.04,0.25±0.11,p=0.05), and ankle dorsiflexion angle (20±10,30±6,p=0.01) were lower in PwH than controls.

In deceleration, PwH had lower ankle dorsiflexion (4±5,15±9,p<0.001) and lower knee flexion (59±12,78±13,p<0.001) angles than controls.

Conclusion: PwH had movement patterns reflecting strategies to decrease joint load, which could be compensation for previous bleeding and could also increase injury risk if higher loads are accidentally encountered. Ankle and knee flexion angles were lower in all tasks except walking, which could potentially serve as screening tools for joint health in the future.

Poster # 205

ROLE OF SOCIAL DETERMINANTS OF HEALTH ON MEDICATION ADHERENCE IN PATIENTS WITH HEMOPHILIA

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Background: Regular prophylaxis in children with hemophilia effectively reduces bleeding and improves quality of life. However, adherence to prophylaxis remains a significant challenge. Impact of socio-demographic factors and contextual factors on prophylaxis adherence is understudied, especially in the Hispanic population, and interventions targeted towards improving adherence are lacking.

Objectives: To investigate the impact of social determinants of health (SDOH) and clinical and contextual factors on adherence to prophylaxis in children with hemophilia.

Design/Method: In this prospective cross-sectional study, parents of children with hemophilia were enrolled from 2018-2023. Adherence to clotting factor concentrate (CFC) or emicizumab prophylaxis was assessed using Hemophilia Regimen Treatment Adherence Scale- Prophylaxis. Total score $\geq$ 57 is defined as the cut off for non-adherence. We assessed SDOH (primary language, insurance, health literacy), clinical characteristics (severity and type of hemophilia, and frequency, type and route of prophylaxis prescribed) and contextual factors (trust in provider, acculturation). Univariate analyses were conducted to identify significant associations between adherence and SDOH, clinical characteristics and contextual factors.

Results: Forty-one parents of thirty-eight children were enrolled. Among the children, 87% had hemophilia A and 13% had hemophilia B. Of the parents, 10 (24%) were of non-white race and 23 (56%) identified as Hispanic. The majority (46%, n=19) of children were on extended half-life CFC prophylaxis, followed by standard half-life CFC (39%, n=16) and emicizumab (15%, n=6). The median Hemophilia Regimen Treatment Adherence Scale-Prophylaxis total score was 29.0 (Interquartile range 27.0, 34.3). Univariate analyses revealed significant associations between prophylaxis route and type but not with frequency. Prophylaxis via peripheral intravenous route was associated with significantly lower adherence compared to prophylaxis via central line (p<0.01), and those on emicizumab had slightly higher adherence than those on standard half-life products (p=0.08). No associations were found with hemophilia type or severity and adherence. Non-white race was associated with higher adherence

(p<0.05) and no difference were identified by ethnicity. Higher trust in providers was significantly associated with higher adherence (p <0.05).

Conclusion: Overall, adherence with prophylaxis was high in this population and associated with less burdensome route of administration. Non-white race and tust in provider were associated with higher adherence. Further evaluation to assess individual factors that contribute to higher adherence is warranted. Our findings can guide tailored interventions to improve adherence in children with hemophilia, including enhancing trust in the healthcare system.

Poster # 206

OPTIMIZING CARE FOR NEONATAL PORTAL VEIN THROMBOSIS: A SYSTEMATIC APPROACH AND ONGOING CHALLENGES

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Background: Neonatal portal vein thrombosis (PVT) is a distinct subset of pediatric deep vein thrombosis wherein it is doubtful that anticoagulation significantly alters the natural history of clot resolution or progression to liver complications (e.g, cavernous transformation, portal hypertension). Current guidelines recommend reserving anticoagulation for occlusive PVT cases, emphasizing the crucial role of consistent PVT grade documentation in radiologic reports. Moreover, there is no consensus on the frequency and duration of ultrasound (US) to survey for liver complications.

Objectives: To enhance neonatal PVT care by standardizing institutional management, minimizing unnecessary anticoagulation, and optimizing imaging checkpoints, we report on practices and outcomes before and after implementing a Neonatal PVT Management Algorithm.

Design/Method: Employing Plan-Do-Study-Act (PDSA) methodology, we developed an algorithm to guide diagnosis, anticoagulation decision-making, and imaging intervals surrounding neonatal PVT. A retrospective electronic medical record search spanning 66 months (February 2012–August 2017) gathered baseline data on PVT grading documentation, anticoagulation utilization, and follow-up imaging. Concurrently, attending hematologists were anonymously surveyed to assess individual practices surrounding new diagnoses. Combining survey and society insights with published data, we established an institutional algorithm that recommended reserving anticoagulation for occlusive PVT cases and foregoing anticoagulation in subocclusive cases, and obtaining doppler US imaging at post-diagnosis timepoints Week 1 and Months 1, 3, and 6. At Month 6, those with unresolved PVT or persistent liver abnormalities were scheduled for yearly surveillance imaging for 5 years. Radiology, engaged as a stakeholder, adjusted their reporting practice to include PVT grading in every imaging report based on established criteria. The algorithm was disseminated electronically across the healthcare system. After 62 months (2018-2023), post-algorithm adherence and outcomes were analyzed.

Results: Documentation of PVT grading improved post-algorithm, with incidence of undocumented/unknown PVT grade improving from 37% (n=7) to 3% (n=2) (p=0.0002). Anticoagulation usage in subocclusive cases decreased from 37.5% (n=3) in the pre-algorithm era to 0% post-algorithm (P=0.0153) with no adverse outcomes. Median duration of anticoagulation for all patients decreased

from 14 to 8 weeks (P=0.0014). However, both pre-and post-algorithm cohorts faced challenges in follow-up imaging adherence. Rates of failure to present for follow-up were identical in both cohorts, with ~50% of patients lost to follow-up by Month 3, and 100% lost by Year 3.

Conclusion: The algorithm positively impacted neonatal PVT management, specifically in systematizing PVT grading and reducing anticoagulation use. However, challenges in follow-up imaging compliance persist, highlighting the need for further refinement in the next PDSA cycle.

Poster # 207

RETROSPECTIVE COHORT STUDY OF VTE RECURRENCE BY WARFARIN OR DOAC USE IN FACTOR V LEIDEN DEFICIENCY

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Background: Factor V Leiden deficiency is a common inherited thrombophilia, that increases the risk of venous thromboembolism (VTE). While both warfarin and direct oral anticoagulants (DOACs) are used in VTE treatment and prevention, their relative efficacy and safety in pediatric patients with Factor V Leiden deficiency remain unclear.

Objectives: This study compared the risk of VTE recurrence, development of anemia, and all-cause mortality in pediatric patients with Factor V Leiden deficiency treated with either warfarin or DOAC therapy.

Design/Method: We conducted a retrospective cohort study using a large, multi-hospital-system database. The time period for this study was limited to January 1, 2000 through December 1, 2023. All patients were under 18 years old and diagnosed with Factor V Leiden deficiency via blood testing. Inclusion criteria were at least one episode of pulmonary embolism or deep venous thrombosis of any extremity, and treatment with warfarin or DOAC. Treatment cohorts were matched based on age and risk factors for VTE including malignancy, asparaginase chemotherapy use, presence of central venous catheter and trauma. Primary outcomes were VTE recurrence, development of anemia, and all-cause mortality. Log-rank tests, relative risk and hazard ratio calculations were performed using commercially available statistical analysis software.

Results: A total of 94 patients on DOACs and 51 on warfarin were included. Compared to warfarin, DOACs were associated with a significantly higher rate of VTE recurrence (hazard ratio: 1.862, 95% confidence interval [CI]: 1.072-3.232, p=0.027). No significant differences were observed in acute blood loss anemia, gastrointestinal bleeding or all-cause mortality risks between the two groups. Notably, among patients without VTE recurrence, DOACs exhibited a lower risk of acute blood loss anemia or gastrointestinal bleeding compared to warfarin (relative risk: 0.488, 95% CI: 0.301-0.792).

Conclusion: Our study suggests that DOACs may be associated with a higher VTE recurrence risk than warfarin in pediatric patients with Factor V Leiden deficiency. However, DOACs potentially pose a lower bleeding risk among patients without VTE recurrence. Further research is warranted to confirm these findings and guide optimal anticoagulation strategies in this population.

Poster # 208

INCREASING ADHERENCE TO RECOMMENDED HBV SEROLOGY TESTING IN PATIENTS WITH HEMOPHILIA

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Background: Patients with hemophilia are at increased risk of abnormal bleeding, often requiring treatment with plasma-derived clotting factors and blood products. While these treatments are relatively safe, they do pose some risk of transmitting infections. Therefore, it is recommended that patients with hemophilia undergo yearly testing for hepatitis B virus (HBV) to detect any infections, assess hepatitis B immunity, and provide vaccinations when necessary. However, at the Yale Hemophilia Treatment Center, we observed a low compliance with these annual testing recommendations.

Objectives: The aim of our quality improvement project is to increase the rate of adherence to recommended annual HBV serology testing for patients diagnosed with hemophilia from a baseline of 41% to 80% within 24-month period from January 2022 to January 2024.

Design/Method: We included 113 adult and pediatric patients older than one year diagnosed with hemophilia followed at the Yale Hemophilia Treatment Center between January 2022 to September 2023. The median age was 20.5 years (range: 1-73 years), 82 patients (73%) were males. Following the identification of key drivers for our project, which included increasing awareness about the screening among patients and staff, along with identifying workflow barriers, we implanted the following interventions: enhancing provider education and awareness about the recommendations, creating a standard order set and checklist within the electronic health records, providing patient education, and streamlining testing with other laboratory investigations. We recorded the percentage of patients that underwent the recommended HBV testing every month and compared the rates of testing before and after implanting the interventions. We utilized statistical process control charts to trend compliance rates over time and identify patterns indicative of any special cause variation.

Results: There was a significant increase in serology testing administration following interventions – the average percentage of tested patients increased from 41% to 69%. The variability in percentage of tested patients also decreased throughout the project, as demonstrated by narrowing of control limits.

Conclusion: Although we did not achieve the target of 80% compliance with annual HBV serology testing, our interventions have significantly increased the testing rates among patients with hemophilia in our center. We aim to meet this target in the next three months, prior to the project's official conclusion, and maintain high testing rates going forward by reinforcing education for both patients and providers.

Poster # 209

IMPROVING PATIENT CARE IN THE COMMUNITY THROUGH A JOINT HEMOSTASIS AND THROMBOSIS-GYNECOLOGY CLINIC

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Background: Postmenarchal women with bleeding or clotting disorders need expertise in both Hematology and Gynecology. Patients typically make two separate trips for each specialist with often redundancy in care. Asynchronous follow-ups are difficult to maintain from both patient/caregiver and provider perspectives, and patients may be lost to follow-up to each service - ultimately leading to inefficient patient care, increased costs, and patient dissatisfaction.

Objectives: 1) Deliver efficient care through a multidisciplinary joint clinic in the community setting with both services to patients ≤ 21 years with abnormal uterine bleeding and a known bleeding or clotting disorder.
2) Improve total visit duration for joint clinic patient to ≤ 90 minutes.

Design/Method: Eligible patients were followed in our multidisciplinary Hemostasis and Thrombosis-Gynecology (HAT-GYN) clinic at Texas Children's Hospital-The Woodlands (TCH-WL) community campus (Apr 2021-Dec 2023). Baseline joint clinic data was obtained from our other two TCH campuses for reference. Our TCH-WL HAT-GYN Care Process Team (providers and Nurse Coordinator) designed "Plan-Do-Study-Act" (PDSA) cycles to improve clinic workflow. Time study sheets were used in clinic to identify additional areas of improvement. Patient and provider surveys were obtained periodically for ongoing feedback.

Results: Median total visit duration for a HAT-GYN patient at other TCH campuses was ~131 minutes. Our Care Process Team has completed two PDSA cycles to date (PDSA 3 ongoing at time of submission). Future PDSA 4 will consist of both providers seeing a patient simultaneously.
PDSA 1 (Jan 2023 - Mar 2023): Nurse Coordinator utilized EMR "Chat" function to communicate patient intake to both providers simultaneously. Median total visit duration ~122 min (range 113-312 min), N= 11 patients.
PDSA 2 (Apr 2023 - Oct 2023): Using additional staff member to help with patient flow. Median total visit duration ~117 min (range 65-185 min), N= 29 patients.
PDSA 3 (Nov 2023 - Jan 2024, ongoing): Preprint "After Visit Summaries" prior to start of clinic (includes educational materials and next follow-up). To date median total visit duration ~123 min (range 69-180 min), N= 11 patients.

Conclusion: At TCH-WL, we have established a multidisciplinary HAT-GYN clinic to provide effective, high quality community-based care to complex patients, a U.S. News and World Report "Commitment to Best Practices" objective. Through this initiative, we strive for a more streamlined clinic with improved patient and provider experiences.

Poster # 210

OPTIMIZING COMMUNICATION AROUND HEMOPHILIA GENE THERAPY: ASSESSMENT OF HEALTHCARE PROFESSIONALS

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Background: Effective communication is essential as we advance the care for persons with hemophilia with innovative treatments like gene therapy. Addressing concerns and disseminating clear and unbiased information is crucial in fostering understanding , improving consent process and overall acceptance of gene therapy. This study focuses on understanding the pivotal role played by healthcare professionals in shaping attitudes and beliefs surrounding gene therapy in hemophilia.

Objectives: To gain comprehensive insight into the expectations, concerns, and effective communication strategies utilized by healthcare professionals caring for patients with hemophilia regarding gene therapy.

Design/Method: Qualitative methodology was employed utilizing audio-recorded interviews with diverse groups of healthcare professionals including physicians, nurses, social workers, pharmacists, and advanced practice providers. A semi-structured interview guide was crafted prior to interviews and piloted to assure the questions posed were effective and pertinent. The interviews were transcribed and uploaded into a qualitative data analysis software (NVivo 14, Lumivero) for coding. Three coders identified overarching themes and subthemes using deductive coding.

Results: A diverse group of 15 healthcare professionals (3 physicians, 2 advanced practice providers, 3 nurses, 3 social workers, 2 pharmacists, 2 academic coordinators) from 4 different academic centers with a median experience in hemophilia care of 15 years (range 1 - 27 years) participated in the study. Three primary themes and multiple sub-themes were identified: 1) Healthcare professionals' perceptions of patients' and families' knowledge of gene therapy included uncertainty about long-term outcomes and side effects, uncertainty around eligibility criteria, misinformation or lack of patient-oriented comprehensive information around gene therapy; 2) Importance of communication included being honest about the word "curative", respecting hemophilia identity, style of medical team communication, frequency of discussions about gene therapy. 3) Influential factors in gene therapy decisions included impact on quality of life, fear and uncertainty after treatment, past experiences with the medical team, and potential financial and emotional costs.

Conclusion: This qualitative study identified valuable perspectives within the discourse on gene therapy for hemophilia B, shedding light on the multifaceted considerations and communication dynamics within the healthcare professional community.This research offers essential qualitative insights that can guide the conversations during consenting process and inform the development of educational programs. These programs would seek to improve comprehension regarding potential adverse effects, uncertainties surrounding longevity of treatment, importance of follow up care, and clearly define the range of variable outcomes.

Poster # 211

HEMOSTATIC DYSREGULATION IN PEDIATRIC AND YOUNG ADULT PATIENTS WITH POST ACUTE SEQUELAE OF COVID-19

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Background: Post Acute Sequelae of Covid-19 (PASC), commonly referred to as "Long Covid", is a complication of acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection that can lead to prolonged debilitating symptoms affecting multiple organ systems. While the underlying mechanism are still to be elucidated, there is evidence that endothelial dysfunction, disturbed hemostasis, and microvascular thrombosis might be a driver of PASC pathophysiology. However, there is limited data, especially in the pediatric population.

Objectives: To describe hemostatic alterations in a cohort of children, adolescents, and young adults with PASC.

Design/Method: We conducted a retrospective study of a cohort of consecutive patients (0-21 years of age) with PASC (new or ongoing symptom >30 days after initial laboratory confirmed COVID-19 diagnosis) who were evaluated at the Children's National Hospital Post COVID Program Clinic. Patients underwent comprehensive hemostatic evaluation that included prothrombotic markers (D-dimer, fibrin monomer, fibrin degradation product), soluble fibrinolysis inhibitors (alpha 2-antiplasmin, plasminogen activator inhibitor-1 antigen), and Kaolin-activated thromboeleastograhpy (TEG). Impaired fibrinolysis was defined as the presence of elevated soluble fibrinolysis inhibitors with a TEG clot lysis at 30 minutes after maximum clot strength (LY30) of <1%. Relevant data were extracted from the electronic medical records and were summarized using descriptive statistics.

Results: A total of 50 patients [27 females, median age 14 years (range 6-21 years)] with PASC were included in this study. All patients reported multiple persistent or prolonged symptoms following a clinically mild COVID-19 illness that did not require treatment or hospitalization. Of these 50 patients, 23 patients (46%) were found to have a hemostatic laboratory abnormality. Hemostatic abnormalities identified in this cohort included elevated prothrombotic markers (15 patients) and elevated soluble fibrinolysis inhibitors (9 patients). Both hemostatic abnormalities were present in only 1 patient. A positive fibrin monomer testing was present in 12 of 15 patients (80%) with elevated prothrombotic markers. Only 2 of these patients showed elevated D-dimers (≥ 0.50 mcg/mL FEU). Of the 9 patients with elevated soluble fibrinolysis inhibitors, 4 patients (44%) showed impaired fibrinolysis on TEG LY30.

Conclusion: Laboratory evidence of dysregulated homeostasis associated with a prothrombotic state was present in a significant proportion of children, adolescents, and young adults with PASC. Further studies are required to determine underlying mechanisms and clinical significance in this population.

Poster # 212

STANDARDIZING THE EVALUATION AND MANAGEMENT OF ADOLESCENTS WITH ABNORMAL UTERINE BLEEDING AND ANEMIA

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Background: Abnormal uterine bleeding (AUB) encompasses a large portion of the adolescent gynecological problems with presentation of anemia and heavy menstrual bleeding. In addition to screening for bleeding disorders, the evaluation of AUB should include non-hematologic causes tailoring the treatment offered. In our free-standing children's hospital, we noted discrepancies in the evaluation and management of patients with AUB. We implemented a quality improvement initiative to

standardize care.

Objectives: Our primary aims are to 1) optimize screening of non-hematologic causes of AUB including thyroid disorder, pregnancy, and sexually transmitted infections to 75% of admitted patients and 2) standardize management of AUB and associated anemia per a treatment algorithm with intravenous (IV) iron, oral iron, and hormonal therapy to 75% of admitted patients.

Design/Method: Baseline data was obtained from 2018 to 2023 for patients aged 11 to 21 years admitted with AUB. A clinical pathway was created in February 2023 using evidence-based medicine with expert input from a multidisciplinary team including adolescent medicine, gynecology, hematology, and pediatric hospital medicine. Interventions implemented to date via PDSA cycles include clinical guideline creation, distribution of guideline among providers and trainees, and guideline publication to our electronic medical record resource site.

Results: Of 46 identified patients from the baseline period, 81% were screened for pregnancy, 61% for TSH, and 9% for *N. gonorrhea* and *C. trachomatous* (GC/CT), while 7% underwent all three recommended screenings for common non-hematologic causes of AUB. Once admitted, 59% of patients received IV iron, 78% received oral iron, and 65% received hormonal therapy, while 28% received combined recommended medical therapies. In the post-intervention period, of 15 identified patients, 33% underwent combined screenings, marking a 371% increase. Individually, screening rates were 73% for pregnancy, 67% for TSH, and 47% for GC/CT. Additionally, 53% of admitted patients received the recommended combined medical treatment, an 89% increase. Specifically, 87% received oral iron, 87% received IV iron, and 80% received hormonal therapy.

Conclusion: The results of our study thus far illustrate improved standardization in the combined screening of non-hematologic etiologies of AUB and in the treatment of bleeding and associated anemia. We hope to further advance our aims through creation of an order set mirroring the pathway and providing education in the form of conferences, emails, and handouts.

Poster # 213

VON WILLEBRAND DISEASE IN PEDIATRIC PATIENTS WITH A POSITIVE BLEEDING PHENOTYPE AND NORMAL APTT

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Background: Despite being the most prevalent congenital bleeding disorder worldwide, Von Willebrand Disease (VWD) is frequently underdiagnosed. The presence of abnormal mucocutaneous bleeding symptoms may trigger consultation with primary care providers (PCPs) for initial evaluation. Abnormal screening coagulation studies, such as prolonged activated partial thromboplastin times (aPTTs), may elicit referral to hematology for specialized coagulation assays. Unfortunately, symptomatic individuals with normal aPTTs might be at risk for delayed diagnosis if VWD-specific assays are not performed upfront.

Objectives: To investigate the prevalence and clinical characteristics of VWD in pediatric patients with bleeding symptoms but normal-for-age aPTTs.

Design/Method: A retrospective chart-review was performed including patients <22 years-of-age diagnosed with VWD between 2015 and 2023 at a single Hemophilia Treatment Center. Only those with normal-for-age aPTTs were included in the analysis. Descriptive/Interferential statistics were performed.

Results: Out of 100 patients with VWD, 57% (n=57) had an initial normal-for-age aPTT. Mean age-at-diagnosis was 13-years (standard deviation (SD) 4-years). The majority were female (n=45, 78.9%) including 35 post-menarchal adolescents (61.4%).

Of the 57 included patients, the mean aPTT was 32.6 seconds (SD 2.0 seconds, range 28.3-35.9 seconds). Despite normal aPTTs, the majority (n=54, 94.7%,) reported presence of bleeding symptoms. Heavy menstrual bleeding (HMB) (n=34, 59.6%), epistaxis (n= 29, 50.9%), and easy bruising (n= 27, 47.4%) were the most commonly reported. Thirty-three percent (n=18) had concomitant iron-deficiency-anemia (IDA).

Ultimately, most patients (n=54, 94.7%) were diagnosed with type 1 VWD, with 9 (15.8%) having VWF levels <30% (15.8%). Type 2B (n=2, 3.7%) and type 2A VWD (n=1, 1.8%) were also identified. Hemostatic management including antifibrinolytics (n=23, 40.4%) and desmopressin (n=12, 21.1%) was often required to control symptoms. The need for on-demand VWF replacement was uncommon (n=1, 1.8%). None required VWF prophylaxis.

Among post-menarchal females, HMB was highly prevalent (n=34, 97.1%). Compared to males and pre-menarchal females, post-menarchal females had higher prevalence of IDA (45.7% vs. 13.6%, p=0.01), with 4 (11.4%) requiring blood transfusions to correct the anemia. These females often required antifibrinolytics (n=18, 51.4%), oral hormonal regimens (n= 12, 34.3%) or other hormonal methods (n=11, 31.4%) to manage their HMB.

Conclusion: Standard screening coagulation studies may not be sufficiently sensitive to identify children with VWD presenting with mucocutaneous bleeding symptoms. Post-menarchal females with VWD are at high-risk for HMB and IDA despite normal aPTTs. The need to perform upfront VWD testing in patients with positive bleeding phenotypes should be encouraged. This practice will minimize suboptimal treatment and inadequate access to specialized care.

Poster # 214

EVALUATION FOR BLEEDING DISORDERS IN CHILDREN PRESENTING WITH BRUISING CONCERNING FOR ABUSE

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Background: Bruising in pre-mobile infants <6 months of age and bruising in the TEN (torso, ears, neck) region in children aged 6 – 48 months of age raises concern for abuse. Similar bruising patterns can also be seen in in children with thrombocytopenia or coagulation factor deficiencies, with or without a history of trauma. Screening for bleeding disorders is often sent as part of the evaluation of children presenting to the emergency department (ED) with bruising.

Objectives: Our objectives were to describe: (1) the hematologic abnormalities found on screening labs obtained as part of an established clinical standard work (CSW) pathway for children <48 months of age presenting to the ED with high-risk bruising (2) the percent who had abnormal screening labs and (3) the percent diagnosed with a hematologic disorder associated with easy bruising.

Design/Method: Clinical and laboratory data were obtained retrospectively from medical records for all patients aged 0 to <48 months who screened positive for high-risk bruising in the Seattle Children's ED between October 2020 and June 2023. Data included patient demographics, medical history, laboratory results, referral to hematology, and diagnosis of a hematologic disorder. All patients presenting to the ED during this period were screened for high-risk bruising. The CSW pathway has been previously published. Only labs that can be resulted during the ED stay are included in the laboratory evaluation, except for von Willebrand factor (VWF) activity, which is included for some patients despite being performed off-site.

Results: 161 children were identified. Seventy percent (113/161) had a complete blood count, 65% (105/161) prothrombin time, 64% (103/161) partial thromboplastin time (PTT), 49% (79/161) VWF antigen, and 16% (26/161) VWF activity. Fifteen percent (24/161) of patients had a significant lab abnormality. The most common abnormality was a prolonged PTT in 12 patients. Of those with a lab abnormality 33% (8/24) were evaluated by a hematologist and 21% (5/24) were diagnosed with a hematologic disorder. Three patients had immune thrombocytopenia, one von Willebrand disease, and one aspirin effect. Three patients had VWF levels below the normal range but were not referred to hematology and had no additional investigation for von Willebrand disease.

Conclusion: It is important to consider an undiagnosed bleeding disorder in young children presenting to the ED with bruising concerning for abuse. Appropriate screening labs and early involvement of a pediatric hematologist for those with an abnormal laboratory evaluation are important to allow for timely diagnosis, intervention, and education.

Poster # 216

HSD3B7-ASSOCIATED BILE ACID SYNTHESIS DEFECT: A RARE CAUSE OF A BLEEDING DIATHESIS IN A CHILD

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Background: Vitamin K is a fat-soluble vitamin crucial to the formation of key factors in the coagulation cascade. Outside the neonatal population, vitamin K deficiencies are either related to medication use or gastrointestinal malabsorption syndromes. Here, we describe a case of vitamin K-dependent coagulopathy secondary to HSD3B7 gene mutations causing a rare bile acid synthesis defect.

Objectives: To highlight a unique cause of vitamin K-dependent coagulopathy caused by HSD3B7 deficiency.

Design/Method: Case Report

Results: A 10-year-old male was referred to the Pediatric Hematology for evaluation of chronic epistaxis

and easy bruising with a prolonged PTT of 48 and INR of 2.5. An extended bleeding workup revealed a normal complete blood count, von Willebrand studies and fibrinogen. Factor levels were suggestive of a vitamin K deficiency: factor II 0.30U/mL (low), factor VII 0.20U/mL (low), factor IX 0.23U/mL (low), and factor X 0.11U/mL (low). A 2-week trial of vitamin K 5mg PO daily resulted in a normalized PTT of 38 and INR of 1.2. However, after cessation of supplementation for 2 months, his INR/PTT once again became prolonged (3.6 and 50s respectively) suggestive of a chronic malabsorptive process despite his lack of gastrointestinal symptoms.

Additional work-up showed elevated liver enzymes including ALP 489U/L, ALT 68U/L, AST 50U/L, GGT 50U/L, and total bilirubin of 21umol/L as well as deficiencies in vitamin A (1.0umol/L), D (25umol/L) and E (<3umol/L). He was referred to Pediatric Gastroenterology who arranged genetic testing which yielded a homozygous mutation in the HSD3B7 gene with a pathogenic sequence variant in c.439G>A, p. Glu147Lys. The variant results in a defect in the 3β-hydroxy-Δ5-C27-steroid dehydrogenase enzyme leading to a congenital bile acid synthesis defect, causing decreased absorption of fat-soluble vitamins. In addition to vitamin K supplementation, cholic acid replacement has been initiated to improve liver biochemistry and prevent progression to cirrhosis.

Conclusion: Bile acid synthesis disorders caused by a HSD3B7-induced 3β-hydroxy-Δ5-C27-steroid dehydrogenase defects are a rare clinical entity with fewer than 100 cases reported in the literature. The majority of patients present under the age of 5 with the most common symptoms being cholestasis and hepatosplenomegaly. This case is unique in that the patient presented at an older age with the primary symptom being a vitamin K-dependent bleeding diathesis. He was treated successfully with vitamin K supplementation with the hope of eliminating the need for supplementation with his ongoing cholic acid replacement.

Poster # 217

EARLY CHOLESTASIS AND VITAMIN K DEFICIENCY PRESENTING AS COAGULOPATHY AND THYMIC HEMORRHAGE

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Background: Bleeding and progressive coagulopathy are established symptoms of early cholestasis, including extrahepatic biliary atresia. We present a patient with bleeding secondary to vitamin K deficiency and cholestasis-induced fat malabsorption with unusual presentation of mediastinal mass.

Objectives: Describe a case of late-onset vitamin K deficiency and cholestasis presenting as jaundice and coagulopathy with associated bleeding into thymic structures

Design/Method: Case report

Results: A 4-week-old term male infant was brought to the ED with fussiness and bruising. Prior to presentation, he was afebrile and followed regularly with his primary care provider for jaundice below phototherapy thresholds. Infant received vitamin K at birth.

In the ED, infant was tachypneic with retractions and grunting. Physical examination was notable for

diffuse jaundice and two 1 cm bruises along shoulder and midline thoracic spine. No hepatosplenomegaly was noted. Chest x-ray was significant for mildly widened mediastinum.

Labs demonstrated elevated WBC 19.68 x10(3)/mcL, Hgb 10.8 gm/dL, Platelet count 287 x10(3)/mcL. LFT notable for mixed direct/indirect hyperbilirubinemia with total bilirubin 11.1 mg/dL, direct bilirubin 5.6 mg/dL, indirect bilirubin 5.5 mg/dL. DAT was negative. Coagulation studies were significantly abnormal, with PT >125 sec and aPTT >250 sec; INR was unable to be completed. Fibrinogen was 406 mg/dL. A repeat set of coagulation studies were similarly abnormal.

Infant received 2 mg vitamin K for three days, 50 IU/kg KCentra, and 15 mg/kg fresh frozen plasma. Factors VII and IX were low, factor VIII was high, and factor V was normal consistent with late-onset vitamin K deficiency bleeding. Coagulation studies normalized after these interventions. An echocardiogram and computed tomography scan of the chest were obtained due to respiratory distress identifying an anterior mediastinal mass bifurcating the thymus. Due to concern for solid appearance of the mass, a biopsy was completed demonstrating only normal thymic tissue, suggestive of bleeding into his thymic structures as cause of mass.

He was able to be discharged with ongoing stability in coagulation labs but with ongoing fat malabsorption and persistent cholestasis. He followed closely with hepatology outpatient and was ultimately diagnosed with biliary atresia with Kasai procedure completed at 8 weeks of age.

Conclusion: Bleeding associated with Vitamin K deficiency and cholestasis may present variably in neonates, including intracranial bleeding, bruising, and coagulopathy; in this case, our patient presented with thymic bleeding and mediastinal mass. Vitamin K deficiency is correctable in the acute setting, however, early identification and further evaluation is indicated to address underlying causes of cholestasis.

Poster # 218

A CASE REPORT OF A PEDIATRIC PATIENT WITH CATASTROPHIC ANTIPHOSPHOLIPID ANTIBODY SYNDROME

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Background: Antiphospholipid syndrome (APS) is a multisystemic autoimmune disorder that involves the presence of persistent antiphospholipid antibodies in the setting of arterial, venous or microvascular thrombosis. Catastrophic APS (CAPS) is the most severe form and involves acute multiorgan failure with predominant microthrombosis. CAPS mortality rate is high (37%) despite optimal therapy

Objectives: To describe a rare case of a fatal presentation of CAPS in a child.

Design/Method: A single subject case report.

Results: On 1/10/23, a 3yo boy with pulmonary embolism (PE) was transferred to our hospital. Current Illness started 12/24/22 with “flu-like symptoms” treated with Tamiflu. On 1/6/23 he required admission to outside hospital (OSH) for hypoxia and fever. He had a negative Respiratory Viral Panel and

COVID-19 PCR, but positive COVID-19 IgG/IgM serology. On 1/10/23, a Chest computed tomography angiogram (CTA) and echocardiogram (ECHO) showed pulmonary embolism (PE) so he was transferred to our PICU. CTA showed left pulmonary artery (PA) occlusive thrombosis, thrombi on right PA and left pulmonary infarct. Doppler showed left lower extremity (LLE) deep venous thrombosis (DVT). Labs showed: negative COVID-19 PCR, negative SARS-Cov-2 IgG and IgM, normal creatinine, high GGT and CRP, thrombocytopenia, low fibrinogen and positive lupus anticoagulant (diluted Russel Viper Venom Test), negative anticardiolipin and anti-Beta-2 Glycoprotein antibodies. Inherited thrombophilia workup was negative. tPA catheter directed thrombolysis/thrombectomy of left PA was done (1/11-1/13) followed by anticoagulation. He was extubated, weaned to room air, yet, a new left upper extremity (LUE) DVT into superior vena cava (SVC) (1/13) and a new right lower extremity (RLE) DVT into inferior vena cava (IVC) were found (1/17). On 1/30, he had further extension of RLE DVT. Hypofibrinogenemia, thrombocytopenia and elevated D dimers persisted. Anticoagulants used: Bivalirudin, Argatroban, Lovenox, Lovenox plus Rivaroxaban (1/30). Immunomodulation: IVIG, Steroids, Rituximab. On 2/3/23, patient was walking and arrested. CTA of head/neck/chest/abdomen showed cerebral sinus vein thrombosis, thrombosis of left internal jugular vein, bilateral PAs, SVC, IVC and left pulmonary vein into left atrium. Patient expired shortly after.

Conclusion: CAPS in children is rare and timely recognition is difficult. The events of this syndrome are described as a “thrombotic storm” where patients present with severe thrombotic events that affect multiple vascular and organ structures, all of which were present in our patient shortly after an apparent viral infection. This case highlights that despite aggressive anticoagulation and immunosuppressive management, a fatal outcome can happen. Further research of CAPS is warranted specially in the pediatric population.

Poster # 219

BLEEDING FROM A TONGUE TIE IN A NEONATE AS A RARE PRESENTATION OF VITAMIN K DEFECIENCY BLEEDING

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Background: Vitamin K defeciency bleeding (VKDB)) in neonates can present as cutaneous, gastrointestinal and intracranial bleeding. Classic VKDB can be seen in neonates not receiving vitamin K supplementation at birth, and late-onset VKDB due to deficiency in breast milk. As neonates are deficient in Vitamin K, and due to the potential for post-frenotomy bleeding, vitamin K administration is essential at birth and prior to frenotomy. Vitamin K dependent procoagulant factors increase within 30 minutes-2 hours after parenteral administration. Spontaneous bleeding from a tongue tie has never been reported. We report a case of a neonate who experienced spontaneous and post-frenotomy bleeding from a tongue tie likely due to vitamin K defeciency as vitamin K injection was not given with home delivery, further accentuated by exclusive breast milk intake.

Objectives: The principal aim of this study is to report an uncommon presentation of Vitamin K Deficiency Bleeding (VKDB) in neonates, thereby enhancing awareness among healthcare providers regarding this particular manifestation. Secondary objectives are to further highligh the crucial significance of vitamin K prophylaxis in all neonates and also to provide some practical insights into the management of post-frenotomy bleeding.

Design/Method: Case report of a neonate who experienced VKDB secondary to a previously unreported cause of spontaneous tear and frenotomy of tongue tie.

Results: A 2-week-old, full term, exclusively breastfed male neonate delivered at home by a midwife without receiving vitamin K injection, developed bleeding from a spontaneously ruptured tongue tie on day 12 of life that continued for one day. The tongue tie was clipped the next day at home by the midwife. One hour later, profuse bleeding started, not stopping with pressure. Following day neonate was taken to the ED, afrin and tranexamic acid were locally applied with prompt hemostasis, vitamin K injection given and admitted for observation. Labs done 6 hours after vitamin K injection showed: hemoglobin 13g/dl, platelets 438,000/ml, PTT 33.9 seconds, and INR 1.15. Head ultrasound was negative. The patient was discharged home with no further bleeding.

Conclusion: Our case adds to the spectrum of presentation of VKDB in neonates, with spontaneous and post-frenotomy bleeding from a tongue tie. Physicians/mid-wives need to be aware of VKDB in neonates with spontaneous/post-frenotomy tongue tie bleeding and ensure vitamin K supplementation at birth and prior to the procedure. Our case report further highlights the importance of vitamin K prophylaxis in all neonates.

Poster # 220

CASE REPORT: A PEDIATRIC PATIENT WITH RECURRENT MECHANICAL VALVE THROMBOSIS TRANSITIONED TO APIXABAN

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Background: Neonatal Marfan Syndrome (NMS) is an autosomal dominant disorder characterized by congenital dysmorphisms and congestive heart failure. Treatment for early onset cardiac disease often requires surgical interventions. In patients with mechanical valve replacement, warfarin is the mainstay of thromboprophylaxis given the breadth of supporting literature. Newer anticoagulation agents have been explored as potential alternatives, but recent adult trials using direct oral anticoagulants have been halted early due to adverse outcomes.

Objectives: We present a case of challenging anticoagulation management in a female toddler with NMS and congenital heart disease palliated with a St. Jude prosthetic mitral valve. We utilized an atypical anticoagulation approach with apixaban to address ischemic strokes and recurrent valve thrombosis.

Design/Method: This publication is a case report for a pediatric patient. Data was obtained through chart review and history obtained from the family.

Results: We present a pediatric patient with NMS, who presented with early onset heart failure and pulmonary hypertension requiring St. Jude mechanical mitral valve replacement at 3 months of age. Following valve replacement, the patient was bridged from bivalirudin (due to heparin failure) to warfarin (goal INR 2.5-3.5). After being therapeutic on warfarin (3 days off bivalirudin), the patient developed an acute ischemic stroke. Three days later, an additional ischemic stroke was identified while therapeutic on bivalirudin (off warfarin), thus aspirin was added. Once stabilized, she was bridged to

warfarin again (same goal INR 2.5-3.5), with continuation of aspirin. Two months later, she was readmitted to an outside institution with mitral valve thrombosis requiring mechanical valve replacement. She was again bridged to warfarin (adjusted INR goal 3.0-3.5), with continuation of aspirin. Twelve months later, she was readmitted to our hospital with second-degree heart block and recurrent mechanical valve thrombosis despite having goal INR. She underwent systemic thrombolysis with tissue plasminogen activator, followed by complete thrombus resolution. After multidisciplinary discussion, she transitioned from warfarin to apixaban for anticoagulation with dual antiplatelet therapy (clopidogrel and aspirin). To ensure appropriate anticoagulation, we used an anti-Xa chromogenic assay calibrated to apixaban for drug effect monitoring, with a goal range of 200-300 ng/mL. During the transition, warfarin was continued (goal INR of 3-4) until the goal anti-Xa level was obtained.

Conclusion: We present a case with unique challenges in thrombosis, most notably a failure of traditional anticoagulation practice standards, and an atypical approach using apixaban.

Poster # 221

REFRACTORY CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME SUCCESSFULLY TREATED WITH MULTIMODAL THERAPY

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Background: Seven-year-old female with recent diagnosis of community acquired pneumonia required hospitalization at our hospital for respiratory failure. Her clinical course was remarkable for microangiopathic hemolytic anemia, acute renal failure requiring dialysis, and development of encephalopathy. She was noted to have a positive lupus anticoagulant and bilateral cephalic vein thrombosis meeting the international consensus classification criteria for probable catastrophic antiphospholipid syndrome (CAPS). She was also found to have significantly elevated soluble terminal complement complex (SC5b-9) [1391 ng/mL, normal <244 ng/mL]. Thrombotic microangiopathy genetic susceptibility panel revealed homozygous deletion of CFHR3-CFHR1. Treatment was initiated with plasma exchange, high dose steroids, and therapeutic anticoagulation; due to clinical concerns for refractory CAPS, rituximab and eculizumab were then added which led to rapid clinical improvement, organ recovery, and normalization of SC5b-9. At the time of this report, patient continues to do well clinically on long-term therapeutic anticoagulation.

Objectives: The goal of this case report is to highlight the successful use of multimodal therapy including eculizumab for treatment of refractory catastrophic antiphospholipid syndrome.

Design/Method: This is a case report developed from patient's chart review.

Results: Catastrophic antiphospholipid syndrome (CAPS) is a severe form of antiphospholipid syndrome (APS) with high mortality characterized by multiorgan failure and widespread thrombosis in the setting of a positive antiphospholipid antibody testing. There is evidence that patients with CAPS have persistent terminal complement activation and a higher prevalence of rare germline variants in complement regulatory genes. A pathogenic mutation in complement regulation in combination with complement activation by antiphospholipid antibodies may predisposed patients to developing CAPS in the setting of a trigger, such as an infection in our patient. Our patient showed evidence of rapid and

sustained clinical response to intensive combination therapy that included eculizumab.

Conclusion: Pathogenic mutations in the complement regulatory genes and activation of complement by antiphospholipid antibodies portends an increased risk for catastrophic antiphospholipid syndrome. Multimodal therapy with early consideration of eculizumab in patients with terminal complement activation may decrease morbidity and risk of mortality.

Poster # 222

NONTRAUMATIC HEMORRHAGIC "BRAIN TUMOR" IN TWO PEDIATRIC PATIENTS WITH MILD/MODERATE HEMOPHILIA A

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Background: Mild/moderate hemophilia A is characterized by factor VIII deficiency (factor VIII levels 1-40%) and presents with bleeding precipitated by trauma or surgery. Nontraumatic intracranial hemorrhage (ICH) with factor VIII level >5% is extremely rare. Here we present two patients with nontraumatic ICH who presented as having pseudotumors, eventually found to have mild/moderate hemophilia A.

Objectives: To describe the presentation, hospital course, and management of two unrelated pediatric patients with mild hemophilia whose sole presentation was an intracranial pseudotumor.

Design/Method: Case series

Results: A 10-month-old male patient presented to the hospital with a one-month history of a progressively enlarging tender 4x4 cm mass on the back of his head, not preceded by trauma and with no associated symptoms. His vital signs were normal and his neurologic exam was nonfocal. Brain MRI revealed a hemorrhagic mass in the left posterior fossa involving the left occipital calvarium suggestive of a brain tumor. Given the ICH he had coagulation studies drawn which showed a prolonged activated partial thromboplastin time (aPTT) of 53.8 seconds, with a normal prothrombin time (PT). His factor VIII assay was 4.2% activity, consistent with mild/moderate hemophilia A. He was treated successfully with recombinant factor VIII, and his brain mass completely resolved within 4 weeks. He was started on prophylaxis with factor VIII and continues on a nonfactor product for prophylaxis.

A 1-day-old male patient of 34 weeks gestation, born via nontraumatic vaginal delivery, was admitted to the NICU for prenatal imaging demonstrating a “brain tumor” of the left cerebral hemisphere causing hydrocephalus. Brain imaging demonstrated a large lobulated hemorrhagic mass in the posterior fossa, dilation of bilateral ventricles, and evolving intraventricular hemorrhage. He developed pulmonary hemorrhage and was noted to have prolonged bleeding at heel stick sites. His aPTT was 104.3 seconds. His factor VIII level was 18.6%, consistent with mild hemophilia A. He was started on daily factor VIII replacement with complete resolution of the brain mass and continues on a nonfactor product for prophylaxis.
Both patients’ siblings were found to have asymptomatic mild hemophilia.

Conclusion: These patients with mild/moderate hemophilia A presented with hemorrhagic intracranial masses mimicking a brain tumor, a very rare clinical presentation without the presence of predisposing bleeding factors such as birth trauma or congenital anomalies. These cases highlight the need to evaluate for inherited bleeding disorders in the presence of hemorrhagic brain lesions.

Poster # 223

OBLIGATE CARRIERS AND MONOZYGOTIC TWIN FEMALES DISCORDANT FOR HEMOPHILIA A WITH VARIABLE PHENOTYPE

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Background: Hemophilia A is a bleeding disorder with X-linked recessive inheritance, which predominantly affects males. Females born to affected males are obligate carriers. The varying disease severity in females is predominantly due to skewed lyonization. Variable presentation or phenotype of Hemophilia A in twins has clinical and genetic significance; two previous reports with Hemophilia A depicted twins born to a normal father/carrier mother and one with de novo mutation and no family history.

Objectives: To report a novel case of obligate carriers and monozygotic twin females discordant for hemophilia A with resultant varying presentation

Design/Method: Case report, retrospective electronic medical record review

Results: A 10-month-old male with severe Hemophilia A, presented with a history of prolonged bleeding from tongue injury, multiple bruises on legs/trunk, and past history of right knee swelling. Exam findings includedhematomas in the abdominal wall, left shin, and multiple ecchymoses on both legs. Laboratory evaluation showed hemoglobin of 11.7g/dL, platelets of 412K/mL, normal prothrombin time, partial thromboplastin time prolonged at 113 seconds and Factor VIII (FVIII) level <1%. Family history revealed severe hemophilia A in deceased maternal grandfather and maternal aunt who is the mother's identical twin. The maternal aunt had FVIII level of <1% and a FVIII mutation, a mis-sense variant c.5822A>T (p.Asn1941Ile) on exon 18. Interestingly, patient's mother never experienced bleeding symptoms, and had FVIII level of 180%. Our patient was diagnosed with severe Hemophilia A, inherited from his mother, an obligate asymptomatic carrier. Interestingly mother's twin sister has severe Hemophilia A, also an obligate carrier.

Conclusion: Our case adds to the spectrum of presentation of Hemophilia A in twins. To our knowledge, this is the first report in Hemophilia A of monozygotic twins who are obligate carriers, with discordant presentation, one with a normal FVIII level and the other with severe Hemophilia A. Our case also emphasizes the importance of knowing that daughters of a male with Hemophilia A are obligate carriers. There is hence and a need for factor level evaluation and genetic counseling for both twins, as the twin females can be affected and regardless of their severity, and both can give birth to affected children. This is illustrated in our report, one twin female with severe Hemophilia A and another, an asymptomatic carrier with an affected son. The varying presentations in the twins is explained by skewed lyonization described in Hemophilia.

Poster # 224

DIAGNOSING CONGENITAL SEVERE FACTOR 7 DEFICIENCY: A PREVIOUSLY UNREPORTED VARIANT IN THE F7 GENE

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Background: Factor 7 deficiency is a rare bleeding disorder with a wide range of bleeding phenotypes among affected individuals. Congenital severe Factor 7 Deficiency diagnosed in infancy, however, is associated with significant clinical bleeding such as intracranial hemorrhage and life-threatening gastrointestinal bleeding. Limited data is available regarding genetic variants in the F7 gene given the rarity of this diagnosis.

Objectives: To report a previously unreported pathogenic frameshift variant defined as c.1027_1039del in a neonate with congenital severe factor 7 deficiency and severe intracranial hemorrhage.

Design/Method: A retrospective case report of a neonate diagnosed with congenital severe Factor 7 deficiency and treated at Texas Children's Hospital in 2023.

Results: Our case describes a patient who presented at 11 days of life with severe intracranial hemorrhage including bilateral subdural hematomas. Initially thought to have suffered from nonaccidental trauma due to a delivery-induced femoral fracture, screening coagulation studies revealed a PT of 37.6 seconds and a factor 7 level of less than 1%. Genetic testing of the F7 gene was done in order to support the running diagnosis of congenital severe factor 7 deficiency. Our patient was identified to have a homozygous, likely pathogenic variant in F7 (c.1027_1039del, p.Gly343Cysfs*19). This genetic mutation is a frameshift variant that results in premature protein termination. This variant has not been reported in ClinVar or gnomAD to date. Our patient was initially treated with frequent factor 7 replacement therapy with significant clinical improvement. This patient continues on daily factor 7 replacement therapy as prophylaxis and has not had recurrent significant bleeding events.

Conclusion: Our case highlights the importance of genetic testing in cases of Factor 7 Deficiency not only to identify novel causative variants but for the family's future family planning and identification of at-risk relatives. Genetic testing in this patient population may also help classify long-term bleeding risks and inform therapeutic clinical decision-making.

Poster # 225

HORMONE REPLACEMENT THERAPY IN A PATIENT WITH ANDROGEN INSENSITIVITY AND FACTOR V LEIDEN

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Background: Factor V Leiden (FVL) is an autosomal dominant genetic condition characterized by an insensitivity to the physiologic anticoagulant, Protein C. Persons with FVL mutations are at increased risk of venous thromboembolism (VTE). Overall incidence of spontaneous VTE in asymptomatic carriers, however, is low and prophylactic anticoagulation is not routinely recommended. In patients with FVL mutation and additional risk factors, prophylactic anticoagulation may be considered. In this report, we describe a case of a patient with heterozygous FVL mutation and complete androgen insensitivity syndrome (CAIS) requiring estrogen hormone replacement therapy (HRT) for pubertal progression and osteoporosis prevention.

Objectives: Describe HRT management in patients with inherited thrombophilia.

Design/Method: Retrospective chart review was performed for diagnostic and therapeutic information of patient with CAIS and FVL.

Results: A 15-year-old girl with asymptomatic, heterozygous FVL mutation presented to Endocrinology with delayed menarche. Physical exam was notable for Tanner stage III pubic hair and breast development. Six months later, labs were obtained and notable for elevated testosterone. Subsequent MRI of the abdomen and pelvis showed testes in inguinal canal and no identifiable uterus. Genetic testing revealed 46 XY karyotype and pathogenic AR gene variant confirming diagnosis of CAIS. As per recommendations for CAIS management, patient underwent gonadectomy with plan to start HRT thereafter. Hematology was consulted for HRT recommendations given heterozygous FVL mutation. On review of literature, oral estrogen therapy has been associated with significant thrombosis risk in patients with heterozygous FVL mutations. Transdermal estrogen replacement, however, has not been shown to have same risk. In discussion with patient and family, taking into account negative family history of thrombosis and patient quality of life concerns, decision was made to proceed with low dose (12.5 mcg) estradiol transdermal patch without prophylactic anticoagulation.

Conclusion: HRT is necessary after gonadectomy to prevent symptoms of hypoestrogenism and maintain secondary sexual features in CAIS. In patients with heterozygous FVL mutations requiring HRT, compounding VTE risk is of concern. Most data regarding management comes from older populations (i.e. postmenopausal women) who have different risk factors than our adolescent patients. Based on available literature, the transdermal estrogen patch may have less thrombotic risk than estrogen containing pills allowing use without prophylactic anticoagulation.
The psychosocial benefit of providing gender-affirming care can't go unnoted. The use and type of HRT and use of anticoagulation in patients with inherited thrombophilia should be discussed, including risks and benefits, with families and individualized to patient needs.

Poster # 226

PORTAL VEIN THROMBOSIS PRESENTING WITH MILD THROMBOCYTOPENIA: AN UNUSUAL PRESENTATION

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Background: Portal vein thrombosis (PVT) is the most common cause of extrahepatic portal vein obstruction in children with a reported incidence of 1 in 100,000 live births and in 36 of 1000 NICU

admissions. Major risk factors for PVT include UVC, sepsis, and thrombophilia. It can result in portal hypertension leading to varices and splenomegaly, which can result in cytopenias from sequestration.

Objectives: The objective of this case report is to raise awareness on this rare presentation of PVT .

Design/Method: Case report

Results: A 13-year old male, seen by our hematology service for mild thrombocytopenia (78000 to 150,000/cu.mm), intermittent mild leukopenia (3800 to 4200/cu.mm), with normal hemoglobin (12 to 13.5 g/dl). Normal CMP, including AST/ALT of 10-15/20-25 U/L, serum albumin 4.5 g/dL, with mild indirect hyperbilirubinemia (positive Gilbert's testing). Evaluation for thrombocytopenia: bone marrow aspirate/biopsy with mild hypocellularity, normal cytogenetics, negative MDS panel and PNH testing. BMF panel showed 2 variants of uncertain significance (DOCK8 and TAOK20), normal coagulation studies except mildly elevated PT (16.4 with INR 1.3), and normal vWD studies (no evidence of type IIB vWD). Almost a year after initial presentation, he presented acutely with an episode of hematemesis and syncope, admitted to our hospital with GI consulted. Labs on presentation were remarkable for significant drop in Hb (8.8 g/dL from 13.5g/dL) and thrombocytopenia (98000/cu.mm down from 102,000/cu.mm) and elevated PT/INR (18.3/1.4) with normal aPTT. Further coagulation factor analysis was remarkable for low factor VII (41%), borderline low factor X (45%), and low protein S (38%), rest of the factors including factors II, VIII, IX, vWD antigen assay, fibrinogen were within normal range. Thrombophilia work-up was negative for factor V Leiden mutation, and Prothrombin gene (20210) mutation He did not have any hepatosplenomegaly on examination, however, ultrasound of abdomen showed cavernous transformation of portal vein with splenomegaly and diffusely increased echotexture of liver. CT abdomen confirmed the diagnosis and demonstrated esophageal and splenorenal varices. EGD also showed the evidence of esophageal varices and portal hypertensive gastropathy. Liver biopsy showed hepatocyte plate atrophy with some regenerative changes consistent with sequelae of cavernous transformation, with no evidence of liver cirrhosis or fibrosis or primary parenchymal liver disease. The thrombocytopenia was deemed secondary to consumption in setting of chronic portal hypertension and splenomegaly. He underwent band ligation of largest varix and remains on PPI therapy.

Conclusion: PVT must be considered among the differentials of etiology of thrombocytopenia in absence of any definitive identifiable etiology.

Poster # 227

GINGIVAL HEMATOMA AFTER MINOR ORAL TRAUMA AS FIRST PRESENTATION OF HEMOPHILIA A

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Background: Mild hemophilia A is associated with a wide variation of factor VIII clotting activity from 5-40%. Individuals with mild hemophilia A can go many years without having a major bleeding event requiring evaluation by a health care provider. Manifestations of mild hemophilia A often occur in the setting of acute trauma or surgical intervention. For pediatric patients, oral instrumentation during routine dental procedures or exams are the first challenge that can led to a prolonged bleeding episode. These individuals may lack a personal or family history suspicious for a bleeding diathesis.

Objectives: It is important to recognize that dental providers may be the first practitioners to raise suspicion for a bleeding disorder after a sentinel event.

Design/Method: Here we discuss a case of a 3-year-old male with no past medical history presenting with a rapidly enlarging left maxillary gingival mass. He presented to his primary dentist and had x-rays done which revealed no damage to the roots of his teeth or the underlying permanent teeth. The mass continued to enlarge and then began to manifest with a slow oozing bleed that did not resolve after gauze packing at home. He then presented to an ED where bimanual pressure for >15 minutes, application of crushed TXA on gauze nor application of Surgicel could stop the bleeding. Parents denied a personal history of frequent epistaxis, gingival bleeding, easy bleeding or bruising, or prolonged bleeding when his umbilical stump fell off. He is not circumcised and has never had any surgeries or major dental procedures. He had no known family history of hemophilia, bleeding or transfusion requirement.

Results: Serum labs revealed PTT of 60.4 seconds that corrected to 37.8 seconds after 1:1 mix with control plasma. Factor IX activity (87%), Factor XI activity (120%), von Willebrand Factor Antigen and Ristocetin Cofactor activity were all within normal limits. Factor VIII activity level was found to be 4% consistent with a diagnosis of hemophilia A. He received two doses of Advate 50U/kg and was initiated on oral Amicar for clot stabilization. He subsequently underwent hematoma evacuation and suturing with the dentistry and bleeding manifestations resolved.

Conclusion: At our center, we provide didactics to dentistry colleagues to increase awareness of the substantial role they play in diagnosing mild to moderate bleeding disorders and ensuring appropriate hematologic referral.

Poster # 228

BIVALIRUDIN IN A PATIENT WITH ACUTE NEPHROTIC SYNDROME RELAPSE AND MASSIVE PULMONARY EMBOLISM

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Background: Thromboembolism (TE) is a serious complication of nephrotic syndrome (NS) and may be associated with urinary antithrombin III (ATIII) loss. To treat venous TE in patients with NS, heparin or low molecular weight heparin is often initiated, but this sometimes requires higher doses and takes more time to achieve therapeutic effect due to acquired ATIII deficiency. Bivalirudin is a direct thrombin inhibitor, doesn't bind albumin, and isn't dependent on ATIII. There is limited data regarding anticoagulation (AC) with bivalirudin in pediatric patients with NS.

Objectives: To describe a successful case of bivalirudin anticoagulation in an adolescent patient with acute and severe nephrotic syndrome relapse and massive pulmonary embolism (PE).

Design/Method: Case report.

Results: A 17-year-old obese female with minimal change disease, steroid-dependent NS, and history of

multiple NS relapses, presented with severe NS relapse and acute hypoxemic respiratory failure and was found to have massive saddle and bilateral PE. Enoxaparin was initially given, and she underwent catheter-directed thrombolysis with tPA at 1 mg/hr divided to both pulmonary arteries for 12 hours. Due to worsening respiratory status, frequent need for ATIII replacement from acquired ATIII deficiency (ATIII 30-40% normal), subtherapeutic anti-factor Xa levels, and normal creatinine clearance, AC was switched to bivalirudin with an initial dose of 0.3 mg/kg/h using total body weight. Intravascular suction thrombectomy was attempted, but there was poor clot retrieval due to large organized clot burden. Bivalirudin was titrated using goal activated partial thromboplastin time (aPTT) of 60-80 seconds. Despite 2 bivalirudin boluses (0.4 mg/kg/dose) and increasing the dose to 0.6 mg/kg/h, the aPTT remained at around 50 seconds. Due to concern for aPTT plateau effect, which has been observed with higher bivalirudin concentrations, thromboelastogram (TEG)-R times and international normalized ratio (INR) were concomitantly followed and remained prolonged between 11-13 minutes and 2.0-2.6, respectively. Bivalirudin was continued at 0.6 mg/kg/h. The patient showed significant clinical improvement. After 72 hours, bivalirudin was bridged to warfarin. Since discharge, she has done well with complete resolution of PE at 3 months, at which point warfarin was transitioned to apixaban due to ongoing NS relapses and risk of recurrent TE. She has not had any complications on anticoagulation, with about 1 year of follow-up.

Conclusion: Bivalirudin can be successfully used for therapeutic anticoagulation in pediatric patients with NS relapse and massive PE. This case also highlights the importance of recognizing the possibility of aPTT plateau effect at higher bivalirudin concentrations.

Vascular Anomalies (301-320)

Poster # 301

ANTICOAGULATION EFFECTS ON QUALITY OF LIFE IN PATIENTS WITH SLOW-FLOW VASCULAR MALFORMATIONS

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Background: Pain from slow-flow vascular malformations (SFVM) is common and may due to slow-flow, swelling, and localized intravascular coagulopathy (LIC) with frequent impact on quality of life (QOL).

Objectives: The objective of this study was to determine if anticoagulation in SFVM would improve QOL, decrease pain and/or improve laboratory markers of LIC.

Design/Method: This multi-institutional prospective nonrandomized observational study included subjects with SFVM and prescribed anticoagulation by their treating physician. Subjects were excluded if anticoagulation was initiated only for peri-procedural interventions or if they were on sirolimus for less than 3 months.

Patient assessments (Peds QL survey, demographic and laboratory data) occurred at study entry, 2 weeks and 4 weeks after starting anticoagulation. Data were assessed for normality and equal variances. Non-normal distributions were log-transformed and then evaluated with repeated measures ANOVA.

When the overall F-test was significant (p<.05), contrasts between entry and 2 weeks and 4 weeks were compared.

Results: Data were available on 35 patients with SFVM. Median age was 20 (range 7-59) years. Patients were predominately female (65.7%) and Caucasian (65.7%). All were started on a direct oral anticoagulant - rivaroxaban (n=33) or apixaban (n=2). Six (17%) patients were stable on sirolimus prior to starting anticoagulation. Four patients were stable on aspirin (81mg to 325mg daily). Seventeen patients utilized compression garments, with the majority less than 50% of the time. Twelve patients experienced minor adverse bleeding events, including heavy menstrual bleeding, rectal bleeding, bruising and epistaxis. 1 patient experienced major bleeding with hematuria requiring cessation of anticoagulation.

D-dimer and pain scores had a statistically significant decrease from 1.2 mg/L FEU to 0.4 mg/L FEU and 4.0 to 2.0 by 2 weeks, respectively. QOL increased significantly from 71 to 75 by 2 weeks.

Conclusion: Patients with SFVM and pain benefit from short-term anticoagulation which is supported by improved QOL, decreased pain and improvement of coagulation parameters. This improvement will need to be carefully balanced with bleeding risks.

Poster # 302

HHT VARIANT RECLASSIFICATION AND IDENTIFICATION OF NOVEL VARIANTS: A SINGLE INSTITUTION REVIEW

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Background: Hereditary Hemorrhagic Telangiectasia (HHT) is a disorder affecting blood vessel development, characterized by excessive bleeding. It is usually inherited with mutations in the ENG, ACVRL1, or SMAD4 genes. The American College of Medical Genetics(ACMG) periodically publishes guidelines to standardize variant classification, with the latest being published in 2015.

Objectives: This study aimed to reclassify variants diagnosed in the Genetic Diagnostic Laboratory(GDL) at UPenn before 2015. The objective was to observe the percentage of variants that were recategorized, and to look for novel variants.

Design/Method: This single institution retrospective study gathered data on patients with HHT diagnosed from 2003-2015, and 7 patients post-2015. Of the 359 patients included, 166 had variants in ENG, 187 in ACVRL1, and 6 in the SMAD4 gene. Variant files were uploaded to QCI, Qiagen's variant calling software which aggregates extensive patient and disease-specific data. Then GDL's internal data was reviewed for each variant, and specific criteria were assigned per ACMG's guidelines. Next, ARUP lab's HHT database and ClinVar were examined for known clinical significance. Each variant was then manually assigned a new classification. For novel variants, UniProt, a resource for protein sequence and annotation data, identified subcellular structures affected by these variants to elucidate any structural patterns. GDL's patient database was then analyzed for familial segregation of novel variants, to better understand pathogenicity. Each novel variant was then mapped based on genetic coordinates to explore

correlation between mutation location and its clinical significance.

Results: Of the 166 ENG patient variants, 44 are now classified as Pathogenic(P), 38 Likely Pathogenic(LP), 77 Variant of Unknown Significance(VUS), 6 Likely Benign(LB), and 1 Benign(B). For our 187 ACVRL1 patient variants, 29 are now classified as P, 72 LP, 79 VUS, and 7 LB. 8% of ENG and 18.51% of ACVRL1 variants were upgraded from benign to LP or P. For ENG, 75% of ENG and 69.76% of ACVRL1 variants were downgraded from suspected pathogenicity to VUS, LB, or B.
We found 88 "novel variants", defined as variants found by GDL and not reported in the ARUP database. Of these, 58 were located in ENG, and 30 in ACVRL1. A majority (51/58) of ENG variants were in the extracellular space, whereas 22/30 of ACVRL1 variants were in the cytoplasmic region.

Conclusion: Considering the significant changes noted in this study, we propose periodic reevaluation and updates of variant classifications. This helps with accurate clinical decision making, patient counseling, risk assessment, and further research and development.

Poster # 303

REAL-WORLD USE OF ALPELISIB IN 26 VASCULAR ANOMALY PATIENTS TREATED AT A SINGLE INSTITUTION

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Background: The oral PI3K alpelisib has shown promise in the treatment of vascular anomalies. However, there is limited data about the real-world use of alpelisib in vascular anomalies patients in the United States, including patient characteristics, insurance approval of the medication, dosing, adverse events, and clinical outcomes

Objectives: To provide real-world evidence of the utility of alpelisib in 26 vascular anomalies patients

Design/Method: Retrospective chart review of patients who initiated alpelisib between December 2019 and December 2023.

Results: Patient diagnoses included LM (n=18), CLOVES (n=2), FAVA (n=1), MCAP (n=1), VM (n=1), FIL (n=1), LVM (n=1), BRBNS (n=1). Median duration for alpelisib was 15.2 months (range 5.3-48.1). Median dose was 50 mg QD (range 25-200 mg QD). *PIK3CA* mutations were identified in 21 patients (mean VAF% 10.4, range 1-49%). *TEK* mutations were identified in 2 patients (VAF 6% and 8%). Three patients did not have a genetic mutation identified due to lack of available tissue or cyst fluid.

Eleven patients were initially treated with alpelisib via compassionate use prior to US FDA approval in April 2022. All 11 transitioned to commercial supply within 3 months. Of the 26 total patients treated, 15 had initial insurance denial and 11 required a Letter of Medical Necessity. Twenty-three patients responded. Four patients had a marked radiologic response (≥20% decreased lesion volume by MRI). Clinical responses included decrease in: bleeding (n=4), swelling (n=10), size via clinical assessment (n=15), pain (n=7). Fourteen reported improved function. Median time to clinical response 31 days (range 9-120 days). Three patients had stable disease.

Of the 5 patients without a confirmed PIK3CA mutation, 3 patients had clinical response; characterized by improvement in: function (n=3), bleeding (n=1), pain (n=1), swelling (n=1), and size by clinical assessment (n=1). The remaining 2 had stable disease. These patients either did not have radiologic decrease in mass size (n=2) or lacked sufficient imaging to determine(n=3).
Adverse events (AEs) occurred in 22 patients. Grade 1-2 AEs included: diarrhea (n=5), nausea (n=4), anorexia (n=4), alopecia (n=6), brittle nails (n=1), rash (n=3), eczema (n=6), headache (n=2), oral mucositis (n=2), behavioral disturbance (n=3), growth suppression (n=1). Grade 3 AEs included oral mucositis (n=1); oral bleeding (n=1), headache (n=1). O

Conclusion: Alpelisib was well-tolerated and had clinical impact in most patients. Even in patients with confirmed PIK3CA mutations, initial insurance denials for the medication were common. No patients had disease progression, highlighting that this may be an important therapy for vascular anomalies patients in the future.

Poster # 304

CLINICAL IMPACT OF GENETIC TESTING IN VASCULAR ANOMALIES PATIENTS

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Background: Recent discoveries have demonstrated that vascular anomalies arise primarily due to somatic variants in cancer genes. While molecular profiling has become a mainstay of diagnostic testing in cancer, its adoption in the clinical care of patients with vascular anomalies has not been ubiquitous.

Objectives: We evaluated the clinical utility of molecular profiling in vascular anomalies patients at a single institution. We report on diagnostic clarification, identification of clinically actionable variants, and use of targeted therapies. Pre-testing diagnoses were established via expert interdisciplinary review of patient presentation, imaging, and histopathology. Post-testing diagnoses incorporated genetic findings identified via molecular profiling.

Design/Method: This is a retrospective chart review of vascular anomaly patients who had genetic testing performed between 2016-2022.

Results: Variants in *PIK3CA* were identified in 45% (142/315) of all patients. Identification of *PIK3CA* variants supported the pre-testing diagnosis in 82% (116 of 142 *PIK3CA* positive cases), namely in PROS (for example, KTS, MCM, FAVA, CLOVES) or isolated LM. Eighty-six percent of all *PIK3CA* variants identified occurred in one of 5 hotspots (C420R, E542K, E545K, H1047L, H1047R). Both targeted NGS and ddPCR testing identified variants at low variant allele frequencies (average VAF = 6.9%). Four patients with a pre-testing diagnosis of CLOVES had variants in PIK3R1. Several patients had variants in the RAS-MAPK pathway: *MAP2K1* (n=10), *NRAS* (n= 5), *KRAS* (n= 8), *BRAF* (n= 4), *SOS1* (n=4). Variants were also found
in *AKT* (n=1), *ARID1A* (m=6), *GNAQ* (n=3), *GNA11* (n=2), *RASA1* (n=3), *PTEN* (n=6). Targeted NGS led to diagnostic reclassification (n=18) and identification of potential germline cancer predisposition (n=12). Molecular profiling demonstrated actionable variants in 67% (166/ 230 patients). As a result of genetic

testing, 39 patients initiated targeted medical therapy [alpelisib (n=19), miransertib (n=8), trametinib (n=12)].

Conclusion: Our study demonstrates the clinical utility of using a precision medicine approach in patients with vascular anomalies, as this testing provided diagnostic clarity, identified actionable variants, and provided support for the use of targeted therapies.

Poster # 305

PATIENTS WITH ARTERIOVENOUS MALFORMATIONS RESPOND TO MEK INHIBITORS

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Background: The use of targeted medical therapies for AVM is emerging. However, data on safety, efficacy, and optimal duration of treatment of AVMs with targeted agents is not well-established. We report our single-institution experience of AVM patients treated with oral MEK inhibitors.

Objectives: To provide real-world data of the use of MEK inhibitors in patients with AVMs

Design/Method: This is a retrospective chart review of treatment and outcomes for 10 AVM patients treated with MEK inhibitors between 2019-2023.

Results: Ten patients with complex AVMs were evaluated by an interdisciplinary team at our center. Patients presented with pain (n=8), bleeding (n=8), discoloration (n=7), anemia (n=1), epistaxis (n=1), swelling (n=3), headaches (n=1), and bruit/thrill (n=3). All patients had biopsy or resection of affected tissue; histopathology was consistent with AVM. Genetic testing of affected tissue was performed using Oncopanel. Patients had mutations in MAP2K1 (n=3), KRAS (n=1), BRAF (n=2), SOS1 (n=3). A causative mutation was not able to be identified in one patient. AVM locations included: face and neck (n=8), lower extremity (n=2). Trametinib dose ranged from 0.4 mg to 2 mg daily. Average treatment was 16 months (range 3- 42). Five patients had marked clinical response, including improvement in pain (n=6), size (n=5), discoloration (n=4), bleeding (n=4), and headaches (n=1). Dermatologic side effects included acne (n=5) alopecia (n=1), eczema (n=1), paronychia (n=2), seborrheic dermatitis (n=1), scalp dermatitis (n=1), and xerosis (n=2). Other adverse events included diarrhea (n=4), anemia (n=1), AST elevation (n=1), CPK elevation (n=1), LDH elevation (n=1), fatigue (n=2), and creatine kinase elevation (n=1). Three patients eventually discontinued the medication due to lymphatic leakage (n=1), rectal bleeding (n=1) and paronychia (n=1). One patient stopped the medication due to edema.

Conclusion: Trametinib led to clinical improvement in most of our patients. Trametinib is a promising treatment for AVMs, though the side effects were intolerable for some, highlighting the need for further studies and the identification of other potential targeted agents.

Poster # 306

COMPARING DDPCR VS NGS FOR DETECTION OF PIK3CA VARIANTS IN PIK3CA-RELATED OVERGROWTH SPECTRUM (PROS)

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Background: Many technologies are now available to support patients with vascular anomalies to support specific diagnoses and the use of matched targeted therapies. Factors that influence the clinical utility of each technique include breadth of targets, sensitivity and specificity. The low variant allele fraction (VAF) of somatic mosaic alterations in patients with vascular anomalies is particularly challenging. We present a comparison cohort of patients with known or suspected PI3K-related overgrowth who had both targeted next generation sequencing (NGS) and PIK3CA droplet digital PCR (ddPCR).

Objectives: To describe the differences in detection of PIK3CA variants by ddPCR and NGS testing in vascular anomalies patients

Design/Method: Patients with vascular anomalies were either enrolled on a clinical sequencing study or tested clinically from Boston Children's Hospital 2018-2022. A subset of patients with known or suspected PROS were evaluated by ddPCR and/or targeted NGS. Clinically (CLIA) validated assays include a targeted DNA NGS with 447 genes including PIK3CA, and a ddPCR assay targeting five known hotspots in PIK3CA (C420R, E542K, E545K, H1047L, H1047L).

Results: One hundred and four patients were evaluated with ddPCR. Of these, 83 (79%) passed ddPCR quality metrics. Of those that passed, 83 (80%) had a positive result with VAFs as low as 1.15%, with 20 (19%) having a negative result. Sixty patients were evaluated by both NGS and ddPCR. Of these, 54 (90%) passed NGS metrics while 52 (87%) passed ddPCR metrics. Thirty-seven cases (62%) were concordant between NGS and ddPCR, with 29 negative concordant cases and 8 positive concordant. Eighteen cases (30%) were discordant, with 12 cases having a PIK3CA variant identified by ddPCR and 6 cases having a PIK3CA variant identified only by NGS. Another 5 cases failed both assays.

Conclusion: One hundred and four patients were evaluated with ddPCR. Of these, 83 (79%) passed ddPCR quality metrics. Of those that passed, 83 (80%) had a positive result with VAFs as low as 1.15%, with 20 (19%) having a negative result. Sixty patients were evaluated by both NGS and ddPCR. Of these, 54 (90%) passed NGS metrics while 52 (87%) passed ddPCR metrics. Thirty-seven cases (62%) were concordant between NGS and ddPCR, with 29 negative concordant cases and 8 positive concordant. Eighteen cases (30%) were discordant, with 12 cases having a PIK3CA variant identified by ddPCR and 6 cases having a PIK3CA variant identified only by NGS. Another 5 cases failed both assays.

Poster # 307

USE OF TARGETED MEDICAL THERAPY IN KAPOSIFORM LYMPHANGIOMATOSIS (KLA)

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Background: Kaposiform lymphangiomatosis (KLA) is a rare and aggressive lymphatic anomaly first described as a distinct entity in 20 patients in 2014 [1]. Overall survival is very poor (51%) [1].

Historically, patients were treated with supportive care and surgical intervention. Recently, new medical therapies have emerged, including the use of mTOR and MEK inhibitors.

Objectives: To describe the use of targeted therapies (mTOR inhibitors and MEK inhibitors) in patients with KLA, an aggressive vascular anomaly

Design/Method: We conducted a retrospective review of clinical features and treatment outcomes for 57 patients diagnosed with KLA. All patients were referred to the Vascular Anomalies Centers at Boston Children's Hospital and Cincinnati Children's Hospital Medical Center between 1995 and 2021.

Results: The median age at symptom onset was 5.4 years (range 0-40.6). Anatomic involvement varied: lung (82%), abdominal (77%), bone (68%). Pleural effusions occurred in 72% and pericardial effusions occurred in 56%. Thrombocytopenia (platelet count <150,0000/uL) occurred in 63% and hypofibrinogenemia (fibrinogen <150 mg/dL) occurred in 50%. Sixty percent of patients required transfusions of blood products. Sixty percent of patients were treated with sirolimus for >6 months. Five-year overall survival was 56% in the non-treated group and 97% in the sirolimus-treated group (log-rank p-value=0.0013).
Seven patients had genetic mutations identified: NRAS (n=5), KRAS (n=1) from tissue (n=4) or cell-free DNA (n=2). Due to toxicity (n=4) or disease progression (n=3) on mTOR inhibitors, 5 patients initiated therapy with trametinib. Three of these patients had no significant adverse events. Two patients stopped trametinib due to lower extremity swelling and are now doing well on selumetinib. Fifteen of the 57 patients died (24%).

Conclusion: Sirolimus significantly improved survival of patients with KLA. Despite this success, some patients have disease progression on sirolimus. There is emerging potential for molecular diagnostics and targeted therapies in KLA patients, particularly in those who become refractory to mTOR inhibition. Evaluating the safety and efficacy of targeted therapies in KLA will be an important area of future research.

Poster # 308

INFORMATION ACCESSIBILITY DYNAMICS IN VASCULAR ANOMALIES CARE: A UNITED STATES CASE STUDY

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Background: Out of 200 children's hospitals in the United States, 27% do not provide any information online about how to access care for patients with vascular anomalies (VAs). Given that these patients struggle to access medical care and 13 states lack multidisciplinary VA teams, it is essential to understand the patient's experience when seeking this care. In the context of rare disease, difficultly accessing care with VA specialists may delay diagnosis, exacerbate manifestations of disease, and prevent effective treatment. A closer examination into the time commitment when contacting children's hospitals is essential.

Objectives: This study aimed to analyze the time required to garner pertinent information regarding VA care.

Design/Method: In a prior study, we identified 54 U.S. children's hospitals that lacked information about VA care on their websites. Using a structured script, team members called each hospital to identify which physicians or clinics managed VAs. Up to three calls were made per hospital. Call duration was recorded. Data analysis was completed using descriptive statistics, Kruskal-Wallis, and Mann Whitney U testing.

Results: Of the 54 centers contacted, all 54 (100%) were successfully reached during the first call. Only 18 (33.3%) centers were able to provide VA care information upon initial contact, necessitating a second call to 36 (66.7%) centers. 12 (22.2%) centers required a third call to obtain this information. Of all centers, only 29.6% successfully provided information regarding physicians or clinics treating VAs. These centers required an average of 1.6 calls with a median call duration of 4.5 minutes (IQR 4.5) to obtain this information. For the centers that did not provide information regarding physicians or clinics treating VAs, the mean number of calls was 2.0 with a median call duration of 3.9 minutes (IQR 5.9). Across all calls placed to each center, there was not a significant difference in duration at the $P<0.05$ level for the three calls ($P=0.458$). Significantly more calls were made to centers that did not provide care information for patients with VAs ($P=0.029$).

Conclusion: Children's hospitals may lack sufficient information regarding treatment for patients with VAs, even upon direct inquiry. Additionally, many of these hospitals do not offer care for such patients, adding a significant hurdle to accessibility due to the substantial time and effort needed for information gathering.

Poster # 309

UPDATED LONG-TERM SAFETY AND EFFICACY OF ALPELISIB FOR PATIENTS WITH PROS: A POOLED ANALYSIS

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Background: *PIK3CA*-related overgrowth spectrum (PROS) is a group of overgrowth disorders with overlapping, phenotypically varied features driven by somatic gain-of-function *PIK3CA* mutations, typically managed symptomatically. Alpelisib, a PI3Kα inhibitor, is the only approved pharmacologic treatment for PROS. EPIK-P1 (NCT04285723), a retrospective chart review of patients with PROS who received alpelisib, was followed by EPIK-P3 (NCT04980833), an ongoing prospective, interventional, open-label, Phase II study with a retrospective period to assess long-term safety and efficacy of alpelisib in patients with PROS from EPIK-P1. We presented EPIK-P1/P3 pooled analysis (retrospective period) results at the Society for Pediatric Dermatology 48th Annual Meeting; here we report updated results with 1-year prospective data.

Objectives: To assess long-term safety and efficacy of alpelisib in patients with PROS in pooled EPIK-P1/-P3 populations during retrospective and prospective periods.

Design/Method: Safety, pediatric growth, and overall clinical benefit (change in severity of PROS-related signs/symptoms, incidence of PROS-related surgeries) data pooled from EPIK-P1/-P3 were described for

each patient from treatment start date in EPIK-P1 to the end of the EPIK-P3 retrospective period. Safety, pediatric growth, and overall clinical response from the EPIK-P3 prospective period (data cutoff August 26, 2023) are presented.

Results: Forty patients (pediatric, N=31; adult, N=9) were treated with alpelisib during the EPIK-P3 prospective period. Median (range) duration of treatment exposure was 60.7 months (47-91) since initiation of alpelisib, and 16.4 months (13-19) since commencement of the prospective period. All-grade treatment-related adverse events (TRAEs) were reported in 3 pediatric patients (9.7%) and 2 adult patients (22.2%). TRAEs led to dose reduction in 1 pediatric patient (3.2%) and no discontinuations. Pediatric patients grew normally after treatment initiation; most had height/BMI trajectories within the 5th-95th percentiles. At the baseline visit, 25 pediatric (80.6%) and 8 adult patients (88.9%) showed improved clinical response; 5 pediatric (16.1%) and 1 adult patient (11.1%) were stable. At the 12-month visit, 9 pediatric (29.0%) and 1 adult patient (11.1%) showed improved clinical response; 20 pediatric (64.5%) and 8 adult patients (88.9%) were stable. One pediatric patient (3.2%) showed a worsened response at both visits.

Conclusion: In these first reported prospective data from EPIK-P3, alpelisib demonstrated a tolerable, manageable safety profile consistent with its mechanism of action, comparing favorably with that in the oncology setting with no new safety signals reported. Pediatric patient growth was normal. Sustained stability or improvement in overall clinical response in the prospective period reinforces the clinical benefit of alpelisib for patients with PROS.

Supported by Novartis Pharmaceuticals Corporation.

Poster # 310

THE MINI-MULTIDISCIPLINARY VASCULAR ANOMALIES TEAM: STEPS TO IMPROVE PATIENT ACCESS AND VOLUME

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Background: Large multidisciplinary teams are important in the management of complex vascular anomalies as multimodal treatment approaches are employed for optimal patient outcomes. At large centers, teams can exceed over 10 disciplines with numerous providers and ancillary support. The coordination of large teams can limit the number of clinics and available patient visits although, frequently, the entire team is not required for each patient.

Objectives: The objective was to create a mini-multidisciplinary team (MMDVT) to improve access, reduce wait time, and execute team strategies without requiring the entire team.

Design/Method: A MMDVT of two providers with specialty support was developed. Evaluation of patient volumes, speed to clinic access, vascular diagnosis, and care coordination was performed with comparison to the traditional team clinic.

Results: Weekly MMVDT clinics were organized for each of the two involved team leaders with simultaneous sessions in the same hallway. Six to eight patients were scheduled per hour in each clinic

session. In less than 4 months, over 200 patient visits were conducted with expedited access to care and included all vascular anomalies diagnosis. Coordination to appropriate treatment was performed via electronic medical record messaging and scheduling. This compares to less than 80 patients in the traditional multidisciplinary team clinic. Better directed referrals to the full multidisciplinary team was a secondary benefit.

Conclusion: Patient access and volumes can be improved with mini-multidisciplinary vascular team clinics in comparison to full teams. We herein explain the process to create and support the MMDVT using available resources and vascular coordinators.

Poster # 311

Dual therapy with beta blockers and sirolimus in an infant with diffuse infantile hemangiomatosis

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Background: Infantile hemangiomas are common, but diffuse neonatal hemangiomatosis and infantile hemangiomatosis are rare. The first line treatment for infantile hemangiomatosis is enteral propranolol.

Objectives: We present the case of a now 12-month-old infant with diffuse cutaneous and hepatic hemangiomas who was treated with intravenous esmolol, steroids, and sirolimus therapy in the setting of critical illness. The purpose of this presentation is to describe a clinical case with successful use of a) dual therapy with beta blockers and sirolimus, and b) intravenous esmolol when oral propranolol is unable to be utilized in diffuse neonatal hemangiomatosis.

Design/Method: A 2-day old late preterm infant presented with diffuse innumerable cutaneous hemangiomas, prompting a hepatic ultrasound which demonstrated diffuse hepatic hemangiomas. Prenatally, fetus was noted to have a "tortuous vessel in the liver." Patient was initially started on oral propranolol at 3 days of life and tolerated maximum dose. Patient remained in the neonatal intensive care unit (NICU) for respiratory distress and development of oral feeding skills. Patient then developed symptoms consistent with necrotizing enterocolitis, requiring bowel rest and cessation of oral propranolol. At that time, patient was transitioned to intravenous steroids for management of her hemangiomas. Patient then decompensated secondary to high output cardiac failure, severe hypothyroidism, and respiratory distress due to severe tracheo-bronchomalacia. Airway evaluation did not reveal hemangiomas. Due to clinical decompensation, she had escalation of respiratory support and could not be given enteral propranolol. A hemangioma on the forearm was biopsied which showed positive GLUT-1 staining consistent with infantile hemangioma. Infant was initiated on triple therapy for hemangiomatosis consisting of steroids, intravenous esmolol, and sirolimus.

Results: Patient stabilized after starting this therapy. Infant was weaned off steroids, and beta-blocker therapy was transitioned to propranolol, which she remains on along with sirolimus. Her cutaneous hemangiomas have reduced in number and are fading as of her recent clinical follow up at 11 months of age. Hepatic hemangiomas have been stable based on imaging.

Conclusion: This is a unique, challenging case of an infant with life-threatening diffuse infantile

hemangiomatosis treated with beta blockers and sirolimus therapy. Patient benefited from intravenous esmolol when enteral beta blocker was not an option due to clinical complications.

Poster # 312

VERRUCOUS VASCULAR MALFORMATION IS PART OF PIK3CA-RELATED OVERGROWTH SPECTRUM

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Background: PIK3CA-related overgrowth spectrum (PROS) encompasses multiple syndromes of tissue and/or vascular overgrowth associated with a hyperactivation of the PI3K/AKT/mTOR signaling pathway. Variants in the gene encoding the catalytic α-subunit of PI3K (PI3KCA) predispose to activation of PI3Kα and Akt-signaling, cellular transformation. Inhibition of the PI3K/AKT/mTOR pathway is of interest in treatment of vascular malformations.

Objectives: We report a case of a 9-year-old female with a progressively enlarging verrucous vascular malformation of the left chest wall associated with a pathogenic variant of PIK3CA.

Design/Method: Literature and chart review.

Results: A 9 year old female who presented at birth with a small and erythematous vascular lesion of the left chest wall, labeled as an infantile hemangioma. Over the following years, it enlarged, developing a violaceous, verrucous appearance with extension into the subcutaneous tissue. The patient reported intermittent bleeding from the lesion with no other associated symptoms. Multiple therapies were attempted including sclerotherapy and coiling without any significant improvement. MRA/MRV showed a predominantly venous lesion with significant adipose proliferation and infiltration of the underlying musculature. Ultimately, diagnosis was obtained via genetic testing of biopsy tissue showing PIK3CA pathogenic variant consistent with PROS. Excision was done, removing 95% of the lesion. Alpelisib was started after surgery to target the remaining soft tissue component of the malformation in an attempt to prevent recurrance.

Conclusion: Verrucous venous malformation may harbor PIK3CA mutation and should be considered as part of the PROS. Tissue and vascular overgrowth can be challenging to treat with traditional interventions such as debulking, amputations and vascular interventional techniques as these lesions often recur. The detection of a pathogenic PIK3CA variant provides the opportunity to direct therapy with inhibitors of the PI3K pathway such as Alpelisib. Further studies are required to explore safety and impact of long term effects of this drug in pediatric patients.

Poster # 313

INFANTILE PULMONARY HEMANGIOMAS: A CASE OF MULTIPLE PULMONARY NODULES IN AN ASYMPTOMATIC PATIENT.

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Background: Infantile pulmonary hemangiomas (IH) can be a challenging diagnosis, it is extremely rare with only a few cases reported in the literature. IH shows the distinctive characteristic of expressing the antigen GLUT-1 in the endothelial cells that differentiates it from with other types of vascular malformations. Those cases exhibit a wide range of clinical presentations including airway compression, massive hemoptysis or respiratory distress. Infantile hemangiomas are the most common benign vascular tumor of childhood, thus pulmonary IH, although rare, should be considered in the differential of an otherwise asymptomatic patient with unexplained pulmonary nodules.

Objectives: We report a case of a 13 month-old female with an incidental finding of multiple pulmonary nodules found to be infantile pulmonary hemangiomas.

Design/Method: Case Report/ Literature review

Results: A 13-month-girl presented to the emergency department with 5 days of intermittent abdominal pain and constipation. Abdominal X-ray revealed a small, round, radiopaque density projecting in the right pulmonary base but was otherwise unremarkable. CT of the chest revealed multiple pulmonary nodules in both lungs with peripheral calcifications and many with faint internal calcifications. CT of the abdomen was normal. Given the CT findings with concerns of malignancy vs. infectious etiology, an extensive workup was done. Infectious work-up was negative for bacterial, viral or fungal infections. The random distribution of the nodules was suggestive of metastatic spread. Work-up including tumor markers, skeletal survey and abdominal imaging was unremarkable ruling out neoplasm. Ultimately, the patient underwent an excisional biopsy of a pulmonary nodule which revealed subpleural capillary proliferations constituted by tightly arranged units containing small vessels with patent lumen and prominent endothelial cells, immunostaining for GLUT-1 was positive. Findings were consistent with infantile hemangiomas. Although some cases had required treatment with medication such as propranolol, in our patient's case there were no life threatening findings and she was managed with supportive treatment. She continues to follow up as an outpatient with imaging alone.

Conclusion: Infantile Pulmonary Hemangiomas are rare but should be considered in pediatric patients with unexplained pulmonary nodules. GLUT-1 receptor is specific for the diagnosis of infantile hemangiomas and can help exclude other causes of vascular malformations.

Poster # 314

PANCREATIC KAPOSIFORM HEMANGIOENDOTHELIOMA WITH POOR RESPONSE TO MEDICAL THERAPY RESULTING IN DEATH

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Background: Kaposiform hemangioendothelioma (KHE) is a rare vascular tumor most commonly found in skin and subcutaneous tissue that can also occur in viscera. Surgical and medical therapies are generally employed for treatment.

Objectives: We present a case of pancreatic KHE that was difficult to diagnose and had a poor response

to medical therapies, ultimately resulting in multiorgan dysfunction and death, to illustrate the complex management and potential complications of these rare tumors.

Design/Method: A 5 month old term female presented with significant vomiting. Labs were notable for anemia, neutropenia, and severe thrombocytopenia (<10K). Platelet count did not improve with transfusion, IVIG, or steroids. Further workup with magnetic resonance imaging (MRI) led to diagnosis of necrotizing pancreatitis complicated by massive ascites and inflammation of adjacent bowel. Workup of the cause of pancreatitis was unrevealing. Additional labs showed hypofibrinogenemia and severely low D-dimer. Despite normalization of lipase and improvement in ultrasound findings, her clinical status did not improve and she developed portal vein thrombosis, obstructive jaundice, hematochezia, fevers, and ongoing transfusion requirements (red blood cells, platelets, cryoprecipitate) and required care in the intensive care unit (ICU).

Results: Four weeks into admission, repeat MRI showed pancreatic soft tissue mass infiltrating into liver and small bowel; biopsy of the lesion showed KHE, and labs were thus felt to represent Kasabach-Merritt phenomenon (KMP). Medical therapy including steroids (8 weeks), weekly vincristine x 5, and sirolimus (12 weeks) was initiated. Surgical resection was not feasible. Despite treatment, she developed progressive complications including infections (bacteremia, pneumonia, multi-organism peritonitis with drug-resistant organisms) that were difficult to clear despite multiple antimicrobials and severe ascites refractory to multiple therapies. Her KMP showed partial response to therapies, with improvement in fibrinogen but continued profound thrombocytopenia and elevated D-dimer. She was considered for multivisceral transplant at multiple institutions but ultimately denied due to infections. She developed bowel necrosis and became progressively more ill with worsening respiratory failure. She died at age 9 months despite efforts by multiple medical teams.

Conclusion: Diagnosis of an uncommon presentation of a rare tumor can be difficult. Balancing the risks and benefits of medical therapies in a critically ill patient with organ dysfunction is challenging, as is dosing medications in this population. Despite good response with combination medical therapy in most patients with KHE, this patient did not have a good response and ultimately died from complications of her KHE. Multidisciplinary input is required for the care of patients with visceral KHE.

Poster # 315

PRENATAL SIROLIMUS IN THE TREATMENT OF CONGENITAL LYMPHATIC MALFORMATIONS

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Background: Vascular Anomalies (VA) are a relatively rare spectrum of diseases that involves vascular tumors and malformations, including lymphatic malformations (LM). The use of sirolimus for infants born with LM has been a promising addition with potential to avoid more aggressive treatments. Maternal sirolimus use for treatment of LM is an ongoing field of investigation with few published reports to date. Describe diagnosis, clinical course and outcome of two infants with LM treated prenatally with sirolimus

Objectives: Describe diagnosis, clinical course and outcome of two infants with LM treated prenatally

with sirolimus.

Design/Method: Case Report.

Results: Two patient cases are highlighted where sirolimus was introduced at 26-30 weeks gestation. In the first case, maternal sirolimus therapy was started at 2mg/day around 28 weeks gestation for prenatal diagnosis of extensive cervical LM. It was titrated up to 12mg/day for goal trough level of 8-12ng/ml and continued up to 24 hours prior to delivery. This patient was able to avoid an EXIT (Ex-utero intrapartum treatment) procedure. LM was soft at birth with a deflated appearance with loose, easily compressible skin. It continued to regress with postnatal sirolimus. Postnatal course was complicated by localized infection causing worsening swelling resulting in need for surgical intervention including local debulking and debridement. Maternal complications included delayed wound healing post-cesarean. In the second case, the mother of an infant with a large anterior neck LM was started on sirolimus at 4mg/day and titrated up to 8 mg/day for goal trough level of 8-12ng/ml, but the medication had to be stopped ten days prior to delivery due to premature contractions and maternal infection. Although there was some stabilization in size prior to delivery, the large mass size required delivery via EXIT procedure with unsuccessful intubation requiring tracheostomy placement. The neonate underwent 85% local mass resection on day two of life and was started on sirolimus five days after surgery without complications, with improvement in mass size.

Conclusion: These two cases highlight the feasibility of maternal sirolimus as an early treatment option for LM. The presenters aim to review/analyze the medical indications for maternal use of sirolimus and to demonstrate the success and risks of its usage. In both cases presented, maternal sirolimus allowed stabilization and even reduction in size of mass. It is imperative to share the cases to prompt further studies and collaboration to grow this sector in the VA field to improve morbidity and mortality in these high risk patients.

Poster # 316

USE OF SYSTEMIC SIROLIMUS IN A PATIENT WITH RECURRENT ERUPTIVE PYOGENIC GRANULOMA: CASE REPORT

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Background: Pyogenic granuloma (PG), also known as lobular capillary hemangioma, is a common, benign, vascular neoplasm of the skin and mucous membranes characterized by an erythematous, dome-shaped papules that bleed easily. These vascular lesions can occur on the head/neck regions, as well as trunk and extremities and are often found in children, young adults and pregnant women. The pathogenesis of PG is still unproven and in many cases it can be triggered by injuries and pharmacological therapies, though cases of spontaneous appearance have been described.

Objectives: Present a case of a patient with recurrent pyogenic granulomas not responsive to validated therapies with excision and propranolol, now receiving treatment with systemic sirolimus.

Design/Method: This is a case report describing the use of systemic sirolimus in a patient as treatment for multifocal recurrent pyogenic granuloma.

Results: A 14-year-old male with remote history of frequent tonsillitis requiring tonsillectomy at age 12 who presented with a two year history of cutaneous lesions on scapular area that have a tendency for bleeding. The lesions had become exquisitely tender to touch causing restriction in daily activities. Patient originally underwent surgical excision of a singular lesion with histopathology consistent with eruptive pyogenic granuloma. He subsequently experienced recurrence about one year later with over 25 new lesions around the site of the original excision. He was referred to dermatology for further evaluation and possible surgical intervention. Given extent of lesions it was recommended that patient undergo trial of systemic propranolol for recurrent eruptive pyogenic granulomas. Patient received four weeks of oral propranolol 60mg PO twice daily without improvement in size or number of lesions, as well as worsening symptoms including pain and bleeding. Due to continued growth of lesions patient was referred to Vascular Anomalies Multidisciplinary Center for assessment and intervention. He was started on oral Sirolimus 0.8mg/m2/dose twice daily with therapeutic trough goal of 8-12ng/mL. After 8 weeks of treatment patient has experienced stability in the number of lesions as well as reduction in size and firmness of the large lesions. Patient has not experienced any adverse side effects such as mouth sores, hyperlipidemia or infections associated with Sirolimus toxicity.

Conclusion: Sirolimus, an mTOR inhibitor used in treatment of vascular malformations, has been shown to have efficacy in patients with various proliferative skin disorders, including PG, and can be considered as a bridge to definitive surgical intervention in disseminated cases.

Poster # 317

CLOVES SYNDROME IN A PEDIATRIC PATIENT: OBSTACLES TO MANAGEMENT

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Background: CLOVES Syndrome is a rare genetic overgrowth syndrome characterized by congenital lipomatous overgrowth, vascular malformations, epidermal nevus, and skeletal anomalies caused by mutations in PIK3CA. These mutations are typically heterozygous somatic activating mutations with no current evidence of vertical transfer. Given its manifestations, these patients require multidisciplinary care.

Objectives: We present the case of a 19-month-old female with confirmed PIK3CA mutation with features predominantly of CLOVES Syndrome including macrodactyly of lower limbs, mediastinal cystic mass, lymphangioma of trunk, and cutaneous vascular malformation nevus. Given this syndrome has under 200 confirmed cases, we hope reporting this case in a pediatric patient can increase familiarity of this syndrome and aid in earlier diagnoses.

Design/Method: Retrospective chart review.

Results: Our patient's diagnosis was suspected prenatally and confirmed genetically days after birth. Early diagnosis allowed the patient prompt establishment with a multidisciplinary team. She was started on PJP prophylaxis and sirolimus, with trough levels maintained at 8-13 mcg/L. At 10-months, she underwent sclerotherapy to mediastinal and abdominal cystic lesions for concern of cardiac compression. At 15-months she underwent third-digit ray resection, epiphysiodesis of second and fourth

digits, and excision of soft tissue of the left foot for concern of macrodactyly affecting ambulation.

Conclusion: With CLOVES Syndrome first described under 20 years ago, treatment options are limited. Clinical trials investigating Alpelisib, a drug that selectively inhibits PIK3 subunits, have been promising, but are not approved for this patient's age. Other systemic therapies block aspects of the PIK3/AKT/mTOR pathway. These include medications like sirolimus which our patient began at 3-days-old and continues to date. These have risks, including exfoliative dermatitis which this patient experienced. Surgical interventions like sclerotherapy may control progression of growths that may risk adjacent organ dysfunction. Given our patient's age, we aspire to offer her more targeted therapies in the future. We also hope that targeted treatments become available to younger patients with CLOVES Syndrome so young patients like ours are able to receive less systemic treatments.

References:
(Garreta Fontelles, Pardo Pastor, Grande Moreillo, Alpelisib to treat CLOVES syndrome, a member of the PIK3CA-related overgrowth syndrome spectrum, 2022.)
(Bruss, Farook, Shah, Baker Sheikh. Sirolimus-Induced Rash in a Kidney Transplant Patient, 2022.)
(Chen, Wang, Xu, Li. Initial dose recommendation for sirolimus in paediatric kaposiform haemangioendothelioma patients based on population pharmacokinetics and pharmacogenomics, 2020.)
(Öztürk Durmaz, Demircioğlu, Yalınay Dikmen, Alanay, Alanay, Demirkesen, Tokat, Karaarslan. A Review on Cutaneous and Musculoskeletal Manifestations of CLOVES Syndrome, 2022.)

Poster # 318

RESPONSE TO DABRAFENIB AND TRAMATENIB IN AN EXTRA-CRANIAL AVM WITH BRAF V600E MUTATION

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Background:
Arteriovenous malformations (AVMs) are blood vessel malformations characterized by shunting of blood through dilated veins and arteries. KRAS is an effector molecule in a MAPK pathway that mediates activation of downstream processes such as BRAF production related to known proliferative disorders such as AVMs. Similarly MAP2K1 mutations that encodes for MEK have recently been implicated in sporadic intracranial and extracranial AVMs. Inhibition of the RAS/MAPK pathway is of interest in treatment of vascular malformations.

Objectives: We report a case with a BRAF V600E mutation and response to treatment with MEK and RAF inhibitors.

Design/Method: Relevant articles were selected for literature review regarding terminology including guidance protocols, latest treatments, outcomes.

Results:
A 22 year old male presented initially at 6 years of age with swelling of the left face involving the cheek and mandible area. The area continued to grow in size with associated pain and rarely intermittent

bleeding from the left buccal mucosa. US and MRI showed evidence of an AVM. He underwent 2 embolizations followed by debulking with some improvement of the swelling. Pathology revealed a BRAF V600 mutation by molecular testing. He was treated with oral Dafrafenib 150 mg twice daily and Trametinib 2 mg daily, showing improvement of the swelling with a 7 month follow up. To our knowledge this is the first case of BRAF V600E mutation described in extracranial AVM. MEK inhibitors have been used with some success in a few case reports.

Conclusion:
Extracranial AVMs continue to present treatment challenges for hematologists, surgeons and other care providers. Treatment with target directed therapies with inhibitors of the RAS-RAF-MEK-ERK pathway such as Trametinib and Dafrafenib have the potential to make a positive impact in the current management of these entities. Looking for the BRAF V600E mutation in biopsies allows for better targeted therapy. Further studies are required to explore safety and impact of long term effects of these drugs in pediatric patients.

Poster # 319

TET2 GENE MUTATION ASSOCIATED WITH GENERALIZED LYMPHATIC ANOMALY

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Background: Generalized lymphatic anomaly (GLA), is a rare congenital multisystem disorder, characterized by multiple lymphangiomas infiltrating different tissues. It has been reported an incidence of 1/4000 in children. While benign and localized, it can lead to complications secondary to mass effects or a diffuse disease. Numerous gene mutations, such as SOX18 and PIK3CA, have been associated with GLA.

Objectives: Report a novel genetic mutation in a child with generalized lymphatic anomaly and describe his clinical course.

Design/Method: Retrospective chart review of the patient's file.

Results: We present a case of a full-term neonate intubated at birth for acute respiratory distress secondary to abdominal distension. In utero at 24 weeks, MRI obtained showed multiseptated cystic structures in the left hemipelvis measuring 5.1 x 4.5 x 0.9 cm with surrounding mass effect, including right displacement of rectum and bladder and left hydroureteronephrosis; findings suggestive of lymphatic malformation. MRI after birth disclosed multiple compartmental intra-abdominopelvic cystic mass crossing multiple soft tissue planes with mass effect measuring 14.9 x 8.5 x 12.3 cm and extension to the spinal canal. The course was complicated by anuria and abdominal distension, requiring fluid drainage. He was stabilized and started on Sirolimus on day 8 of life. After 5 months on a stable dose of sirolimus, repeat US showed improvement in the size of the septated cystic lesion, measuring 3.1 x 1.5 x 1.9 cm and only localized to the left lower quadrant with no bilateral hydroureteronephrosis. The genetic analysis yielded a 46, XY karyotype. Sequence analysis of the 34 genes encompassed by the somatic overgrowth and vascular malformation panel failed to identify any significant variants. However, comprehensive whole-genome sequencing uncovered a TET-2 gene mutation. Intriguingly, this mutation was also observed in the mother's germline, suggesting a hereditary nature of the genetic

alteration. TET-2 gene encodes an iron and 2-oxoglutarate-dependent oxygenase which is an enzyme responsible for conversion of 5-methylcytosine (5mC) to 5-hydroxymethylcytosine (5hmC) involved in DNA methylation.

Conclusion: TET-2 gene regulates gene expression and cellular function; it is associated with various disorders, mostly blood-related disorders (e.g. MDS, AML, MPN) however, none have been reported in association with GLA's. A new connection to lymphatic anomalies could be hypothesized. This patient has a novel mutation that may be related to lymphatic anomalies. While these mutations are typically somatic in nature, in this family, it was found to be germline

Poster # 320

A POSITIVE RESULT YOU DON'T WANT – TUBERCULOSIS AND THE USE OF SIROLIMUS IN VASCULAR ANOMALIES

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Background: While the number of cases of tuberculosis (TB) has decreased over 30 years, cases are increasing in the USA over the last two years. Several states are above the national rate and experiencing significantly increasing numbers (9.9% growth in Texas 2021-2022). Many institutions screen for TB prior to initiating immunosuppressant drugs, such as sirolimus. This presentation highlights two cases of TB in vascular anomalies (VA) patients who utilize sirolimus, reviews literature of TB screening, and proposes a decision-making tree to aid vascular anomalists in screening and treating patients for TB.

Objectives:

1. Review the screening process for tuberculosis.
2. Understand the indications for further treatment and testing for a positive TB test in this unique population.
3. Apply current tuberculosis guidelines to patients who are immunosuppressed with sirolimus for vascular anomalies.

Design/Method: Case 1: 16-year-old female with Klippel Trenaunay syndrome (KTS) presented with worsening of symptoms (pain and lymphatic drainage) requiring initiation of sirolimus. As part of protocol, T-SPOT was obtained and returned positive. Further work up confirmed latent TB. Initiation of sirolimus treatment was held until cleared by TB experts.
Case 2: 30-year-old female with Generalized Lymphatic Anomaly(GLA), well-controlled on sirolimus, presented to acute care facility with active extrapulmonary TB. Sirolimus was held during the acute phase of her disease and restarted after cleared by TB experts.

Results: Treatment of VA during TB infections has many variables, including urgency of initiating treatment with sirolimus and status of the TB disease (latent (LTBI) versus active). In cases where sirolimus can be delayed/held, it is recommended that treatment is delayed one month for LTBI, or in active disease held until the TB symptoms start to improve. In VA that require concomitant TB treatment with sirolimus, the patient should be monitored closely when initiating LTBI treatment.

Conclusion: While working with immunosuppressive drugs, it is important for vascular anomalists to understand the screening processes for TB and the treatment goals while on these agents. Through these case examples and literature review, a clearer pathway for future cases is outlined and will expedite more efficient and improved care for this rare disease population.

Hematopoietic Stem Cell Transplantation (401-414)

Poster # 401

SINGLE-HLA EXPRESSING CELL LINE SCREENED VST SHOW CLINICAL EFFICACY DESPITE LOW HLA CONCORDANCE

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Background: Immunocompromised patients suffer significant morbidity and mortality secondary to viral infections. Virus specific T-cells (VSTs) are safe and effective in treating CMV, EBV, BK, and adenovirus infections following hematopoietic stem cell transplant (HSCT). Early studies suggested a high degree of HLA-concordance was essential to third party (TP)-VST efficacy and persistence. However, recent studies demonstrated similar clinical outcomes between patients infused with donor derived- (DD-) and TP-VSTs despite disparate HLA concordance. Maximizing the degree of HLA match often guides TP-VST selection; however, this does not directly assess VST response to viral antigens, and thus may be a suboptimal approach. Single HLA-expressing cell lines (SALs) loaded with viral peptide can be co-cultured with VSTs to objectively measure HLA restriction. We hypothesize using SAL screening of VSTs (SAL-VSTs) to inform product selection will improve clinical response rates.

Objectives: To assess clinical outcomes of patients infused with SAL-VSTs compared to historical controls at Cincinnati Children's Hospital Medical Center (CCHMC).

Design/Method: All HSCT recipients who received SAL-VSTs at CCHMC were analyzed. Clinical response was determined as previously described for viremia, and as recorded by clinician assessment per study protocol (ClinicalTrials.gov NCT02532452) for invasive disease (ID).[1] For patients with multiple infusions of one VST, responses were determined using final infusion data.

Results: Twenty infusions for 9 patients were analyzed. Two subjects had multiple infusions with the same product (one patient had 11 infusions, one had 2). Median age was 10 years (range 1-70). Patients were infused for: viremia (n=4), ID (n=2), both viremia and ID (n=3). Of 7 patients infused for viremia, 6 had objective response (OR) (86%). Of 5 patients infused for ID, 5 responded (100%). 9/9 patients had overall clinical response (OCR) to either viremia or ID (100%). HLA typing was reviewed for all patients, and median number of HLA matches was 2/10 (range 2-8).

Conclusion: Patients infused with SAL-VSTs have robust clinical response rates. SAL-VST ID response and viremia OR was comparable to historical TP-VSTs at CCHMC.[1] Additionally, SAL-VST OCR rate was comparable to OCR from historical institutional data (range: 56-70.3% across viruses), and to TP-VST OCR from other groups. Though limited by sample size, the robust response of SAL-VSTs indicate these products are efficacious, and preliminary data suggests possibly more efficacious for ID than historical

products. Their ability to induce response despite low total number of HLA matches suggests that product selection based on presumed HLA restriction is crucial.
1. Galetta, *Transplant Cell Ther,* 2023.

Poster # 402

RSV INFECTION AND MORTALITY AMONG PEDIATRIC HEMATOPOIETIC CELL TRANSPLANT RECIPIENTS

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Background: RSV causes significant morbidity for children, ranging from a peak of 1.3 to 5.0 hospitalizations per 100,000 between 2018 and 2023 per CDC data. While it is known that immunocompromised status increases the risk of serious infections, the true prevalence of RSV in pediatric Hematopoietic Cell Transplant (HCT) recipients remains unknown.

Objectives: To describe the prevalence, demographics, and use of preventative therapeutics against RSV in pediatric HCT recipients during initial and subsequent hospitalizations.

Design/Method: In this retrospective case-control study, information was collected from centers participating in the Pediatric Health Information System database on children <18 years who underwent hematopoietic cell transplant with an initial transplant discharge date between 1/1/09 and 12/31/18. PRISM 10.1.1 was used to complete unpaired t-test evaluations and Chi square/Fisher's exact tests comparing patients with and without RSV during initial transplant admission.

Results: Of the 11,022 patients identified, the majority of patients were male (58.8%) and white (60.1%). Transplant type included 5890 allogeneic and 3445 autologous, while 1744 were classified as "other" HCT. Patients received HCT for malignancy (72.3%), aplastic anemia (7.5%), immunodeficiency (6.9%), sickle cell disease (4.8%), HLH (2.4%), thalassemia (2.0%), and genetic etiologies (2.0%). There were 234 patients whose diagnoses were unknown.
134 patients (1.2%) tested positive for RSV during the initial transplantation and 623 others (5.7%) were hospitalized for RSV following the initial transplant admission. Between those who had RSV during the initial transplant and those who did not, there was a statistically significant increase in mortality (OR 2.21, 95%CI 1.28-3.68, p=0.002), length of stay (67 vs 48 days, p<0.0001), hospital cost ($1,218,962 vs $825,184, p<0.0001), need for ICU (OR2.69, CI 1.57-3.07, p<0.0001) and ventilator support (OR2.69, CI 1.8 - 3.97, p<0.0001); and patients were a younger age (5.9 vs 7.9 years, p<0.0001).
Of those who had RSV during the initial transplant, there was no difference in mortality among those who did not receive palivizumab (8/76) compared to those who did (8/57) (p=0.59). Patients with RSV who received palivizumab were younger (4.5 vs 6.9 years, p=0.01), had a higher length of stay (81 vs 57 days, p=0.03), and higher cost of admission ($1,515,318 vs $1,015,355, p=0.01).

Conclusion: RSV during initial admission for HCT confers an increased risk of mortality, need for intensive care and ventilatory support, and cost. There is no significant difference in mortality among those with RSV who have received palivizumab and those who have not.

Poster # 403

HAPLOIDENTICAL HEMATOPOIETIC CELL TRANSPLANTATION FOR PATIENTS WITH ACQUIRED SEVERE APLASTIC ANEMIA

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Background: Currently, allogeneic hematopoietic cell transplantation (HCT) using an HLA-haploidentical family donor is considered as a feasible treatment option for patients with refractory/relapsed severe aplastic anemia (SAA) who cannot find a suitably matched donor.

Objectives: We evaluated the outcome of haplo-HCT using an ex vivo TCRab-depleted graft with minimal GVHD prophylaxis in pediatric patients with acquired SAA who were mostly treatment-naïve. In this study, all patients received minimal GVHD prophylaxis with no immunosuppressants or MMF alone.

Design/Method: Between December 2015 and November 2022, 31 pediatric patients with acquired SAA received haplo-HCT using ex vivo TCRαβ-depleted peripheral blood stem cells at our center. Conditioning regimen consisted of total body irradiation (TBI 400 or 600 cGy), fludarabine 180 mg/m^2, cyclophosphamide 100 mg/kg and r-ATG 3-7.5 mg/kg. Of 31 patients, 12 patients did not receive any immunosuppressants (no IS) post-transplant, while the remaining 19 patients received only mycophenolate mofetil (MMF) for one month after transplantation. None of the patients received calcineurin inhibitor as a GVHD prophylaxis. Donors were father in 11, mother in 9 and sibling in 11. Of the 31 patients, 27 received upfront haplo-HCT for treatment-naïve SAA, whereas 4 received salvage haplo-HCT for refractory/relapsed SAA.

Results: Of 31 patients, 16 were male and the median age at transplant was 10.7 years (range, 1.4–22.6). Thirty of the 31 patents achieved neutrophil engraftment at a median of 10 days (range, 9–12 days) after Haplo-HCT. One patient failed to achieve primary neutrophil engraftment for which the patient received two more rounds of Haplo-HCTs and eventually achieved stable engraftment. No patients experienced late graft failure. The CI of acute GVHD (aGVHD) ≥ grade 2 and ≥ grade 3 were 40.4% and 10.2%, respectively. No patient developed grade 4 aGVHD. Two patients developed chronic GVHD, of which one had mild and the other had moderate chronic GVHD. At a median follow-up of 49 months (range, 12–97 months), only one patient with treatment-naïve SAA died of TMA at 206 days post-transplant and all 30 survivors remained transfusion-independent. The failure-free survival and overall survival were 94% ± 4.4% and 97% ± 3.2%, respectively.

Conclusion: Our HLA-haploidentical HCT using minimal GVHD prophylaxis after depletion of $\alpha\beta^+$ T cells showed an excellent outcome in pediatric patients with refractory/relapsed or treatment-naïve SAA. Future study is warranted to verify the feasibility of this approach and evaluate the long-term complications such as infertility and second malignancies and so on.

Poster # 404

HOW TO IMPROVE THE SLEEP OF HOSPITALIZED PATIENTS UNDERGOING SCT: PARENT AND PROVIDER PERSPECTIVES

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Background: Pediatric patients undergoing stem cell transplants (SCT) experience lengthy hospitalizations that are intended to support healing. However, the hospital environment, treatment side effects, and care practices can place patients at risk for disrupted sleep, which may negatively impact their quality of life and the recovery process.

Objectives: This quality improvement project aimed to identify barriers to SCT patients and their families getting good quality sleep in the hospital as well as potential intervention targets.

Design/Method: We conducted 8 semi-structured focus groups: 4 with family caregivers of SCT patients and 4 with medical providers. Each group had 3-6 participants and was audio-recorded and then transcribed. Two members of the study team independently coded transcripts in NVivo using descriptive content analysis. Each complete idea expressed during the focus groups was captured under a single code. Initial codes were collapsed into broader categories and organized into a hierarchy. We used an audit trail to detail methodological and coding decisions. Consensus meetings were used to resolve coding discrepancies. We included family partners and medical providers in these meetings to verify the credibility and reliability of codes.

Results: Participants described patient and caregiver sleep as non-restorative and interrupted. They also described multiple negative impacts of getting insufficient sleep in the hospital, such as compromised emotion regulation and communication challenges. Barriers to sleeping well included loud noises (e.g., monitors / pump alarms, trash pulls), bright lights, monitoring health at night (e.g., vitals), room entries, comfort issues (e.g., uncomfortable beds, especially for parents), and difficulties relaxing. Proposed interventions included altered procedures (e.g., retiming medications or vitals), noise masking / reduction, clustering care, light reduction / use of dim lighting when needed, establishing a consistent schedule, use of protected sleep periods, and staff training.

Conclusion: Pediatric patients and their families undergoing SCT often face challenges with sleep during extended hospital stays. Both healthcare providers and family caregivers have pinpointed areas needing improvement. In response, our team has implemented several changes, such as minimizing pump alarms, enhancing staff training, and redesigning patient rooms to allow hallway access to trash bins, thereby reducing noise disturbances. We believe these modifications could be adapted to enhance patient care in other medical facilities. Additionally, this initiative aligns with the growing movement towards establishing 'sleep-friendly' hospital environments.

Poster # 405

COMPARING REGIMENS USED FOR ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION FOR SICKLE CELL DISEASE

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Background: The use of allogeneic hematopoietic cell transplantation (HCT) as a curative therapy for sickle cell disease (SCD) is increasing with the emergence of novel conditioning regimens, alternative

donor sources, expansion to adults, and changing indications. The lack of comparison of outcomes of the combination of conditioning regimens, graft-versus-host disease (GVHD) prophylaxis, and serotherapy remains a gap in the field.

Objectives: To evaluate event-free survival (EFS), overall survival (OS), and GVHD outcomes of combinations of conditioning regimen, T-cell depletion, and GVHD prophylaxis for SCD HCT.

Design/Method: We examined de-identified records of HCT for SCD retrieved through curesickle.org on patients transplanted from 1991 - 2022 in the United States and submitted to CIBMTR. We studied HCT outcomes from HLA-matched sibling donors (MSD), haploidentical relatives (haplo), and HLA-matched unrelated donors (MUD), using recent and current regimens.
For MSD, we compared TBI 300/400 cGY + sirolimus + anti-thymocyte globulin (ATG)/alemtuzumab (Hsieh et al. 2014); Busulfan and Fludarabine (Bu, Flu) + calcineurin inhibitor (CNI) and methotrexate (MTX) + ATG/alemtuzumab (Krishnamurti et al. 2019); Fludarabine and Melphalan (Flu, Mel) + CNI and MTX + ATG/alemtuzumab (King et al 2015); with Busulfan and Cyclophosphamide (Bu, Cy) + CNI and MTX/prednisone + ATG/alemtuzumab (Walters et al. 1996). For haplo, we compared TBI, Cy, and Flu + post-transplant Cy (PTCy) and sirolimus with/without Mycophenolate + ATG (Bolaños-Meade et al. 2012); with TBI, CY, Flu, and thiotepa + PTCy and sirolimus with/without Mycophenolate + ATG/alemtuzumab (De La Fuente et al. 2018). For MUD, we compared Flu, Mel + CNI, MTX, and methylprednisolone + alemtuzumab (Shenoy et al. 2016); with the Krishnamurti regimen.
Chi-squared test, log rank test and cox regression model were used for analysis. Propensity score matching was performed for age and donor type.

Results: For MSD, EFS was higher with the Krishnamurti (EFS 91.2%, p=0.002) and Walters (EFS 91.1%, p<0.001) regimens than with the Hsieh regimen (EFS 74.7%). The risk of aGVHD was higher with the Krishnamurti regimen (14.9%) than with the Hsieh regimen (5.8%, HR: 3.13, 95%CI: 1.04, 9.42, p=0.043). For haplo, aGVHD was higher with the De La Fuente regimen (26.2%) than with the Bolaños-Meade regimen (8.7%, HR: 3.67, 95% CI: 1.44, 9.35). For MUD, the Krishnamurti regimen had higher aGVHD (55.2%) compared to the Shenoy regimen (28.2%, HR: 3.08, 95%CI: 1.35, 7.00, p=0.007).

Conclusion: Current approaches for HCT for different donor types have largely comparable outcomes, but there are significant differences in individual outcomes that should be carefully considered.

Poster # 406

RETURN TO SCHOOL EXPERIENCES OF ADOLESCENTS AFTER ALLOGENEIC HEMATOPOETIC CELL TRANSPLANTATION

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Background: Return to school (RTS) after allogeneic hematopoietic cell transplantation (HCT) can improve health-related quality of life and promote positive adjustment, academic progress, and socialization. However, this process can present substantial challenges for HCT recipients after a prolonged absence from school during treatment.

Objectives: To explore challenges associated with RTS, as well as potential keys for a successful transition, from the perspective of adolescent HCT recipients

Design/Method: From August 2020-June 2021, we conducted semi-structured interviews over video with English-speaking adolescents who underwent HCT for malignant or non-malignant conditions at our institution and had returned to in-person school post-HCT. To gain an in-depth understanding of typical challenges regarding the post-HCT return to school process in this population and potential areas for improvement, we conducted a qualitative study utilizing conventional content and thematic analysis.

Results: : Nineteen patients (mean age at interview 17.5 years [range 12-22], mean age at HCT 13.8 years [range 10-18], 74% for malignant indication) participated in one-on-one interviews. Four global themes emerged from adolescents' experiences with RTS: (1) challenges of returning to school, (2) facilitators of a successful return to school experience, (3) overall perception of returning to school, and (4) recommendations to improve the RTS process for future patients undergoing HCT. Under the global theme of "challenges of returning to school", there were three sub-themes: (a) academic, (b) social, and (c) physical. Under the global theme of "keys for a successful return to school experience", there were two sub-themes: (a) support from peers and (b) support from non-peer allies. Under the global theme of "overall experience of returning to school", there were three sub-themes: (a) adjusting to a new life, (b) fulfilling academic duties, and (c) finding purpose. Under the global theme of "recommendations to improve the RTS process", there were five sub-themes: (a) to have peer support, (b) to establish connections, (c) to have mental health support, (d) to have a go-to point of contact navigator), (e) to have academic support.

Conclusion: Following HCT, adolescent patients experienced several challenges with RTS and described having strong sources of support as critical to a successful transition, physically, mentally, and socially. Our findings highlight important gaps in support and potential areas for improvement. Potential patient centered interventions may include age-appropriate resource toolkits, peer support, and navigation. Providing adolescents with additional assistance may optimize academic and social reintegration into school after HCT.

Poster # 407

A QUALITY IMPROVEMENT EFFORT TO IMPROVE WEIGHT LOSS AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Pediatric hematopoietic stem cell transplant (HSCT) is standard of care for a growing number of malignant and non-malignant conditions. Weight loss and severe malnutrition commonly occur after HSCT and increase patients' morbidity.

Objectives: We performed a quality improvement initiative during a 9 month span to reduce severe weight loss by 50% in the first 100 days following allogenic HSCT in pediatric patients (≤19 years).

Design/Method: In our QI protocol patients were included in a baseline and interventional evaluation. The baseline data was a retrospective review of sequential pediatric HSCT recipients - transplanted between February and November 2022 - to identify the rate of significant weight loss and location of care. Significant weight loss was defined as a weight-for-age z-score change of ≤ -0.7 compared to pre-transplant weight. Excluded patients included those with prolonged admissions (past day +45), those with significant complications leading to readmission, or relapse. Weights were monitored weekly. Three main and overlapping intervention cycles were performed. Participants in nutritional huddles and interventional planning included providers, nutritionists, and patients/caregivers occurred at days +30, 60, and 90 post-HSCT and were performed on all patients included in the interventional group. Handouts with instructions and recommendations such as initiating enteral feeds, increasing feeds, starting appetite stimulant were provided. Finally, we liberalized post-HSCT diet based on recent literature.

Results: Thirty-three pediatric patients were included in the baseline study. Outpatient clinic was identified as the primary setting for patients at risk for weight loss within the first 6-8 weeks post-HSCT via pareto chart. Twenty patients were initially included in the intervention phase (HSCT between January-August 2023), with 18 evaluated as 2 patients were excluded for relapse (n=1) and for multiple readmissions (n=1). After implementation of the three-pronged interventions, the number of patients experiencing significant weight loss decreased from 30.3% at baseline to 11.1% (10 patients to 2 patients). Both patients who failed at the three-month period after the intervention refused enteral tube feedings. Some patients developed significant weight loss but recovered by the 3-month mark with above interventions. The two groups baseline and interventional, were comparable for age and HSCT disease indication.

Conclusion: Weight loss is a common problem post-HSCT, particularly in the outpatient setting. Implementation of nutritional huddles, increasing patient education, and liberalizing post-HSCT diet decreased significant weight loss in patients in this QI study. Further QI studies to validate these data are merited as these low-cost interventions may improve nutritional support and decrease morbidity after HCT.

Poster # 408

HEMATOPOIETIC STEM CELL TRANSPLANT IN THE PEDIATRIC/AYA BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM

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Background: Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare hematologic malignancy typically associated with older patients. With more attention being paid to the presence of BPDCN in the pediatric and AYA population, prognostic indicators have still not been established, hindering standardized treatment approaches, and rendering the role and timing of hematopoietic stem cell transplant (HSCT) ambiguous.

Objectives: We reviewed the international, published experience in utilizing HSCT as consolidative treatment of BPDCN in the pediatric, adolescent, and young adult population.

Design/Method: Literature review was performed to identify all published cases of patients 20 years old and younger who underwent therapy for BPDCN including HSCT at some point in their treatment between 2000 to the present.

Results: We identified 21 case reports of patients with BPDCN in which the median age was 9 years, 11 were male (52.3%). Regarding disease site at diagnosis, skin positive findings were in 15 patients (71.4%), with 3 (14.3%) patients presenting with skin only disease. Peripheral blood, bone marrow, and lymph node disease was found in 5 (23.8%), 12 (57.1%), and 12 (57.1%) patients respectively. Only 3 (14.3%) patients had CNS findings. In terms of initial therapy, 10 patients (47.6%) received ALL, 4 (19.0%) AML, 4 (19.0%) NHL, and 2 (9.5%) CHOP based regimens. One patient received Tagraxofusp monotherapy. Regarding donor source, 1 patient underwent autologous, 1 syngeneic, and 19 allogeneic HSCT (3 matched siblings, 2 haploidentical, 1 mismatched, 2 from cord blood, and remaining matched or unspecified). Regimens varied widely and were largely myeloablative and/or TBI based when reported. 18 (85.7%) were in complete remission at time of HSCT (14 in CR1, 3 in CR2, 1 in CR3), and 3 (14.3%) had persistent disease. Two patients underwent second HSCT after first and second relapse. Median overall survival was 16 (3.29-156) months. Three died of disease, 1 from pulmonary toxicity after conditioning, and 2 from therapy related myeloid disease.

Conclusion: The role of HSCT in the treatment of pediatric and AYA patients remains controversial. While there is more success in the initial therapy of these patients, especially when an acute lymphoid leukemia-based regimen is utilized, definitive indicators of increased risk for relapse are illusive. The role of post HSCT maintenance therapy, either with intrathecal prophylaxis and/or targeted therapeutic agents (e.g. tagraxofusp), remains unclear in this population. Further study is needed as to predictors of relapse, and thus those who would benefit most from early HSCT.

Poster # 409

YOUTH DECISION MAKING INVOLVEMENT BEHAVIORS IN REAL-TIME STEM CELL TRANSPLANT DECISIONS

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Background: Youth prefer to be involved in treatment decisions, as they are expected to adhere to medications and daily expectations of treatment. Yet youth voice is minimally present in treatment decisions like stem cell transplant (SCT) that require frequent medications and social isolation to be successful in curing cancer and chronic illness. The youth-parent interaction offers a target to investigate youth decision making involvement (DMI) in SCT decisions as youth look to their parents to buffer and facilitate exchange of health information.

Objectives: The purpose of this study is to identify barriers and facilitators to youth DMI behaviors in the SCT decision by investigating youth-parent interactions.

Design/Method: We used mixed-methods and report our quantitative survey findings from 10 youth-parent dyads (n=20) of which we achieved data saturation in our qualitative data. Youth and parents independently completed the 5 subscales of the DMI Scale two weeks after their SCT consultation visit:

youth expressing, youth seeking, parent expressing, parent seeking, and joint/options. The 3-5 items on each subscale were averaged, with higher subscale scores indicating that DMI behavior occurred more, capturing the types of involvement rather than a total level of involvement. We used descriptive statistics to summarize the survey data

Results: Youth were 8-16 (median 12) years of age. All had a nonmalignant diagnosis. Youth and parent mean scores were similar on all DMI subscales. On a 4-point Likert scale ranging from 'Not At All' to 'A Lot', mean youth expressing subscale scores (youth-reported 2.3, SD=0.74 and parent-reported 2.3, SD=0.90) were less than parent expressing subscale scores (youth-reported 3.1, SD=0.53 and parent-reported 3.2, SD=0.75). Mean youth seeking subscale scores (youth-reported 2.3, SD=0.82 and parent-reported 2.5, SD=0.99) were also less than parent seeking subscale scores (youth-reported 3.2, SD=0.59 and parent-reported 3.4, SD=0.60). Youth-reported (2.8, SD=0.59) and parent-reported (2.7, SD=0.60) mean subscale scores of discussing options were fairly neutral. One item from the joint/options subscale measuring parents soliciting questions from youth was high, mean scores of 3.4 (youth-reported) and 3.5 (parent-reported).

Conclusion: Youth and parent scores indicated agreement that youth-initiated seeking and expressing behaviors were less than parents in real-time SCT decisions. Parents sought youth questions and opinions about SCT, told youth their opinion was important, and listened to youth. Forthcoming mixed methods analysis will include data triangulation of individual interview and behavioral observations from SCT consultation visits. This comprehensive understanding of the barriers and facilitators to youth DMI behaviors will inform a family intervention in SCT decisions.

Poster # 410

INCREASING PALLIATIVE CARE TEAM INVOLVEMENT IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT PATIENTS

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Background: Palliative care facilitates communication, helps with physical and psychological symptom management, and assists in goals of care and advance care planning discussions. Multiple organizations, including the American Academy of Pediatrics and American Society of Clinical Oncology encourage palliative care engagement and their involvement with hematopoietic stem cell transplant (HSCT) patients has been shown to be beneficial as HSCT is associated with a high degree of morbidity and possible mortality.

Objectives: To increase the number of PaCT consults for patients receiving HSCT for our targeted diagnoses from 48% to 75% by December 2023.

Design/Method: Chart review was conducted for patients who underwent HSCT from July 2020 to July 2022. Demographics documented included reason for and date of HSCT, date of PaCT consult and living status. A targeted diagnosis list was compiled based on which patients were felt to benefit most from palliative care involvement: relapsed or refractory leukemias and lymphomas, myelodysplastic syndrome, high risk myeloid leukemias and metabolic disorders, such as Hurler syndrome. The first plan-

do-study-act (PDSA) cycle included discussion of the project at division meetings and education regarding palliative care and evidence of its involvement in HSCT patients. The second PDSA cycle involved revision of the HSCT referral form to include the question “Is PaCT consulted.” During this time, PaCT also started attending the weekly transplant team meetings to discuss current and upcoming patients.

Results: Baseline data from July 2020 to July 2022 revealed 48 patients underwent HSCT, 25 of whom had a targeted diagnosis. PaCT met 12 of the 25 patients (48%). From the initiation of the project on 1/1/23 to 11/30/23, 14 patients with a targeted diagnosis underwent HSCT. Eight of the 14 patients (57%) received a PaCT consult.

Conclusion: Palliative care involvement in pediatric oncology is well established, but its role in HSCT patients continues to be explored. As HSCT patients receive more intense therapy, have frequent deaths in intensive care units and can have limited opportunity for end of life planning due to rapidly changing clinical courses, early integration of PaCT could allow for decreased symptom burden and distress for both patients and families. Future PDSA cycles to further increase involvement include adding PaCT consultation to the transplant evaluation order set in the electronic medical record and review of the comments on the completed HSCT referral forms to identify possible barriers in the PaCT consultation process.

Poster # 411

ACUTE PERICARDIAL EFFUSION AFTER HEMATOPOIETIC CELL TRANSPLANTATION: SINGLE CENTER EXPERIENCE

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Background: Pediatric hematopoietic cell transplant (HCT) is associated with significant morbidity and mortality. Pericardial effusion (PEF) is an underestimated complication that occurs post-HCT in 5-17% of adult HCT recipients. In pediatrics, prior literature addressing risk factors, incidence, etiology, management, and outcomes of PEF post-HCT suggests a prognostic impact on survival.

Objectives: We report a retrospective review study evaluatingincidence, associations, and clinical course of clinically significant PEF (cPEF) following HCT in a large single-center pediatric cohort. We describe our current clinical experience and inform ongoing scientific needs.

Design/Method: We performed a retrospective study evaluating 703 allogeneic HCT recipients between January 2010 and December 2020. ICD-10 codes were queried for a PEF diagnosis. We defined cPEF as symptomatic with moderate-large effusion, clinical or echocardiographic evidence of tamponade, necessity of medical interventions or pericardiocentesis or a combination of the above. Outcomes in patients with cPEF were described.

Results: We identified 141 patients with a PEF diagnosis; 68 were excluded based on PEF being diagnosed: pre-HCT, or after second HCT. Of 703 patients, PEF was diagnosed in 10% (73/703) of patients, while cPEF was identified in ~6% (40/703). Median time to PEF development was 92 days post-

HCT (1-403 days).
Among 40 patients with cPEF, 58% (n=23) were male; the median age at transplantation was 13 years (0.2-22 years). The indication for HCT was malignancy in 68% (n=27). Myeloablative conditioning was used in 70%. Around half of patients were managed with observation alone. Twelve patients were managed medically with diuretics, corticosteroids, NSAIDs or other anti-inflammatories. Pericardiocentesis was performed in 20% (n=8), fluid analysis was unrevealing except for CMV detection in one patient. We noted aGVHD in 30% (n=12) and cGVHD in 5% (n=2). TA-TMA was present in 45% (n=18) and CMV infection in 43% (n=17) patients. Ultimately, 24 patients (60%) had resolution of cPEF. At 1-year post-HCT, 19 patients with cPEF were alive.
Landmark analysis demonstrated that, out of the patients that remained alive at day 92, the patients that had already developed cPEF had a significantly higher risk of death (HR=2.579, p=0.0167) compared to those that had not yet developed any PEF. Further analysis including 502 patients without PEF is ongoing.

Conclusion: In our cohort, the incidence of PEF was comparable to what has been previously reported. Clinically significant PEF post-HCT is multifactorial. TA-TMA, CMV infection, and aGVHD commonly co-occurred with cPEF. Prospective studies identifying optimal screening, associations, and management of cPEF after pediatric HCT are necessary.

Poster # 412

INFLAMMATORY BOWEL DISEASE FOLLOWING ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANT IN SICKLE CELL DISEASE

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Background: Gastrointestinal complications (GICs) are prevalent following allogeneic hematopoietic cell transplantation (HCT), with graft-versus-host disease (GvHD) being a primary concern. However, diagnostic challenges arise from non-specific symptoms, potentially obscuring rare etiologies such as inflammatory bowel disease (IBD). This study explores three patients with sickle cell disease (SCD) who developed IBD-like features following allogeneic HCT.

Objectives: The primary objective is to enhance awareness of IBD as a potential complication of allogeneic HCT, particularly in patients with SCD, as early detection and treatment is crucial. The secondary objective is to review current literature and identify areas for future research.

Design/Method: We conducted a retrospective analysis of three patients with SCD who underwent allogeneic HCT and subsequently developed signs and symptoms resembling IBD.

Results: Patients #1 and #2 underwent non-myeloablative and reduced intensity conditioning HCT from their matched siblings, respectively, while patient #3 received a myeloablative haploidentical second HCT. All patients received peripheral blood stem cell grafts and sirolimus for GvHD prophylaxis. The patients developed diarrhea, weight loss, and additional gastrointestinal symptoms within two years of transplantation. GvHD and sirolimus toxicity were initially considered, however, symptoms persisted despite appropriate GvHD treatment and discontinuation of sirolimus. The patients subsequently

developed clinical, endoscopic, and pathological features suggestive of IBD, including colonic ulcers and non-caseating granulomas. Colonic ulcers were distributed in a pattern consistent with gut-associated lymphoid tissues (GALT) in patients #1 and #2. Symptoms resolved with IBD-directed therapies in all patients. Patient #1 and #3 are alive, in remission from IBD on infliximab and mesalamine, respectively, with stable mixed donor chimerisms. Patient #3 is alive, off IBD therapy without symptoms, and with full donor chimerisms. Genetic analysis identified a variant of unknown significance (VUS) in ANKF1 in patient #1, while genetic analysis was not performed in patients #2 and #3.

Conclusion: Limited literature exists regarding the development of IBD following HCT. The diverse inflammatory pathologies observed emphasize the need for vigilance in diagnosis and management of GICs post-HCT. Factors such as autoimmune dysregulation, conditioning regimen, and immune reconstitution may contribute to the pathophysiology of IBD in this patient population. Genetic factors, suggested by the VUS in patient #1, may play a role. However, further exploration of GALT's involvement and its modulation by conditioning regiments is warranted given the endoscopic findings in our patients.

Tarantino et al., Clin Hematol Int, 2021.
Van Haaften-Visser et al., Journal of Biological Chemistry, 2017.
Koboziev et al., Ann N Y Acad Sci, 2010.

Poster # 413

PROLONGED SARS-COV-2 RNA POSITIVITY IN TWO CHILDREN UNDERGOING STEM CELL TRANSPLANTATION

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Background: The outcome of prolonged SARS-CoV-2 RNA positivity in nasopharyngeal swabs in immunocompromised individuals, particularly allogeneic hematopoietic stem cell transplant (also HSCT) recipients, remains unknown.

Objectives: We present our experience with two children who had prolonged positive SARS-CoV-2 RNA in nasopharyngeal samples after allo-HSCT.

Design/Method: During the COVID-19 pandemic, transplant patients were required to undergo regular SARS-CoV-2 testing upon admission. Those who tested positive were transferred to the COVID unit. Once negative results were achieved, they returned to the Hematology/Oncology floor.

Results: 16-year-old male diagnosed with high-risk AML (t(15;17) and FLT3 mutation-positive) was initially treated with the AML-MRC-15 protocol. Due to a lack of response, he underwent allo-HSCT from an HLA fully matched sibling. On day 11, he developed febrile neutropenia, and broad-spectrum antibiotics were initiated. A nasopharyngeal swab was positive for SARS-CoV-2 RNA, leading to the patient's transfer to the COVID unit. Four days later, he tested negative and was returned to the SCT unit. On day 35, grade 3 graft versus host disease (GVHD) of the skin and intestinal system developed, and a steroid was administered in addition to cyclosporine. Steroids controlled the GVHD, however, BK hemorrhagic cystitis and CMV reactivation occurred. On day +43, he tested positive for SARS-CoV-2 again and remained positive until day +140. SARS-CoV-2 RNA returned to negative on day 145 as the

steroid gradually decreased but GVHD flared up again. The patient died of multiple complications and sepsis on day +200.
A 9-year-old girl with severe aplastic anemia underwent unrelated allo-HSCT, but she developed anaphylaxis during DMSO product infusion and did not get an adequate number of stem cells. During febrile neutropenia, SARS-CoV-2 PCR was positive. After the first allo-HSCT failed, a second transplant from the haploidentical brother was performed. Similar to the first case, the clinical course involved the development of grade 2-3 skin and intestinal GVHD, prompting the addition of steroid therapy. Although steroids stabilized the GVHD, complications such as BK hemorrhagic cystitis and CMV reactivation occurred. The positive SARS-CoV-2 RNA test persisted until day +160. With GVHD controlled through extracorporeal photopheresis and ruxolitinib, steroids were gradually reduced over time, resulting in the return of SARS-CoV-2 RNA to negative status. On day 360, the patient was doing well.

Conclusion: Our experience suggests that prolonged immunosuppression in children receiving steroids, who developed GVHD and underwent allo-HSCT, resulted in the reactivation of several viruses, including CMV and BK, and also contributed to the persistence of SARS-CoV-2 RNA positivity

Poster # 414

23-YEAR-OLD FEMALE WITH CHYLOTHORAX AND DVT AFTER BONE MARROW TRANSPLANT (BMT)

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Background: Chylothorax occurs when chyle leaks into the pleural space creating an effusion. Though rare in children, it most commonly occurs as a result of cardiothoracic surgery; however, other less common causes include trauma, malignancies, autoimmune conditions, and upper extremity thrombosis. When resulting from a thrombosis in the setting of an oncologic diagnosis, a chylothorax can be difficult to manage. The principal treatment includes eliminating long-chain triglycerides from the diet, but somatostatin analogs, glucocorticoids, pleurodesis, or surgical intervention may be warranted.

Objectives: To describe a case of a 23-year-old female diagnosed with a chylothorax and upper extremity DVT after BMT.

Design/Method: Case Report

Results: A 23-year-old female with T-Cell lymphoblastic leukemia received treatment per AALL0434. When in remission, she underwent a mismatched unrelated PBSC transplant after a preparative regimen of fludarabine, TBI, and post- cyclophosphamide per ACCESS stratum 1 regimen B. She engrafted on day +30 with conversion to donor blood type on day +41. Her course was complicated by sinusoidal obstruction syndrome with HRS, which was treated with defibrotide and resolved by day +38.
At the time of her initial T-cell ALL diagnosis, she was noted to have a large left leukemic effusion and mediastinal mass, both of which resolved prior to transplant. However, shortly after engraftment, serial chest x-rays used for evaluation of chest pain and a new oxygen requirement demonstrated an enlarging left pleural effusion. On day +41, she underwent chest tube placement and was diagnosed with a chylothorax. Initial treatment for this high output effusion included diet modification, albumin infusion, and IVIG. Investigation into the cause of this chylothorax revealed an acute thrombus of the left internal jugular vein, innominate vein and subclavian vein for which lovenox was started on day +46. Due to her

persistent high output effusion despite diet modification and octreotide, on day +59 she underwent a thoracic lymphangiogram with thoracic duct coil and glue embolization. There has been resolution and no recurrence of the chylothorax. For her DVT, she was transitioned to apixaban and the clot resolved.

Conclusion: BMT patients are at high risk for DVT given their malignancy, central lines, and limited activity. Though extremely rare, a chylothorax can result from an upper extremity DVT. This case illustrates the importance of having a low suspicion for a chylothorax in any high-risk patient with a persistent and refractory pleural effusion.

General PHO (501-521)

Poster # 501

TEACHING THE PATIENT EXPERIENCE TO PEDIATRIC ONCOLOGY TRAINEES

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Background: To address the increasing shortage of residents applying for pediatric hematology/oncology fellowships, we need to show the advantages of our field to students while still in medical school. A career in Pediatric Hematology/Oncology offers more work variety and patient continuity than any other field of medicine, with outcomes that are excellent, facts that are underappreciated by students who usually have only a passing exposure to the field. Allowing students to interact with oncology patients and learn the patient experience may increase desire to apply to this specialty.

Objectives: Since 2008, we have offered an innovative clinical rotation to third and fourth year students, designed to provide insights on family function during illness, health systems issues, and the complexity of interdisciplinary care for the acutely ill. For two weeks, students are relieved of clinical duties and spend time with several children and their families on the pediatric oncology service, interacting with them wherever they are: in clinic, the inpatient unit, waiting rooms, hallways, or the OR. Students create a daily narrative about their experiences, which is submitted to the course director at the end of the rotation.

Design/Method: Using qualitative methods, a trained research team analyzed the 120 student narratives submitted from 2008 through 2019. Statements that exhibited humanism were extracted and reduced to five common themes.

Results: The narratives revealed: 1) A heightened sense of empathy; 2) The ability to self-structure clinical time and experiences; 3) Enhanced communication with both team members and patients, especially during “down time” in waiting rooms; 4) An appreciation of and empathy for family dynamics during acute and chronic illness; 5) Insights into important system issues such as hospital admission, consent processes and prolonged waiting times.

Conclusion: This study demonstrates the power of a brief, immersive experiential teaching method that counters empathy drift and burnout, enhances medical student humanism, and in the process sparks interest in pediatrics and pediatric oncology, by highlighting the patient experience. By processing

experiences through narrative, students' sense of empathy was reinvigorated during a critical time in their medical training. For pediatric hematology/oncology specifically, we believe that offering a similar rotation at more medical schools may increase interest in the field among students at a formative time in their training.

Poster # 502

CURRENT APPROACHES TO MEDICAL EDUCATION AMONG PEDIATRIC HEMATOLOGY/ONCOLOGY FELLOWSHIP PROGRAMS

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Background: Application of evidenced-based practices are often lacking in medical education. Increased recognition that traditional methods of knowledge delivery are often less effective than those based in relevant learning theories has led to improved ability to meet the needs of adult learners. Significant variation occurs in education approaches among GME training programs, including Pediatric Hematology/Oncology (PHO).

Objectives: In order to gain a greater understanding of the design and implementation of curricula for PHO trainees, we designed a study to assess current approaches to education and identify potential opportunities for incorporation of evidence-based practices related to established theories.

Design/Method: A national survey was distributed to directors of ACGME-accredited PHO programs to investigate current trends in education design. This research was approved by the IRB at Seattle Children's Hospital. Respondents were contacted via email, and the survey was distributed by REDCap. Data were collected from April-July 2023. Quantitative data were analyzed descriptively. Free-text responses were analyzed with directed content analysis. Consideration was given to how programs reported using evidence-based practices guided by learning theory to support deeper learning and self-direction among their fellows. Codes were collaboratively combined and organized into categories.

Results: Of the 77 eligible participants, 46 completed the survey (59.74% response rate). Participants represented a spread of geographic regions and class sizes. On a 5-point Likert scale, respondents reported a wide range of familiarity with adult learning theory (range 1-5, median 3) and self-regulated learning (range 1-5, median 2). 100% of programs reported utilization of traditional lectures format, >90% board style questions, case-based learning, independent reading, and journal club. 70% of programs incorporated chalk talks, and 50% online modules or simulation. Program directors recognized varying levels of need for development in several domains, including incorporation of educational frameworks, support for structure and content of didactics, and implementation of feedback related to education sessions.

Conclusion: Differences in approaches were described after data review, revealing a wide range of familiarity with and application of specific educational theories. While programs employed active learning strategies to varying degrees, the most common method of education delivery across programs was a traditional lecture format. Analysis of free text responses revealed that efforts to consider principles of adult learning theory and self-regulated learning are not consistent among programs. Through this study, we propose potential opportunities for targeted education and curriculum

development, including faculty development for education sessions, increased incorporation of active learning strategies, and intentionality in considering underlying fundamental educational theories.

Poster # 503

FEASIBILITY OF A VIRTUAL PEDIATRIC HEMATOLOGY-ONCOLOGY CURRICULUM FOR PEDIATRIC RESIDENTS IN GUYANA.

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Background: Approximately 80% of pediatric cancer patients live in low-and-middle income country (LMIC) where the cure rate ranges between 5 and 50%, compared to the 80% cure rate seen in high-income countries (HIC). Amongst the factors that contribute to these disparities is the scarcity of trained professionals in hematology-oncology, which often translates into poorer quality of care and missed diagnostic and therapeutic opportunities. In recent years, there has been increased interest in closing the educational gap for physicians in resource-limited countries. International partnerships that allow twinning between HIC and LMIC have been successful, but they have mostly targeted providers seeking post-residency education. Virtual learning has been proposed as a sustainable alternative for training clinicians residing in limited resource areas. To our knowledge, there are no current virtual educational initiatives in pediatric hematology-oncology (PHO) that target international pediatric residents.

Objectives: To evaluate the feasibility of a virtual curriculum in PHO for the pediatric residents at Georgetown Public Hospital Corporation in Guyana.

Design/Method: We conducted a prospective cohort study where all pediatric residents at the Georgetown Public Hospital Corporation (GPHC) in Guyana (a LMIC) were included. At GPHC, PHO patients are cared for by pediatric residents with no formal PHO education. Our intervention consisted of eight, two-hour long, live-streamed, synchronous sessions delivered throughout the month of October, 2023. The first hour was devoted to case-based discussions of patients with a hematologic or oncologic diagnosis whom the residents cared for during the year prior to the curriculum, followed by a one-hour lecture that covered the epidemiology, presentation, diagnostic testing, and treatment of the discussed diagnosis. Participants completed a post-intervention knowledge test and a curriculum evaluation survey to assess the impact of the curriculum.

Results: One hundred percent of eligible residents completed the curriculum evaluation (n=13) and agreed that the curriculum increased their knowledge in pediatric hematology and oncology. One hundred percent of residents reported that the content of the curriculum aligns with the needs of pediatric healthcare professionals at GPHC. Ninety two percent (n=12) of residents reported feeling more confident in diagnosing and managing common pediatric hematologic and oncologic conditions while 100% of residents felt more confident in applying what they learned in real patient encounters.

Conclusion: Delivery of a virtual PHO curriculum to residents at GPCH was feasible and increased perceived knowledge and confidence among residents.

Poster # 504

EVALUATING THE IMPACT OF AN UNCONVENTIONAL ELECTIVE IN NARRATIVE MEDICINE AND PEDIATRIC ONCOLOGY

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Background: Empathy, an essential component of a humanistic approach to medicine, declines throughout medical training, often due to the nature of the training itself. An emphasis on patient-centered care may combat this decline, particularly when combined with narrative reflection. Narrative medicine is a growing field of study and is a beneficial adjunct to psycho-oncology, which explores the psychological, social, and behavioral components of cancer care.

Objectives: Combining aspects of both narrative medicine and psycho-oncology, an immersive elective was created for medical students that entailed shadowing pediatric cancer patients. Rather than focusing on the medical aspects of care, students participated in a curriculum that explored the illness experience and health systems issues surrounding these patients and their families. Students reflected on their observations/experiences in a journal they submitted at the conclusion of the rotation. Analysis of the narratives has shown how such a rotation can instill humanistic values in students.

Design/Method: To analyze the elective's impact on students, a survey was sent to sixty-five current students who took the elective between 2021-2023. Students were given several statements to grade on a Likert scale developed from prior qualitative analyses of outcomes.

Results: Thirty-five students completed the survey (54% response). The majority strongly agreed/agreed that the elective led to the following positive outcomes: increased empathy and humanism, improved communication skills and meaningful engagements with patients/families. The experience also provided insight into systems issues faced by cancer patients and their families.

The elective taught students to create a narrative that helped process their feelings and reactions to difficult medical situations while significantly enhancing their professional development. From the created narratives, several common themes emerged: increased understanding of patient and family experiences in oncology, improved ability to process emotions in difficult situations, improved communication skills, and improved understanding of healthcare systems.

Conclusion: Teaching methods such as this unique opportunity during the clerkship experience show the potential to promote development of medical students' ability to connect and communicate with patients in an impactful way. Further study is underway to determine if such learning experiences may contribute longitudinally to increased levels of medical student empathy and humanism, and in the process, combat "burnout" and promote interest in Pediatric Oncology among students at a formative time in their training.

Poster # 505

TRENDS FROM BEHAVIORAL HEALTH SCREENING IN A PEDIATRIC HEMATOLOGY ONCOLOGY CLINIC

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Background: Patients presenting to an outpatient Pediatric Hematology and Oncology (PHO) clinic are often treated for illnesses that are associated with significant and emotional distress. Adolescent and young adult (AYA) patients, specifically, are at an important stage of psychological development, and when receiving a diagnosis of chronic illness or experiencing a life-threatening event, these patients are expected to have increased levels of uncertainty and mental distress.

Objectives: The objective of this study is to identify trends within the AYA PHO population, specifically different diagnoses that may be at higher risk for mental health conditions.

Design/Method: A mental health screening process with PHQ and GAD questionnaires was implemented in an outpatient PHO clinic. Data was compiled on questionnaire scores, diagnosis category, and if patient is on active treatment for 316 participants. Diagnoses from clinic were separated into five categories: coagulation, benign hematology, brain tumors, solid tumors, and leukemia/lymphoma.

Results: A Kruskal-Wallis test resulted in a p-value of 0.024 for diagnosis category versus PHQ2, indicating median PHQ2 scores differ for at least one diagnosis category. A Dwass, Steel, Critchlow-Flinger multiple comparisons method was applied for the post-hoc pairwise multiple comparisons. With a corresponding p-value of 0.0362, there is sufficient evidence that the PHQ2 score differs between coagulation and leukemia/lymphoma, with higher averages for coagulation disorders. Another Kruskal-Wallis test resulted in a p-value of 0.453 for diagnosis category versus GAD2, indicating insufficient evidence that median GAD2 scores differ for at least one diagnosis category

Conclusion: Initial screeners used for depression within an AYA PHO population are significantly higher within patients with coagulation disorders. This information may help clinics target mental health resources to at risk groups.

Poster # 506

DEVELOPING TOOLS TO IMPROVE THE RESIDENT EXPERIENCE ON THE PEDIATRIC HEMATOLOGY ONCOLOGY ROTATION

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Background: The demands of pediatric residents have increased due to patient complexity, duty hour restrictions, and increasing documentation requirements with less time to complete tasks. This is exacerbated on inpatient pediatric hematology oncology (PHO) rotations due to higher acuity, limiting educational opportunities and leading to reduced resident satisfaction and sentiments of inadequate learning in this subspecialty. Standardized tools with key points about essential PHO educational topics can serve as a guide while on rotation and as a long-term reference to augment their experience even during a busy inpatient rotation.

Objectives: To investigate the feasibility, utilization, and impact of an educational tool bundle for

pediatric residents on the inpatient PHO rotation.

Design/Method: An educational tool bundle was created, including resident expectations and a booklet of PEARLs for 15 key topics from the ABP content specifications plus associated articles. The bundle was sent electronically prior to the rotation and available in paper format in their workroom. A central checklist was used to track topics covered; feedback was collected at the end of the rotation via an anonymous survey.

Results: An average of 6 topics were covered per rotation. Of the residents that provided feedback, 100% utilized the educational PEARLs and indicated these were valuable both at the time of rotation as well as a reference for future practice; more than 50% preferring to have both paper and electronic formats. Additionally, 86% of participants found having expectations ahead of time prepared them for the rotation. For the associated articles, 43% reviewed some of the articles with 29% indicating they were likely to refer to them in the future. All respondents suggested electronic format alone would be sufficient.

Conclusion: Standardized educational tools improve the resident learning experience serving as a reference both on the PHO rotation as well as in their future pediatric career. Based on their feedback, the most vital components included a document outlining expectations to prepare residents for the rotation and a guide to essential PHO topics with key take-home points. Next steps will be to compare in-training exam results pre and post implementation to assess for improvements in knowledge acquired. Additionally, the information in the PEARLS can be refined through input from outside PHO experts and later validated through implementation at other pediatric resident programs to create standardized tools that can be replicated and disseminated amongst pediatric residency training programs.

Poster # 507

COMFORT ROUNDS: IMPLEMENTING DEBRIEFING SESSIONS FOR PEDIATRIC HEMATOLOGY/ONCOLOGY TEAM MEMBERS

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Background: Pediatric hematology/oncology (PHO) is an intense field in which team members care for seriously ill children and witness death as a regular part of their job. Repeated exposure to high levels of treatment and disease related morbidity and mortality, particularly without opportunity to formally acknowledge and share the experience, puts PHO team members at high risk for developing compassion fatigue. When health care workers experience compassion fatigue, this can impact their overall well-being as well as patient care. The opportunity to debrief difficult patient cases at expected and regular intervals is an effective way to mitigate this risk and strengthen care teams.

Objectives: Establish routine debriefing sessions

Design/Method: This project was conducted at a tertiary pediatric cancer center. Participation was open to any team members who participated in the care of PHO patients. Debrief sessions were held once per month and moderated by a resilience and wellbeing nurse leader. Participants were requested to

complete pre- and post- surveys created by the research team to assess mood/emotions before and after the sessions.

Results: A total of six sessions were held over six months. The number of participants ranged from 8-17 people and included medical assistants, school liaisons, parent hosts, infusion nurses, floor nurses, nurse educators, pediatric residents, PHO fellows, PHO attendings, PHO nurse practitioners, members of the pediatric palliative care team and pharmacists. All participants indicated that the debrief sessions were helpful. All but one participant had the same or increased mood score on pre and post survey results. Topics discussed including coping with recent patient deaths, difficult patient conversations, approaching code status discussions, and finding joy and gratitude in our work. In asking for feedback, participants expressed appreciation for these sessions and asked for more to be scheduled.

Conclusion: Historically at our institution, there was a lack of a consistent and formal setting to debrief difficult patient circumstances and collectively share experiences. Implementing routine sessions was a feasible and effective method for coping with traumatic patient events and promoted healthy emotional practices. These sessions were widely accepted across multiple disciplines and the feedback on the sessions was uniformly positive. Continuing scheduled debriefs has potential to improve care team member professional quality of life and emotional health. Resulting in better care for patients as well as improved job satisfaction and mental health for care team members. Future directions include sustaining this initiative by continuing sessions at regular intervals and working to increase accessibility and engagement.

Poster # 508

IMPROVING FELLOW CONTINUITY CLINIC WITH MULTIPLE SPECIALTY CLINICS: A QUALITY IMPROVEMENT INITIATIVE

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Background: Continuity clinic is an integral component of graduate medical education, but barriers often impede effective training. In the Pediatric Hematology/Oncology fellowship program at St. Jude Children's Research Hospital, fellows have a weekly continuity clinic day during which they longitudinally manage patients in 5 subspecialty clinics, each in a separate location in the hospital. Prior to this initiative, feedback from fellows and faculty indicated that clinic structure and workflows negatively impacted the fellow educational experience and readiness for independent practice.

Objectives: The aim of this initiative was to increase fellow satisfaction with education and workflow in continuity clinic from baseline scores of 2.25 and 1.83 (scale from 1 to 5, with 1 representing 'very dissatisfied' and 5 representing 'very satisfied') to a goal of 3.5 for each.

Design/Method: A multidisciplinary team of key stakeholders was formed, and a fishbone diagram was completed to identify contributing factors. A baseline survey to assess fellow satisfaction was completed in June 2022, then repeated regularly during an intervention period (July 2022-June 2023) and a follow-up period (July 2023-December 2023). A separate survey assessed as balancing measures the satisfaction of faculty, advanced practice providers (APPs), and nurses with the workflow, educational

experience, and patient care. A key driver diagram was developed to demonstrate the theory for improvement.

Results: Five key interventions were implemented and refined through iterative plan-do-study-act cycles using the Model for Improvement: 1) assignment of a clinical mentor for each first-year fellow, 2) enhanced APP support during clinic days, 3) limitation of 8 patient visits per clinic day, 4) adjustments to the scheduling template, and 5) development of guidelines for the fellow primary patient panel. The average response rate to the fellow survey was 57%. Fellow satisfaction with the educational experience increased from a baseline of 2.25 (SE=0.25) to an average of 4.11 (SE=0.16) during the final quarter of the intervention period. Fellow satisfaction with clinic workflow increased from a baseline of 1.83 (SE=0.27) to an average of 3.78 (SE=0.22) over the same period. Both increases were sustained during the follow-up period. There was no significant decrease in faculty, APP, or nurse satisfaction on any measure at any point.

Conclusion: Key interventions led to sustained improvement in the educational experience and workflow of fellows in a longitudinal, subspecialty continuity clinic.

Poster # 509

QUALITATIVE ASSESSMENT OF A PEDIATRIC HEMATOLOGY/ONCOLOGY FELLOWSHIP PROGRAM: THE FELLOWS' VIEW

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Background: In 2021 and 2022, the pediatric hematology/oncology fellowship program at St. Jude Children's Research Hospital was placed on probation status by the Accreditation Council for Graduate Medical Education. To address this, multiple changes were implemented in the areas of program leadership, curriculum, staff professionalism/anonymous reporting system, faculty development, clinic efficiency, faculty evaluation, feedback of fellows, and fellow wellness. The program was reaccredited in April 2023.

Objectives: To explore perceptions of the fellowship program by fellows during and after probation status.

Design/Method: Semi-structured interviews were conducted with current and recently graduated fellows from June to July 2023. The interview focused on their perceptions of the program and implemented changes during and after probation. Interviews were transcribed and analyzed using rapid qualitative analysis techniques by two researchers.

Results: Twenty-three fellows were invited and 19 (83%) agreed to participate. Favorable themes included a positive outlook after probation (e.g., happiness and optimism) (n=12), established program leadership (n=15), comfortable reaching out to leadership (n=14), development of a structured curriculum (n=14), and a coordinated effort to improve fellow wellness (n=14). Unfavorable themes were negative emotions during probation (e.g., shock, disappointment, and stress) (n=14), inefficient separation of five subspecialty clinics (n=13), and challenges with clinic scheduling (n=12). Identified

improvements after reaccreditation included program leadership (n=19), curriculum (n=18), faculty development and fellow wellness (n=13 for each), and staff professionalism, faculty evaluation, and fellow feedback (n=12 for each). Fewer interviewees identified improvements in clinic efficiency (n=10) and reporting unprofessionalism (n=7). Consistent themes identified across multiple items emphasized the importance of institutional culture change and support to sustain improvements.

Conclusion: Implementation of multiple changes led to positive emotions of fellows. Program leadership followed by curriculum were the most frequently identified aspects of improvement. Clinic efficiency and reporting unprofessionalism need further improvement, although fellows seem comfortable reporting to the program leadership for the latter. The overall improvements were seen by many of the fellows, however, ongoing improvements and persistent institutional support are required to ensure the continued advancement of the fellowship program.

Poster # 510

IMPROVING HANDOFF DOCUMENTATION THROUGH THE EHR: A QUALITY IMPROVEMENT PROJECT

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Background: Since the original I-PASS study in 2013, documented handoff has been an essential communication tool in the clinical management of patients across the country and, when used appropriately, results in an overall reduction in medical errors. Recent studies have demonstrated improved accuracy without significant increase in burden of handoff with direct incorporation in the electronic health record (EHR).

Objectives: To improve handoff documentation and accuracy on the inpatient pediatric oncology service at MD Anderson by creation and implementation of an EHR incorporated handoff.

Design/Method: This quality improvement project employed the Plan-Do-Study-Act (PDSA) method to systematically address and enhance the inpatient handoff process. A baseline survey was created with eleven questions to evaluate confidence, perception, and importance of current handoff documentation. The first cycle evaluated the previous process and results led to the creation of a new EHR integrated handoff. This document was oncology service specific and built with common preset phrases. Periodic feedback was elicited from fellows to assess confidence and accuracy of the handoff. Three months after introduction, an interim survey was collected to prepare for the next PDSA cycle.

Results: In July 2023, a presurvey was administered to 12 fellows, of which 10 responses were collected with an 83.3% response rate. From this initial survey, a documented EHR handoff was developed and distributed to fellows for use during inpatient service. A post implementation survey was collected in September 2023, and 10/12 responses were obtained. On pre-implementation, 50% of fellows reported dissatisfaction and 70% lacked confidence in the previous handoff process. Post-implementation, only 10% of surveyed fellows were dissatisfied and 10% lacked confidence in the new process. Of the fellows surveyed, 50% reported satisfaction with the new process. In addition, whereas the previous system saw 80% of fellows perceiving frequent inconsistencies in handoff materials, only 30% perceived frequent inconsistencies with the new process. Direct feedback was elicited with positive feelings towards efficiency and ease of use with the new system process. In addition, note templates were created from

the new handoff process for daily documentation.

Conclusion: Accurate and reliable handoff documentation integrated in the EHR improves handoff experience and provider confidence in patient care. Through development of a service specific EHR integrated handoff for the inpatient pediatric oncology service, we have improved confidence and satisfaction of handoff methods, along with improved perceived efficiency. Future directions will include continued improvement in written handoff and broader institution of these methods in the pediatric oncology department.

Poster # 511

EXPLORING CLINICIAN COMPASSION IN THE PEDIATRIC HEMATOLOGY/ONCOLOGY OUTPATIENT SETTING

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Background: Compassion is an emotional response to the pain and suffering of another, involving an authentic desire to help. The role of compassion is especially vital in the pediatric hematology/oncology outpatient setting where both patients and caretakers often have to cope with heavy and life-altering diagnoses. However, there is little research dedicated specifically to studying compassion in this subspecialty.

Furthering work in this area requires valid and feasible ways to measure clinician compassion in the pediatric hematology/oncology outpatient setting. We previously developed a 5-item compassion measure to assess patient experiences of clinician compassion that can be used in conjunction with the Clinician and Group Consumer Assessment of Healthcare Providers and Systems (CG-CAHPS) visit survey and recently validated its use in the pediatric outpatient setting, including the pediatric hematology/oncology outpatient setting.

Objectives: The objective of this study is to explore the results of a recently validated 5-item compassion tool used to measure patient assessments of clinician compassion in the pediatric hematology/oncology outpatient setting.

Design/Method: In this cross-sectional study, the 5-item compassion measure was incorporated into CG-CAHPS surveys and completed by parents of patients less than 18 years old. Surveys were distributed from February 2023 to September 2023 at a U.S. academic healthcare system. Responses were measured on a 5-point Likert scale and a descriptive analysis was completed, including frequencies, percentages, and 95% confidence intervals.

Results: The median patient age was 7 years, and 33% of patients were female. Additionally, 58% of patients were African-American and 25% of patients were Caucasian. All responders reported that their provider was “very good” at showing interest in their child as a whole person, being considerate of their child’s needs, and showing their child care and compassion during their visit. All responders reported that their provider was “good” (8%) or “very good” (92%) at caring for their child’s psychological or emotional well-being during their visits, and all responders reported that their provider was “good” (17%) or “very good” (83%) and gaining their child’s trust during their visit.

Conclusion: The 5-item compassion measure, newly validated for use in the pediatric hematology/oncology setting, measures how patients perceive compassionate care provided by pediatric hematologists/oncologists. Here, we explored the preliminary data with a descriptive analysis. Continuing, larger-scale studies can be used to identify gaps in compassionate care across various demographic groups or to test the efficacy of targeted interventions.

Poster # 512

IMPROVING PROCEDURAL CONFIDENCE AND SKILL WITH SIMULATION TRAINING IN PEDIATRIC HEMATOLOGY/ONCOLOGY

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Background: Procedural skills are critical in Pediatric Hematology/Oncology (PHO), as diagnosis and treatment often rely on bone marrow (BM) evaluation. Inadequate-for-interpretation BM specimens may lead to harm, through diagnostic delays and repeat procedures. Institutional data from 2006-2011 revealed 12.2% of BM biopsy (BMB) specimens were inadequate. Limited literature exists on procedural simulation in PHO. We developed a novel simulation-based curriculum for PHO trainees at The Hospital for Sick Children to strengthen procedural confidence and skill.

Objectives: This study aimed to reduce the number of inadequate BMB specimens obtained by trainees by 50% in one year and increase trainee confidence in procedural skills.

Design/Method: We developed an educational workshop for first-year fellows (Y1F) including hands-on training of BMB with manikin model. Outcomes included inadequate specimen rate and pre- and post-participant confidence. Data were collected on operator and pathology interpretation for all BMB samples from July 2022-June 2023 (pre-intervention) and July 2023-September 2023 (post-intervention). Statistical analysis was completed using Fisher's exact test for categorical variables and by t-test for quantitative variables.

Results: In the pre-intervention period, 161 BMB were performed: trainees n=97 (60.2%; Y1F n=43), staff physicians n=44 (27.3%), nurse practitioner/physician assistants (NP/PA) n=18 (11%), and unknown provider n=2 (1.2%).The inadequate specimen rate for trainees was 12/97 (12.4%), Y1F 4/43 (9.3%), staff physicians 9/44 (20.4%), and NP/PA 3/18 (16.7%). In the first three months post-intervention, trainees performed 41 (82%) BMB (Y1F n=18). The inadequate specimen rate by operator type was: trainees 6/41 (14.6%), Y1F 4/18 (22%), staff physicians 2/5 (40%), NP/PA 1/4 (25%). There was no significant difference in the rate of inadequate BMB specimens between timepoints (24/161 (14.9%), vs. 9/50 (18%), p=0.66). By 5-point Likert scale, Y1F confidence post-intervention increased for equipment selection (3.5 to 4.2, p=0.02), performing the procedure (3.1 to 4.2, p=0.01), and sample collection (2.85 to 4.2, p=0.001). Overall comfort in completing BMB was 3.3 pre-intervention and 3.9 post-intervention (p=0.18).

Conclusion: Procedural simulation training is a helpful tool to increase operator confidence. The post-intervention inadequate specimen rate was not significantly different from baseline. First-year fellows completed proportionally more BMB than in the pre-intervention period. Fellows perform the most

BMB. We expect targeting improvement toward this group will have the largest impact on patient harm reduction. Evaluation is ongoing to fully characterize the potential impact of procedural simulation training on specimen adequacy in the longer post-intervention period.

Poster # 513

IMPROVING SHARED SITUATIONAL AWARENESS TO IMPROVE SAFETY

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Background: Pediatric oncology and stem cell transplant (SCT) patients are vulnerable to communication errors that lead to undetected decompensation given patient complexity, large medical teams, and use of novel therapies. Poor interdisciplinary communication impedes the creation of shared situational awareness (SSA) – a mental model of a patient's clinical status and potential trajectory. Research has shown that improving SSA can reduce medical errors and enhance early recognition of decompensating patients (1, 2).

Objectives: To improve SSA on the oncology and SCT units to achieve smart goal of reducing emergent transfers (ET) and acute respiratory decompensations (ARD) events by increasing the average time between events by 20% over a 5-month period, from 26 to 31 days.

Design/Method: An interdisciplinary team analyzed past unanticipated decompensation events and current workflows. Key drivers included effective interdisciplinary communication, standardized workflows, and shared mental models of patient acuity. Based on analysis and review of literature (1,2), a new "watcher" pathway was implemented in iterative PDSA cycles on oncology and SCT units starting July 2023. The pathway is initiated when a care team member is concerned a patient is at risk for decompensation (a watcher) and includes a multidisciplinary huddle to discuss and document a structured SSA plan (concern, plan, and care escalation criteria). The primary outcome metrics were ETs and ARDs, defined as the transfer of patients from the acute care floor to the ICU where the patient received intubation or Bipap, vasoactive medications, or ³3 fluid boluses in the 60 minutes before or after ICU transfer, as markers for unanticipated decompensation events given ET are a predictor of poor patient outcomes (1,2). Data was collected by chart review 12 months prior to and 5 months after implementation. Special cause variation was determined by SPC t chart. Additional outcome metrics included a nursing survey. The process metric was watcher pathway usage.

Results: The watcher pathway was used over 60 times in five months with over 95% compliance during implementation. The average time between ETs and ARDs increased to 50 days (an 100% increase), though have not yet achieved special cause variation on SPC t chart. The nursing survey completed by 64 nurses showed improvement in self-reported SSA.

Conclusion: New watcher pathway improved SSA and met smart goal with increased number of days between unanticipated decompensation events by 100%. Sustainability planning is ongoing.

1 Brady Pediatrics 2013
2 Sosa Pediatrics 2021

Poster # 514

SEVERE REACTIONS TO RITUXIMAB IN CHILDREN

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Background: The anti-CD20 antibody rituximab is frequently administered for various conditions. While usually well tolerated, severe reactions may occur including anaphylaxis and rituximab-induced serum sickness (RISS). While anaphylaxis is usually well-recognized, RISS is a rare delayed hypersensitivity reaction that may be confused with severe infection or in some circumstances with primary disease flare-up.

Objectives: Our study objective was to extend our knowledge about severe infusion-related reactions to rituximab in children and adolescents, focusing on RISS and anaphylaxis.

Design/Method: We conducted a single-center retrospective study on children and adolescents who received rituximab between 2014 and 2021. Anaphylaxis was defined according to the diagnostic criteria proposed by the World Allergy Organization. RISS was defined as patients presenting fever and at least rash and/or arthralgia, 1 to 30 days following infusion, with no other confirmed pathologies explaining the symptomatology.

Results: 1534 rituximab infusions in 391 patients were included. Main indication was auto-immune disease (61% of patients). RISS was diagnosed in 7/391 patients (1.8%), all of whom had an auto-immune disease such as immune thrombocytopenia (ITP, 4/7 RISS patients). Mean time from infusion to RISS was 9 days (ranging from 6 to 12 days). Six patients had fever, rash and arthralgia. C-reactive protein or sedimentation rate were increased in all patients and complement was decreased in 83%. Three patients required admission to intensive care unit due to hemodynamic instability. All patients had complete resolution of symptoms within a few days of corticosteroids and/or intravenous immunoglobulins. Patients who received standard dose (375mg/m^2 vs 500mg/m^2) were at lower risk of developing RISS (RR 0.14, CI 0.03-0.74, p=0.016). Furthermore, occurrence of RISS was associated with greater chance in achieving partial or complete remission in ITP patients (RR=3, CI 1.47-6.14, p=0.033). Seven patients developed anaphylaxis (1.8%); five successfully received further infusions using desensitization protocols.

Conclusion: RISS is a rare hypersensitivity reaction. Our study suggests that it may be more frequent when rituximab is administered for an autoimmune condition, such as ITP. The classical triad of fever, rash and arthralgia appeared to be more frequent in children compared to adults, and biological inflammation and/or low complement can further support the diagnosis. In contrast with anaphylaxis, RISS should be considered as a contraindication for further rituximab therapy. Further studies are needed to evaluate if risk to develop RISS is associated with dose or quality of response in patients with ITP.

Poster # 515

TIME TO POSITIVITY ANALYSIS OF PAIRED CENTRAL AND PERIPHERAL BLOOD CULTURES FOR FEBRILE NEUTROPENIA

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Background: Central Line Associated Blood Stream Infections (CLABSIs) are potentially life-threatening complications for immunocompromised pediatric hematology/oncology (PHO) and bone marrow transplant (BMT) patients. For febrile neutropenia workup, established guidelines have historically recommended drawing blood cultures from both central and peripheral sources when a central venous line (CVL) is present and CLABSIs are determined by differential time to positivity (DTP) of central culture positivity ≧ 2 hours prior to peripheral culture. Our institution preferentially utilizes paired blood cultures for fever and neutropenia workup; however, institutional practices vary nationwide, as peripheral cultures are not always feasible in acutely ill pediatric patients, may delay antibiotic administration, and contamination with skin flora may cause false positive results.

Objectives: Our study retrospectively reviews our institutional experience with paired blood cultures during fever and neutropenia workup, aiming to answer if the addition of peripheral cultures and therefore DTP criteria were useful in determining CVL retention.

Design/Method: This study was approved by our Institutional Review Board. We reviewed all reported blood culture encounters from January 2020 through December 2021 in the emergency center (EC), PHO and BMT outpatient clinics and inpatient units, and our intensive care unit (ICU) for all patients diagnosed with hematology or oncology diagnoses. Positive paired cultures were assessed for DTP and if this criterion influenced CVL removal.

Results: During 2020-2021, 60 paired positive cultures were drawn: 44 from the EC and outpatient clinics, 12 from PHO floors, 2 from BMT, and 2 from the ICU. All but 2 cultures grew congruent microbes (96.7%). The DTP was over 120 minutes in 19/60 (31.7%) of cases. Central lines were removed in 34/60 (56.7%) of cases; only 9/34 (26.5%) of line removals were in cases where DTP was greater than 120 minutes. The most common documented indications for line removal were due to the infecting organism (19), sepsis (10), and persistent positive cultures (6); only twice were CVLs documented as removed solely due to DTP criteria. Twelve cases occurred where peripheral cultures were positive but central were negative; of these, 4 were considered contaminated from skin flora (25%).

Conclusion: CLABSIs were infrequently clinically defined by recommended DTP criteria, and the presence of CLABSI in and of itself was not a determining factor for line removal. Future directions include comparative outcome analyses of paired positive versus central-only positive cases.

Poster # 516

FEVER IN PEDIATRIC SICKLE CELL & ONCOLOGY: DECREASING TIME TO PRESENTATION FOR OUTPATIENT CARE

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Background: Pediatric oncology and sickle cell patients are at an exceedingly high risk of morbidity and mortality secondary to infection, especially when treatment is delayed. These patients have impaired immune responses, and fever can sometimes be the only indication of infection.

The Children's Hospital at Montefiore (CHAM), the only tertiary care center in the Bronx, cares for more than 900 patients in the sickle cell division and over 50 new cancer diagnoses annually. After developing fever, it often takes patients several hours to days to present to the hematology/oncology clinic. Barriers to care include poor comprehension of the emergent nature of fever in this population, as well as social obstacles such as insufficient access to transportation.

Objectives: We began a quality improvement initiative to improve fever education and decrease infection-related morbidity. Our SMART aim is to decrease the average time between fever to clinic presentation in pediatric oncology and sickle cell patients at CHAM by 25% from June 2023 to June 2024.

Design/Method: Our first plan-do-study-act (PDSA) cycle consists of a visual aid in the form of a magnet. The magnet includes temperatures at which patients should seek care (100.4 °F for oncology, 101.0 °F for sickle cell) and the clinic phone number. Three months of baseline data were collected including time of first fever, time to call clinic and time to clinic presentation. Data was collected via creation of a standardized clinic sick visit note. Parallel data was collected after the introduction of the magnet, as well as an addendum to the note template, remarking if the patient was given a magnet.

Results: This initiative has led reduced time between patients calling clinic and subsequently presenting for care. The mean time decreased by 19%, from 2.25 hours (n=26) to 1.83 hours (n=22) (p=0.68). The median time decreased by 7%, from 1.49 hours (n=26) to 1.30 hours (n=22) (p=0.68). Specifically in oncology patients, the mean time decreased from 3.01 hours (n=9) to 1.19 (n=3) for a 60% decrease.

Conclusion: This project has shown that implementation of a simple visual aid improves time of presentation to care in these vulnerable populations. Our next PDSA cycle will include expanding patient education on the importance of fevers and utilizing the clinic's social determinants of health (SDOH) screener to identify at-risk patients and connect them with the hospital's community health worker for transportation services.

Poster # 517

TOOL FOR AN APPROPRIATE GOLDEN HOUR MANAGEMENT IN SEPSIS

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Background: Timely initiation of appropriate antimicrobials is vital for better outcomes of sepsis in pediatric hemato-oncology (PHO)unit. Conventional blood culture remains the gold standard to establish the microbial etiology but it typically takes 48-72 hours to report. There is a need for an affordable test that can rapidly and reliably identify the pathogen.

Objectives: 1)To describe the clinico-microbiological profile of infections in febrile immunocompromised children

2)To find the correlation between the blood culture reports by direct MALD-TOF and the conventional culture.
3)To study the clinical impact of MALDI-TOF in terms of

A. Escalation
B. De-escalation
C. Duration of Time
D. Morbidity

Design/Method: This prospective study was conducted in the PHO-unit between June-2022 and July-2023 Children upto 18-years from PHO-unit presenting with fever were enrolled.
After stabilization, detailed secondary assessment for identifying focus of infection was done. Blood was drawn for BACTEC-cultures (central and peripheral, where applicable), hemogram and other investigations as required. When the blood culture bottles incubated in the automated system BD-BACTEC™FX signalled as positive, process for classical ID using MALDI-TOF/Conventional Biochemical was followed. In parallel, an aliquot was subjected to a lysis-centrifugation method (LCM) and used directly for the identification by the MALDI-TOF. Clinical, laboratory characteristics and outcomes were analysed. Time to pathogen identification by direct MALDI TOF and conventional method and concurrence between the 2 methods were analysed.

Results: We had 187 children in the cohort ranging from 3.5months to 7-years including 67% boys. B-Acute lymphoblastic leukemia (B-ALL) was the most common primary diagnosis. Among the subjects, 92% received chemotherapy and 8.2% were post-HSCT recipients. Neutropenia was present in 52% including 17% profound neutropenia.
Out of the 187 blood cultures, 51 (27.5%) were positive including 22-GPC, 25-GNB and 4 Candida species. Acinetobacter and Klebsiella were the commonest.
Out of the 53 culture-positive cases, 29(56%) were identified by direct broth MALDI-TOF including 50% concordance in GPC and 68% concordance in GNB. Results were obtained as early as 6- to 40-hours with direct MALDI-TOF.
CLABSI was seen in 19% necessitating removal in 8% cases. Other foci included PICC line site infections (2%), gastro-intestinal(10%) and respiratory(17%) cases. Mortality was noted in 3% due to resistant-GNB sepsis.

Conclusion: Identification of the bacterial growth by direct MALDI-TOF is possible atleast 12 hours before the conventional technique and is promising, as every hour in PHO-unit is crucial.

Poster # 518

GRANULOCYTE TRANSFUSION SAFETY IN PEDIATRIC PATIENTS WITH SEVERE NEUTROPENIA

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Background: Pediatric oncology and stem cell transplant patients are at high risk for severe bacterial infections due to the myelosuppressive effects of treatment. Even with the rapid initiation of empiric antibiotics, mortality in this patient population occurs at around 3% in febrile neutropenic cancer patients. Prognosis is worse in children with proven bacteremia, with mortality rates of 9%.

Granulocytes harvested from healthy donors can temporarily raise the functional neutrophil counts in transfusion recipients. Studies of the efficacy of granulocytes have yielded varied results, but there is a paucity of data in the pediatric population.

Objectives: To determine the safety of granulocyte transfusions in pediatric patients with severe neutropenia.

Design/Method: We completed a retrospective cohort study of 74 neutropenic pediatric oncology patients with various infections who received granulocyte transfusions at the Maria Fareri Children's Hospital at Westchester Medical Center from 2011-2019. The medical record was reviewed for patient age, underlying medical condition, indication for granulocyte transfusion, duration of fever, time to resolution of infection, mortality, granulocyte dose, adverse reactions to the granulocyte transfusion, and changes in absolute neutrophil and platelet counts post transfusion.

Results: The majority of patients receiving granulocytes were either Stem cell transplant recipients, patients with hematologic malignancies, or both. There were 34 patient transfusions that had an ANC increment of >1000 cells/µl following granulocyte transfusion. The median ANC increment in this subset was 2130 cells/µl. For the patients who did not increment, the median ANC was 100 cells/µl. The platelets increased by a median value of 5,500 platelets/µL in the 34 patient transfusions that incremented and 3,500 platelets/µL in those that did not increment. Adverse events related to granulocyte transfusion occurred in 5 patients (7%), with 3 patients having a fever during the transfusion (CTCAE grade 1), 1 having hypothermia (CTCAE grade 2), and 1 having joint pain (CTCAE grade 1). All of the patients that had adverse events were in the high incrementing group except for one patient with fever. 3 patients died during the period they received granulocytes: 2 due to infectious complications and one due to seizure. 30 day survival was 89.1% and 100 day survival was 75.7% from the initiation of granulocyte transfusions.

Conclusion: Granulocyte transfusions can be safely administered to pediatric patients with severe neutropenia. Although this data is an important step to understanding the role of granulocyte transfusions in the management of documented infections in severely neutropenic pediatric patients, further studies are needed to determine efficacy.

Poster # 519

SLEEP DISTURBANCES AMONG HOSPITALIZED ONCOLOGY AND BMT PATIENTS: WHAT HELPS AND WHAT GETS IN THE WAY

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Background: Hospitalized pediatric oncology and bone marrow transplant (BMT) patients face sleep disruption due to factors such as poor lighting, noise, medical routines, and physical discomfort.

Objectives: This study aimed to describe 1) sleep disturbance and sleep-related impairment and 2) barriers and facilitators to sleeping in the hospital among pediatric oncology and BMT patients.

Design/Method: The study involved 17 BMT and 8 oncology patients, aged ≥5 years. They and their parents completed PROMIS questionnaires characterizing sleep disturbance and sleep-related impairment after being admitted for 5 nights while receiving chemotherapy. These measures are normed using the general population, where the average t-score is 50 with a standard deviation of 10. T-scores >60 indicated problematic sleep disturbance or impairment. Using a measure created for this study, participants evaluated the extent to which factors identified in prior research affected their sleep. Bedside light intensity was measured in lux using Condor ActTrust actigraphs and then compared to established guidelines, which suggest indoor light should be ≤1 lux at night and ≥250 lux during the day. Staff recorded nighttime room entries.

Results: Over a third of hospitalized patients (35%) experienced problematic sleep disturbance and 23% endorsed sleep-related impairments, based on parent- or self-report. Top patient-reported barriers to sleeping well included vital sign checks, room entries, loud sounds, bright lights, medical procedures, and pain. Top sleep facilitators included reducing light in the room, pain / sleep medications, and having family nearby. Light never reached the recommended threshold during the daytime (median = 15.55 lux, range = 3.49-125.63) and was too bright at night (median =1.03 lux, range = 0.28-9.44). Recorded room entries averaged 5 per night (range = 2-18).

Conclusion: All patients endorsed barriers to sleeping well in the hospital. Over a third reported concerning levels of sleep disturbance or related impairments, and one experienced 18 room entries in a single night. Objective measurements indicated that patients are routinely exposed to too bright light at night and light that is too dim during the day. Given the important role sleep plays in recovery and health, it is crucial that hospitals make environmental changes to decrease light exposure at night and practice changes to reduce staff-related sleep disturbances. Advocacy efforts are needed to support the recent call for a "sleep friendly" hospital designation, which will spur the necessary cultural shift to prioritize patient sleep.

Poster # 520/Late Breaking Abstract

MIDLINE CATHETER SAFE & RELIABLE PERIPHERAL ACCESS IN CHILDREN WITH BLOOD DISORDERS & MALIGNANCIES

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Background: Delivering high-quality medical care to pediatric patients with hematological disorders and malignancies often requires reliable central venous access. In addition, they often require extra venous access for frequent blood extraction, delivering a non-compatible concomitant infusion, or merely because the original permanent line is occupied with prolonged infusions.

Objectives: This study aimed to assess the safety and reliability of midline catheters as an alternative peripheral venous access option in pediatric patients with hematological disorders and malignancies.

Design/Method: We conduct a retrospective analysis for prospectively collected data, including age, gender, primary diagnosis, insertion & removal indications, and complications that include CLABSI, deep venous thrombosis (DVT), or extravasations. The inclusion criteria were all pediatric patients with hematological disorders and malignancies who had difficult intravenous access or needed an extra

peripheral line in addition to the permanent line during the study period. Exclusion criteria included patients with established CLABSI and DVT, patients requiring emergency central venous catheter lines, and pediatric patients without hematological disorders and malignancies.

Results: 70 pediatric patients were included in the analysis, all of whom underwent midline catheter placement for various therapeutic and diagnostic purposes at our center between January 2023 and December 2023. 30 patients diagnosed with childhood malignancies and blood disorders were included. The median age was 36 months with 66 % females and 33 % males. The median platelets count at the insertion time was 101 x 10^9/L .The success insertion rate was 100%. The most common site of insertion was left cephalic vein 37% followed by right cephalic vein 30%. The most common catheter size was 22G 8CM. The most common reason for placing a midline was new oncological diagnosis 30 % followed by frequent blood extraction and prolonged infusions 23 % each. The average dwell time was 8.9 days. One patient developed localized venous thrombosis and one patient developed localized hematoma at the insertion site.

Conclusion: Preliminary findings indicate a high midline catheter insertion success rate, with minimal procedural complications observed across the patient cohort. The midline catheters demonstrated prolonged dwell times, suggesting durability as a viable option for long-term venous access needs. Notably, the study identified midline catheters as a reliable conduit for delivering critical therapies in pediatric patients with hematological diseases and malignant disorders and their role as an adjunctive venous access strategy.

Poster # 521

FINANCIAL CHALLENGES FACED BY CAREGIVERS DURING PEDIATRIC CANCER TREATMENT AND POST SCT

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Background: Caring for children with cancer or undergoing stem cell transplantation (SCT) often includes unanticipated financial costs. These costs and often, financial distress, may generate coping behaviors (suboptimal treatment adherence, health care delays), collectively termed “financial toxicity.” Identifying modifiable factors that are associated with financial distress is an important step toward addressing financial toxicity.

Objectives: We describe financial distress for families of children and adolescents ages 0 to 21 years following a diagnosis of cancer or from SCT.

Design/Method: We conducted a prospective, observational study using quantitative surveys among parents of patients aged 0-21 years with cancer or undergoing SCT who speak English or Spanish. Parents completed surveys at three timepoints from treatment initiation through 1 year. The survey measured financial distress using the Personal Financial Wellness Scale (PFWS), household material hardship (food, housing, transportation, utility insecurity), clinical and financial coping behaviors, and sociodemographic information. We used descriptive statistics to characterize the participants and their

financial distress, household material hardship, coping behaviors, and factors associated with worsened financial distress. Among a subset of participants, we conducted semi-structured interviews to further explore financial distress and financial coping behaviors.

Results: Of 28 participants, baseline PFWS showed high financial distress (PFWS score ≤4) in 46%, moderate (PFWS score 4.1-6.9) in 36% and low (PFWS score 7-10) in 18%. More than half (57%) had an oncology diagnosis and 43% received SCT. Regarding household material hardship, 14 families (50%) reported difficulty paying the rent/mortgage, 8 families (28.5%) lacked reliable transportation for work/medical appointments, 3 families (10.7%) received notices threatening to turn off utilities due to lack of payment, 10 families (35.7%) were worried that food would run out, and 7 families (25%) stated that they ran out of food and could not afford more. Most (n=23, 82%) received financial support from existing resources, and 25 (89%) used at least one coping behavior (Cutting back on spending for family birthday/holiday celebrations being the most common followed by cutting back on spending for clothing/transportation/home utilities) in an effort to overcome their financial distress.

Conclusion: At baseline, the majority of families reported either moderate or high financial distress, and household material hardship were also endorsed by many families of children with cancer or following SCT. Our preliminary findings show that at baseline, families may already be experiencing financial hardships.

General Oncology, Cancer Predisposition, AYA, Survivorship, and Palliative Care (601-696)

Poster # 601

INCIDENCE OF GERMLINE FINDINGS IN PEDIATRIC, ADOLESCENT AND YOUNG ADULT CANCER PATIENTS AT UCSF

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Background: Certain germline mutations are known to be associated with inherited predisposition syndromes. The UCSF500 Cancer Gene Panel test utilizes next-generation sequencing to target and analyze 529 cancer genes. The test identifies mutations that are present in both tumor and germ cells that may drive tumor growth and guide targeted therapies. The UCSF500 test can be ordered as a tumor-normal test in order to simultaneously profile the somatic mutations of the tumor and to screen for inherited germline mutations.

Objectives: The primary objective of this project was to determine the incidence of pathogenic germline mutations in pediatric, adolescent, and young adult (AYA) patients with cancer who have undergone UCSF500 testing across age groups and tumor types since 2015. A secondary aim was to determine the most common germline altered genes involved across tumor types.

Design/Method: We analyzed results for patients age 0-39 years at cancer diagnosis with UCSF500 tumor-normal testing performed between January 2015 and March 2023. Additional data points examined include pathological diagnosis of tumors standardized using the OncoTree oncology, age of patient at sequenced tumor collection, and germline gene alterations in patients with germline-positive findings.

Results: A total of 1259 patients underwent germline testing. Overall, 18.2% (229/1259) of cancer patients had a pathogenic germline mutation. The incidence of a germline mutation was 21.6% for ages 0-2, 16.9% for ages 3-5, 14.1% for ages 6-13, 19.7% for ages 14-18, 23.8% for ages 19-33, and 10.9% in ages 34-39. *TP53*, *NF1*, and *MUTYH* were the most prevalent germline alterations, respectively accounting for 13.5%, 12.4%, and 6.6%. Notably, germline mutations were found in 77.8% of Malignant Peripheral Nerve Sheath Tumors with 85.7% being *NF1*; 72.7% of neurofibromas with 63.6% being *NF1*; 52.4% of retinoblastomas with all being *RB1*; 33.96% of osteosarcomas with 55.6% being *TP53*; 30.2% of glioblastomas with 21.1% being *PMS2*; and 28.0% of rhabdoid tumors with 71.4% being *SMARCB1*.

Conclusion: Our findings highlight the importance of screening for germline mutations given the high incidence of pathogenic germline findings across cancer diagnoses. This allows for appropriate genetic counseling, family testing, and patient surveillance screening procedures, which can lead to improved outcomes for those with cancer predisposition syndromes.

Poster # 602

COMPARISON OF RATES OF MALIGNANT NEOPLASMS IN 11,149 CHILDREN WITH AND WITHOUT NEUROFIBROMATOSIS-1

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Background: Neurofibromatosis-1 (NF1) is known to be associated with higher incidence of benign and malignant neoplasms in adulthood but large populations studies on childhood malignancies are not available.

Objectives: To compare the rates of malignant neoplasms based on primary tumor location between children with and without NF1.

Design/Method: This was a retrospective cohort study based on the TrinetX platform global collaborative network on patients

Results: There were 1,852 patients with NF1 who had a diagnostic code for a malignant neoplasm compared to 39 in non-NF1 population. The relative risk (RR) of malignant neoplasm at any site in children with NF1 was 43.58 (95% Cl 34.62-65.14). Relative risks of malignant neoplasms in central nervous system (RR 107.31[95% Cl 64.64-175.44], n=1,717 vs 16 in non-NF1), hematologic sites (RR 9.53 [95% Cl 5.79-15.70], n=162 vs 17 in non-NF1), endocrine system, particularly adrenal gland (RR 3 [95% Cl 1.47-6.13], n=30 vs 14,196 ([95% Cl 1978-101879] n=90 vs none in non-NF1) was also significant. Rates of malignancies of bone, thyroid, reproductive organs, and skin were too few (n

Conclusion: The study highlights the disproportionate rates of certain malignant neoplasms in children with NF1. Central nervous system, hematological, mesothelial and soft tissue, adrenal gland based tumors are found in significantly higher rates. There is no association with uncommon childhood malignancies such as those of bone, thyroid, skin, and reproductive organs. This is the largest cohort of pediatric NF1 studied and is limited by possible inaccuracies in diagnostic codes. We aimed to circumvent this by comparing with a control population without NF1 to simulate real world data. Since

our results suggest a higher index of suspicion for certain malignancies in NF1 population, this could be helpful to clinicians to refine existing screening protocols to allow for cost-effective and targeted testing.

Poster # 603

PAIRED TUMOR-NORMAL GENETIC TESTING IN PEDIATRIC ONCOLOGY: CAREGIVER UNDERSTANDING AND EXPERIENCE

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Background: Tumor-normal paired (TNP) genetic testing is becoming standard practice for most pediatric cancer types to inform cancer diagnosis and identification of underlying cancer predisposition. Ideally, TNP genetic testing is coupled with counseling to ensure that patients and their caregivers understand the implications of germline genetic testing for the patient and their family. However, such counseling is often limited due to a shortage of dedicated genetic counselors and time constraints in the setting of a new cancer diagnosis or relapse.

Objectives: To understand baseline caregiver genetic knowledge, distress, and decisional satisfaction with TNP testing, and describe development and initial implementation of education video to augment limited genetic counseling.

Design/Method: Caregivers were approached for participation after consenting to TNP testing for their child in the setting of cancer diagnosis or relapse (NCT05472714). Participants completed surveys of genetic knowledge, distress, and decisional satisfaction both before and after return of genetic testing results. During the year of observational data collection, we also developed an educational video for families to support pre-test counseling, including possible test results, next steps for the patient and family members, and legal protections available to patients undergoing genetic testing. The video was recently introduced to oncology teams to share with families in context of TNP testing, with data collection ongoing.

Results: Caregivers without exposure to the video reported a large range of genetic knowledge and relatively high satisfaction and low distress across both time points. Controlling for baseline genetic knowledge, there was a statistically significant difference in genetic knowledge post results in caregivers who watched the educational video prior to post-result survey (n=9, mean 86%, SD 8.3%), those who watched the video during the post-result survey (n=23, mean 73%, SD 27.1%) and those who did not watch the video (n=110, mean 60%, SD 23%)(p=0.034). There were clear limitations in distributing the video intervention in the setting of new diagnosis which require further analysis in year 2 of the study, and complete feasibility and acceptability data is pending.

Conclusion: Preliminary results suggest improvement in genetic knowledge for caregivers of patients undergoing TNP testing with addition of an educational video. Over the subsequent year, we will continue distribution of an educational video to all caregivers of patients undergoing paired TNP genetic testing.

Poster # 604

A CALIFORNIA POPULATION-BASED ASSESSMENT OF CANCER CONCORDANCE IN TWINS

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Background: Twin cancer concordance rates have been used to estimate the relative contribution of genetic and non-genetic influences on cancer development. Accuracy of these estimations has been historically limited by ascertainment bias in the case of selected cohorts and due to challenges in assembling sufficient sample sizes and diagnostic information for population-based cohorts.

Objectives: Identify pediatric and adolescent/young adult (AYA) twin cancer concordance rates through a population-based registry assessment in California from 1982-2022.

Design/Method: Twin pairs with cancer (diagnosed in one or both) aged 0-39 were identified using linked California birth records from 1982-2017 and California Cancer Registry data from 1988-2022. ICD-O-3 histology and site codes were used to classify diagnoses into 12 broad groups and 69 recode subgroups as defined by the International Classification of Childhood Cancer, Third Edition (November 2012). Concordance was defined as siblings in a twin pair with cancers in the same ICCC-3 recode subtype category.

Results: A total of 1243 individual cancers were diagnosed across 1182 twin pairs, 816 being same sex pairs and 366 opposite sex pairs. Concordant diagnoses were identified in 13 (1.1%) pairs overall, including 2 of 249 (0.8%) leukemias, myeloproliferative diseases, and myelodysplastic diseases, 1 of 133 (0.8%) lymphomas and reticuloendothelial neoplasms, 1 of 214 (0.5%) CNS and miscellaneous intracranial and intraspinal neoplasms, 1 of 48 (2.2%) neuroblastoma and other peripheral nervous cell tumors, 2 of 16 (12.5%) retinoblastomas, 1 of 90 (0.1%) soft tissue and other extraosseous sarcomas, 3 of 93 (4.5%) germ cell tumors, trophoblastic tumors, and neoplasms of gonads, and 2 of 225 (0.9%) other malignant epithelial neoplasms and malignant melanomas. By specific subgroups, concordance was identified in 1 of 194 with lymphoid leukemias (0.5%), 1 of 32 (3.1%) for acute myeloid leukemia and 1 of 52 non-Hodgkin lymphomas (1.9%). No concordant cases were identified for renal, hepatic, malignant bone tumors or other and categories. Leukemia (OR=1.62, 95%CI=1.11-2.36, P=0.011) and bone tumor diagnoses (OR=2.93, 95%CI=1.21-7.33, P=0.011) were significantly associated with being born baby A (first one out) compared to B.

Conclusion: Here, we present population-based concordance rates of cancer in twins. Concordance across all cancers was low at 1.1%. Surprisingly, the concordance rates of 0.5% for lymphoid leukemias and 3.1% for acute myeloid leukemia were below the previously described rate of 10-25% for childhood acute leukemias. This low rate of concordance indicates that acquired genetic, epigenetic factors and unshared exposures likely contribute more heavily to leukemogenesis than previously appreciated in pediatric acute leukemias.

Poster # 605

EVALUATING THE UTILIZATION OF MOLECULAR TESTING IN A SINGLE CENTER PEDIATRIC ONCOLOGY PRACTICE

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Background: Molecular testing in pediatric oncology has led to improved diagnostics, risk stratification, prognostication, and treatment options for patients. Advancements in molecular techniques led to the emergence of Precision Medicine; a branch of oncology care that targets specific molecular alterations identified in the tumor cells of individual patients through drug development and utilization. The incorporation of precision medicine in the care of oncology patients has led to improved outcomes, often with less toxicity. Despite these recognized benefits, significant practice variation remains in the pursuit of molecular testing amongst providers. Given these observations, we evaluated the historical use of molecular testing at our institution to identify potential gaps in the care of our patient population.

Objectives: Evaluate for changes in the rate of molecular testing in pediatric oncology patients over a 10-year period. Additional objectives included analyzing the trend of molecular testing over time, examining patients most likely to receive molecular testing, assessing the yield of testing, and characterizing the impact on patient care.

Design/Method: A retrospective chart review was performed on all pediatric oncology patients diagnosed at Akron Children's Hospital (ACH) from 2012-2021. Demographic data including age, gender, diagnosis, stage/risk group, and primary/secondary/relapsed disease was collected. The types of molecular testing assessed included gene panels, FISH, karyotype, methylation, RNA sequencing, whole exome of tumor, and germline testing. Results of testing and impact on patient care was evaluated. Descriptive statistics, Wilcoxon Rank Sum, and Chi-Square tests were used to assess, describe, and analyze data by cohort.

Results: Of 943 patients screened, 811 patients met inclusion criteria. 77.3% of patients had at least one molecular test performed. A significant increase was observed in number of molecular studies obtained in the 2012-2016 vs 2017-2021 cohorts ($p < 0.0001$). Patients identified as "high-risk" were 4.4x more likely (95%CI 2.83-6.89, $p < 0.0001$) to have molecular testing performed. In those who underwent testing, an alteration of any kind was found in 63% of patients.

Conclusion: This review highlighted the increasing utilization of molecular testing in pediatric oncology. The results indicate that further analysis is needed to identify patients who would most benefit from molecular testing. The high percentage of alterations identified demonstrates the importance of further studies to increase our understanding of the clinical impact of specific alterations and the development of targeted therapies for pediatric oncology patients. Information from this study will contribute to the development of an algorithm at our institution to guide molecular testing for future patients.

Poster # 606

ROLE OF MEDICAL STUDENTS IN A PEDIATRIC ONCOLOGY PRECISION MEDICINE CLINIC

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Background: Significant effort has been devoted to better understand tumor biology and driver mutations to provide precise therapy specifically targeting tumors, a novel approach entitled precision medicine. This approach is expected to address relapsed disease and limit the sequelae of intensive therapies. Precision medicine commonly relies upon next-generation sequencing (NGS), which provides a vast amount of data to be interpreted and integrated into cancer care. This approach raises new questions and opportunities for growth and education of new trainees.

Objectives: Since its inception in 2021, the Precision Medicine Clinic (PMC) at Cook Children's Medical Center (CCMC) has evolved to fulfill the goal of precision medicine: providing comprehensive cancer treatment options tailored to genetic sequencing results. We describe the impact of a PMC on educational opportunities for all disciplines, especially medical students. Aims in initiating the PMC include providing universal NGS testing for pediatric cancer patients at CCMC, helping to personalize treatments and avoid toxicity. In fulfilling these aims, we have added the unique aspect of integrating medical students to present at interdisciplinary PMC meetings.

Design/Method: PMC meetings create a centralized platform to compile, discuss, and provide recommendations on patient cases guided by the above principles. Meetings consist of a PMC report presentation and discussion.
Reports are frequently created and presented by a medical student volunteer, a unique feature. Reports consist of an outline of the patient's clinical course, relevant laboratory studies and imaging, NGS results, and treatment options and studies specific to the NGS results. Reports are checked for accuracy and completeness by a pediatric oncologist. Attendees include pediatric oncologists, researchers, pharmacists, molecular pathologists, the solid tumor coordinator, medical students, and medical science liaison.

Results: Since January 2022, our PMC has held over 75 meetings. Thirty-three students have presented cases, many at multiple meetings. All medical students enrolled in the pediatric hematology/oncology 4th-year clinical elective (25 students in this period, from both medical schools in Fort Worth, Texas) completed at least one presentation, leading to career exploration, scientific inquiry, and student-led research initiatives.

Conclusion: The importance and impact of early exposure to precision medicine through our PMC for medical students cannot be understated. The clinical environment, therapy modalities, and technologies, particularly pertaining to pediatric oncology, evolve at a pace that cannot be matched by medical school curricula, and the application of precision medicine continues expanding. This exposure has provided medical students with experience in interpreting NGS results while engaging with a robust interdisciplinary team.

Poster # 607

CREATION OF A TUMOR MOLECULAR TESTING REGISTRY: AN UPDATE

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Background: Precision medicine represents an exciting and rapidly-developing frontier in medicine, particularly for pediatric patients with rare or relapsed/refractory malignancies, for whom traditional therapies have proven ineffective. The use of targeted therapies based on the genomic profile of a pediatric patient's tumor is increasing exponentially. The evidence supporting the use of targeted therapies in this population, however, is quite limited.[1]

Objectives: We aim to create a comprehensive and dynamic registry of every patient who has underwent next-generation sequencing (NGS) of their malignancy to quantify the impact of NGS on treatment decisions and patient outcomes at our institution.

Design/Method: We designed a REDCap database that collects the following information for each patient:
1) Demographic information, including age and current status.
2) Initial diagnosis information, including age at diagnosis and type of malignancy.
3) Relapse information, including age at relapse and site of relapse.
4) NGS information, include timepoint at which NGS was performed, genomic variants, and immunotherapy markers, such as PD-L1 expression.
5) Treatment information, including whether NGS results contributed to treatment and if so, what genomic variant was targeted.

Results: To date, 82 patients have been entered into the database. 52.44% (43/82) are female, and 47.56% (39/82) are male. Ages range from <1 year of age to 29 years of age. 76.83% (63/82) of patients were diagnosed with a solid tumor, including 12.20% (10/82) with osteosarcoma, 10.98% (9/82) with Ewing sarcoma, and 10.98% (9/82) with rhabdomyosarcoma. 9.76% (8/82) of patients were diagnosed with leukemia, and 8.54% of patients (7/82) were diagnosed with Langerhans cell histiocytosis (LCH). 20.73% (17/82) received treatment recommended in their NGS reports. 35.29% (6/17) patients received targeted therapy at first relapse, and 29.41% (5/17) patients received targeted therapy at initial diagnosis. Six patients had LCH and received trametinib for *BRAF* or *MAP2K1* mutations. Of these six patients, five are stable on trametinib therapy, and one discontinued trametinib therapy after imaging surveillance revealed no evidence of recurrence. Three patients received nivolumab and ipilimumab for high microsatellite instability or high PD-L1 expression. Of these three patients, one is currently being treated with this regimen, one is deceased, and one has relapsed.

Conclusion: We continue to build an extensive database comprised of patients who underwent NGS of their malignancy at our institution. We will continue to monitor the outcomes of patients who receive targeted therapies as the field of precision medicine advances.

1. Lee, *JCO Precis Oncol*, 2021.

Poster # 608

SUCCESSFUL DEVELOPMENT OF A MULTIDISCIPLINARY CANCER PREDISPOSITION PROGRAM

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Background: There has been rapid expansion of the identification of germline variants that increase risk for cancer in pediatric patients, and this growing population is often without a medical home. Patients with a concern for or a diagnosis of a Cancer Predisposition Syndromes (CPS) require individualized counseling and follow up care, which is best provided in a centralized multidisciplinary clinic.

Objectives: Described the development of a multidisciplinary program to provide care for patients with concern for or a known CPS.

Design/Method: We established a multidisciplinary program for Cancer Predisposition patients in 2020. The clinical program was initially staffed by a single genetic counselor (GC) and one pediatric oncologist. With increasing referrals and identification of patient needs, our team has grown to including multiple GCs, a pediatric oncology physician's assistant, a nurse coordinator, a pediatric psychologist, and a pediatric oncologist. We aim to describe our program's successful growth from 2020 – 2023.

Results: Referrals to our program have increased from 2020 – 2023; 44 in 2020, 90 in 2021, 88 in 2022, and 74 so far in 2023. The referrals were received from a variety of clinics including primary care, pediatric oncology, gastroenterology, general genetics, dermatology, endocrinology, general surgery, and patient/parent self-referral. The most common referral sources were pediatric oncology (25.4%), primary care (25.0%), and the gastroenterology (6.5%). Patients were referred for a family history of a known CPS (34.5%), personal history of a known CPS (28.9%), personal history of cancer with concern for an underlying CPS (14.7%), and family history with concern for underlying CPS (12%). The patients seen in our clinic have positive testing for a over 25 unique CPS, the most common being PTEN Hamartoma Syndrome (15%), Familial adenomatous polyposis (12.7%), Li-Fraumeni Syndrome (10%), Hereditary paraganglioma/pheochromocytoma syndrome (7.5%) and Multiple Endocrine Neoplasia Type 2A (7.5%). Approximately 33% of patients have met with our psychologist since adding that service to our program in 2023.

Conclusion: Our experience demonstrates the increasing need for establishing programs to care for patients with cancer predisposition syndromes. The referral and diagnosis pattern are very heterogenous, requiring a team of subspecialized multidisciplinary team to be able to provide comprehensive care. Programs that integrate many subspecialties can be successfully implemented at mid-sized institutions.

Poster # 609

GENETIC COUNSELING IN CANCER SURVIVORSHIP CLINIC

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Background: Childhood cancer survivors are more likely than their cancer-free counterparts to have a pathogenic germline mutation in a cancer predisposition gene (CPG). CPG mutations increase the likelihood of subsequent malignancies. Surveillance for individuals with CPG mutations has been shown

to lead to earlier diagnosis, which is associated with improved prognosis and overall survival. Knowledge of a predisposition can help providers incorporate recommended cancer surveillance into survivorship care. While there is a demonstrated utility for genetic counseling in childhood cancer survivorship clinics, many do not have genetic counselors (GCs), creating a barrier to genetic testing for patients. We hypothesize that having a GC embedded in survivor clinic can help facilitate testing to elucidate more survivors at additional cancer risk and coordinate management with the goal of decreasing survivor mortality.

Objectives: The objective of this study is to evaluate the impact of a full-time GC embedded in a cancer survivorship clinic.

Design/Method: This retrospective chart review analyzed the number of patients seen for genetic counseling, the number of tests completed, and actionable results received after full-time GC coverage began in the Aflac Survivor Clinic on August 1, 2022. The percentage of patients seen in the first year with embedded GC coverage was compared to those seen between 8/1/21-7/31/22 when survivor patients were seen on a consult basis.

Results: One year prior to GC integration, 15.0% of survivors (144/960 visits) had engaged with genetic counseling (10.9% prior to the visit, 4.1% at their survivor visit). After embedded GC coverage, 26.1% of patients (247/943 visits) engaged with genetic counseling – 15.4% cancer prior to their visit and 10.8% during their survivor visit. Since the integration of GC, genetic testing was ordered and completed for 76 patients. Of those who completed testing, 48 had negative results, 18 (23.7%) had uncertain or carrier results, and 10 (13.1%) had positive results. Positive results included variants in the following genes: *ETV6*, *WT1*, *TP53*, *RB1, CHEK2*, and *ATM*. One patient was found to have a secondary malignancy shortly after testing resulted, presumed to be related to their CPG variant. All positive results have either pediatric management implications or cascade testing recommendations.

Conclusion: A GC embedded in a survivorship clinic increased the number of patients with GC contact by 75%, which can facilitate testing for patients and families, and identify predispositions to guide tailored cancer surveillance.

Poster # 610

MATURE B-CELL LEUKEMIA WITH TP53 MUTATION: CONSIDERATIONS IN ADOLESCENT AND YOUNG ADULT POPULATIONS

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Background: The classification of aggressive B-cell lymphomas is multifactorial and delineated by clinical, pathological, and molecular features. High-grade B-cell lymphoma, not otherwise specified (HGBL, NOS) is a heterogeneous category of aggressive B-cell lymphomas with Burkitt-like or blastoid morphology without characteristic cytogenetics.[1] Differentiating HGBL from other neoplasms is difficult, with expert diagnostic consensus in about 50% of cases.[2] HGBL therapy is typically determined by histology in adults (R-CHOP versus DA-EPOCH-R) and by clinical presentation in pediatrics (COP/R-COPADM backbone), with maintenance chemotherapy, more intrathecals, and etoposide. However, when histology is indeterminant, as in HGBL, NOS, adults similarly direct therapy by clinical presentation

given the paucity of data in this subgroup and frequent need for treatment intensification.[1] Somatic TP53 mutations are found in 30% of HGBL, NOS but the need for treatment intensification in these cases is unclear.[2]

Objectives: The objective of this case study was to discuss the classification and treatment decisions in an AYA patient with a rare and aggressive subtype of mature B-cell neoplasm, including the similarities/differences in classification and treatment options between children and adult patients in the setting of a familial TP53 mutation.

Design/Method: In this case, we discuss a 15-year-old male who presented with acute facial swelling, facial droop, headache, hypertension, and hematuria and was subsequently found to have a high-grade B-cell neoplasm, NOS (MYC, BCL-2, BCL-6 normal) with CSF and >70% marrow involvement. Additional work-up revealed intraparenchymal brain lesions, scalp lesions, bilateral hydronephrosis, and a germline TP53 mutation. Mother was also known to have this mutation and history of sarcoma, breast cancer, and B-cell lymphoma treated with R-CHOP.

Results: Given stage 4, CSF+ high-grade B-cell neoplasm with *TP53* mutation, we proceeded with therapy per ANHL1131 (COP/R-COPADM backbone) after consideration of adult regimens. Our patient's neurological symptoms improved following pre-phase therapy. Serial MRIs throughout therapy demonstrated eventual resolution of scalp lesions but stable intraparenchymal lesions, suggesting an alternate etiology (e.g., low-grade glioma), for which he is being monitored. Our patient completed ANHL1131 with continued remission of disease and stable intraparenchymal lesions at 5 months off-therapy. Confirmation of germline *TP53* mutation prompted further evaluations and referral to genetics clinic for the patient and his relatives.

Conclusion: This case demonstrates the importance of appropriate B-cell neoplasm classification and treatment intensification in a unique population with multiple treatment options, elevated risk of recurrence, and potential future need for chemotherapy and radiation in the setting of a germline mutation.

[1]Olszewski, Blood, 2022
[2]Zayac, Blood Advances, 2023

Poster # 611

MEDIASTINAL MASS INCREASES RISK OF UPPER EXTREMITY DVT IN PEDIATRIC AND AYA PATIENTS WITH MALIGNANCY

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Background: Cancer associated thrombosis (CAT) is common among adult oncology patients, with well-recognized risk-stratification systems to guide thromboprophylaxis. The prevalence and risk-factors of CAT in pediatric, adolescent, and young adult (AYA) patients remain under-investigated and the benefit

for thromboprophylaxis in this population has not been clearly established. The role of a mediastinal mass as a potential CAT risk-factor in pediatric patients remains controversial.

Objectives: (1) To identify risk-factors associated with upper extremity (UE) deep venous thrombosis (DVT) and lower extremity (LE) DVT or pulmonary embolism (PE) in pediatric and AYA patients with pediatric-type malignancies. (2) To determine if the presence of a mediastinal mass impacts risk of developing UE DVT compared to LE DVT or PE.

Design/Method: Pediatric and AYA patients (≤39 years-of-age) with pediatric-type malignancies (leukemia, lymphoma, central nervous system, sarcoma, germ cell, renal, hepatic, adrenal) requiring chemotherapy between 2012-2022 were included. Non-pediatric-type malignancies (ex: breast, colon, skin) were excluded. Through natural language processing, thrombosis events were identified from 30 days before to one year after diagnosis. A mediastinal mass at diagnosis was also recorded. All events were adjudicated by team members. Data was analyzed using Excel and SPSS.

Results: A total of 978 patients were identified. The mean age-at-diagnosis was 25-years (standard deviation 10-years). The most common diagnoses were lymphoma (31%), leukemia (20.8%), and sarcoma (18.5%). Of the 176 (18%) patients with a mediastinal mass, 76.7% had lymphoma, 8.5% had leukemia, and 8.5% had sarcoma.

A total of 207 thrombotic events in 157 (16.1%) individuals were identified. Seventy-one (7.3%) had UE DVT and 47 (4.8%) had LE DVT or PE. Individuals with a mediastinal mass, compared to those without, were 2.5-times more likely to develop UE DVT (14.2% vs. 5.7%, $p<0.001$) across all diagnoses. This increased risk persisted when stratified by diagnosis, including lymphoma (11.9% vs. 5.9%, $p=0.066$), leukemia (33.3% vs. 11.6%, $p= 0.017$), and sarcoma (13.3% vs. 6.6%, $p=0.34$). A mediastinal mass was not associated with an increased risk of LE DVT or PE (4% vs. 5%, $p=0.57$), suggesting that a local effect on the UE vasculature is a key risk-factor.

Conclusion: In pediatric and AYA patients with pediatric-type malignancies, CAT is a prevalent complication. A mediastinal mass at diagnosis was associated with development of UE DVT, but not LE DVT or PE, suggesting a local prothrombotic effect. Although further studies are needed, providers should consider thromboprophylaxis in pediatric and AYA patients with pediatric-type malignancies, especially in those with a mediastinal mass.

Poster # 612

GEOGRAPHIC DISTANCE TO CARE AND FINANCIAL TOXICITY DURING PEDIATRIC CANCER TREATMENT

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Background: Children with cancer and their families can experience substantial adverse financial effects resulting from their care—also termed financial toxicity. Families living in geographically remote locations face unique barriers to accessing subspecialty medical and support services, potentially increasing risk for financial toxicity and its severity.

Objectives: To explore how geographic distance between permanent residence and treatment center shapes families' experiences with financial toxicity during and early after cancer treatment.

Design/Method: We conducted in-depth, semi-structured interviews with a purposive sample of English- and Spanish-speaking adult caregivers of children with cancer who received myelosuppressive treatment. We included households defined as "geographically distant", based on a calculated drive time of ≥60 minutes from permanent residence. Caregivers completed interviews 3-18 months following an initial cancer diagnosis, a period chosen to balance the accumulation of financial challenges after treatment initiation while minimizing recall bias. Interviews were double-coded by three investigators through an inductive coding approach and regular consensus-building meetings. We performed a qualitative thematic analysis of interview transcripts focused on elucidating contributors to financial toxicity and its effects on patients and families, specifically focused on lived experiences impacted by geographic distance to care.

Results: We interviewed 14 caregivers, all of whom were geographically distant. Most (57%) caregivers reported a travel time of 1-4 hours. The sample included diverse caregiver characteristics and diverse household size, composition, income, and location. Distance to care was almost universally reported as provoking or exacerbating financial toxicity. We identified four themes around financial toxicity that were most salient among geographically distant families: (1) troubles maintaining employment and/or income due to challenging logistics and relocation for care; (2) excessive out-of-pocket costs related to travel and housing; (3) separation from prior support networks limiting adaptive response behaviors and familiarity with resources; and (4) disruptions of the family unit and roles regarding complex caregiving duties, resulting in reduced income, difficulty affording household necessities, and higher levels of finance-related stress. Most families who reported financial toxicity felt that geographic distance to care directly impacted one or more aspects of their experience.

Conclusion: Geographically distant families of pediatric patients with cancer can experience substantial financial toxicity and caregiving challenges throughout treatment, with distance to care perceived as a critical factor intensifying negative experiences. Interventions and/or policies are needed to mitigate the development and effects of financial toxicity for geographically distant families, who may require creative solutions specific to their unique support needs.

Poster # 613

PRECISION SEDATION: REDUCING GENERAL ANESTHESIA FOR LUMBAR PUNCTURES IN LEUKEMIA & LYMPHOMA PATIENTS

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Background: Children and adolescents with leukemia require multiple lumbar punctures (LPs) for the delivery of intrathecal chemotherapy. In North America, this procedure is most commonly done under general anaesthesia (GA), typically using propofol. There is a growing body of evidence that cumulative exposure to propofol is associated with risks of neurocognitive impairment.

Objectives: The primary objective of this quality improvement (QI) project was to implement and

evaluate a practice of Precision Sedation (PS) matching the level of sedation or anesthesia required for each child needed to provide adequate control of discomfort and anxiety to safely complete each LP. The overarching goal is to limit the use of GA to only those patients who require this level of support.

Design/Method: Patients aged 5-18 who required LPs as part of leukemia and lymphoma therapy were included. Patients in induction or scheduled for concomitant bone marrow aspirate/biopsy were excluded. Eligible patients were approached by the primary care team, provided with educational materials, and could elect to participate. Anaesthetic options included: local (EMLA patch), minimal (oral lorazepam and/or IV midazolam), moderate (IV midazolam and nitrous oxide) or GA (IV propofol). Parent presence during the procedure, child life support, iPad, virtual reality and/or music were offered as distraction methods. Experience surveys were distributed to participants after each procedure.

Results: Between February and October 2023, 18 patients aged 5-18 (6 [5-9]; 5 [10-14]; 7 [15-18]) elected to undergo PS. 59 LPs were completed without GA, the majority (85%) of which were completed with minimal sedation. 15 patients have undergone multiple LPs with PS, including five patients who have had 5+ procedures. Two patients opted to resume their LPs with GA. Of the unique survey respondents (10), all were extremely or moderately happy with the medicines they received for their LP and 30% reported having no pain during the procedure. Patients who underwent LPs without GA increased by ~10% relative to pre-project rates.

Conclusion: With this QI project of PS we have established a practice that allowed a subset of patients to safely, and without excess distress or discomfort, undergo sequential LPs with minimal or no sedation. Additional observed benefits included decreasing length of time in the hospital on procedure days and relief from the requirement to be fasting. Our future directions include expanding this practice to a broader group of patients, ensuring every patient is approached at diagnosis and including other subspecialties' patients.

Poster # 614

MODELING THE GLOBAL BURDEN OF PEDIATRIC CANCER TO IMPROVE ACCESS TO CARE

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Background: In many low- and middle-income countries (LMICs), a significant number of children with cancer die without being diagnosed or treated. Research indicates that this lack of diagnosis may be the single largest contributor to childhood cancer mortality in these regions.

Objectives: Our objective was to develop a model to estimate the total subnational incidence of pediatric cancers accounting for detection bias from undiagnosed cases to guide health systems to improve access to care and reduce the number of children who are not diagnosed and treated

Design/Method: We developed and validated the Pediatric and Adolescent Cancer Total Incidence Model (PACTIM), which uses data from the Surveillance, Epidemiology, and End Results program to produce age-, sex- and disease-specific prediction intervals of case counts for a population. We used data from high-income countries (HIC) from GLOBOCAN 2020 and from subnational registries in HICs

from the International Incidence of Childhood Cancer study to validate the PACTIM predictions. The primary validation metric was predictive accuracy, defined as the percent of predictions that fell within the PACTIM prediction interval. We estimated global incidence and non-diagnosis rates in 2020 and created a website for public access to the model.

Results: The PACTIM achieved the desired predictive accuracy for national and subnational registries in HICs and in LMICs that used higher-quality registration methods across all geographic contexts. Predictive accuracy progressively decreased as national wealth decreased, with low-middle- and low-income countries yielding the lowest accuracy scores, a trend that is consistent with under-registration and under-recognition of cases in these regions. For 2020, we estimated 327,719 cancer cases in children 0-14 years (95% prediction interval [PI]: 288,084–371,339) and 127,658 cases in adolescents 15-19 years (95% PI: 103,305 – 158,666) worldwide. Based on cases actually reported, approximately 37% (95% PI: 28-44%) of pediatric cases and 43% (95% PI: 29-54%) of adolescent cases were likely undiagnosed. The model may be accessed at https://mzobeck.shinyapps.io/pactim_app/.

Conclusion: The PACTIM accurately estimates the incidence of pediatric cancers in HICs and in LMICs that use higher-quality registration methods across all geographic contexts, which is evidence that the predictions of total incidence for regions with incomplete registry data are also accurate. We found that a substantial number of cancer cases go undiagnosed or unreported in LMICs. Reducing the number of undiagnosed cases and increasing access to care is critical for improving pediatric cancer survival rates. The PACTIM offers essential data for policymakers to bolster healthcare access for children with cancer worldwide.

Poster # 615

BARRIERS AND FACILITATORS TO ADEQUATE INFORMED CONSENT FOR CHILDHOOD CANCER CLINICAL TRIALS

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Background: To participate in childhood cancer clinical trials, parents and legal guardians must provide informed consent, a fundamental ethical right. There are scarce data on perspectives of parents of children with cancer on barriers and facilitators for adequate informed consent in diverse populations.

Objectives: To assess parent-reported barriers and facilitators to adequate informed consent in a convenience sample that included a significant number of Hispanic parents.

Design/Method: Twelve qualitative semi-structured interviews and 224 open-ended surveys were conducted with 236 parents of children with newly diagnosed cancer at Rady Children's Hospital San Diego, a large quaternary children's hospital in California. Fifty-three percent of participants were Hispanic and 38% of Hispanics used Spanish for medical communication. Four main codes (informed consent concepts and delivery; desired clinical trial information; motivations and emotions related to clinical trial enrollment; and potential areas for intervention) were used as a coding guide for analysis. Interviews and surveys were transcribed and coded for thematic analysis by three independent coders trained in qualitative methods to identify key barriers and facilitators.

Results: Four main themes were identified as barriers: 1) Complexity of the informed consent forms and discussion (lengthy, confusing, not available in Spanish, and heavy use of medical jargon); 2) parents feeling emotionally overwhelmed, anxious, and pressured around the informed consent; 3) parents viewing the clinical trial as the only treatment option; and 4) mistrust and fear of clinical trial procedures. Four facilitators to adequate informed consent were identified: 1) simpler explanations of study procedures; 2) provider training and flexibility for accommodations when delivering the informed consent, including additional time for decision-making and psychosocial support; 3) active promotion of voluntariness and trust; and 4) supplemental education in lay language, including request for peer-education, decision aids, and navigation to "bridge the provider-patient gap."

Conclusion: We identified key barriers and facilitators to adequate informed consent in a diverse sample of parents. Findings can inform potential interventions to enhance informed consent for childhood cancer clinical trials, including the use of decision aids, peer-navigation, and interventions tailored to the language and culture of the individual.

Poster # 616

ANTICOAGULATION THERAPY IN CHILDREN WITH CANCER AT RISK OF THROMBOCYTOPENIA: A RETROSPECTIVE STUDY

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Background: Patients with solid tumours or lymphomas have an increased risk of thromboembolism (TE) and thrombocytopenia due to their disease and treatments. The prevalence of TE in these patients is estimated at 8%, 600 times greater than in the general paediatric population. Anticoagulation therapy (ACT) strategies, notably evidence-based recommendations for low molecular weight heparin (LMWH) dose adjustments, for these patients with concurrent thrombocytopenia in the literature remain limited.

Objectives: The study's objective was to investigate the safety and efficacy of McMaster Children's Hospital's institutional ACT LMWH protocol in patients with solid tumours or lymphomas aged 0-18 years with TE who are thrombocytopenic or at risk of thrombocytopenia.

Design/Method: In this retrospective study, we reviewed the records of 39 patients that received LMWH ACT at McMaster Children's Hospital between January 2007 and December 2020. Data extraction and analysis focused on demographics, underlying disease and treatment, TE diagnosis, TE treatment, platelet counts during ACT, TE outcome, bleeding episodes, and invasive procedures.

Results: A total of 55 TEs were diagnosed in 39 patients [mean age: 7.5 years (range: 0.1-18 years)]. Among these patients, 12 (30.8%) were diagnosed with more than 1 clot. Symptomatic TEs occured in 14 patients (35.9%). Deep vein thrombi (38.8%) were the most common TEs, followed by cardiac-related thrombi (5.9%), superficial vein thrombi (4.7%), and pulmonary emboli (4.7%). The most common underlying malignancies included neuroblastomas (15%), osteosarcomas (15%), and hepatoblastomas (10%). The median duration of LMWH ACT was 3.1 months (range: 0.36-12.03 months), with 37 patients (94.9%) completing a full LMWH course. There were 26 procedures undergone by 20 patients (51.3%) during ACT, with 24 (92.3%) occurring without bleeding complications. There were 4 patients (10.3%)

who experienced a bleeding event, 2 of which were surgical bleeds, however none were associated with ACT as platelet and anti-Xa levels were normal at the time of the bleed. Complete resolution was achieved by 26 patients (72%), partial resolution was seen in 6 patients (16.7%), and 4 patients (13.3%) remained stable. In 1 patient, a mass initially diagnosed as a thrombus was revealed after their ACT to be a rhabdomyoma.

Conclusion: These findings provide further evidence that administering full-dose LMWH ACT is safe and effective in paediatric patients with concurrent thrombocytopenia or risk of thrombocytopenia.

Poster # 617

SOCIAL DETERMINANTS OF HEALTH & POST-TRAUMATIC STRESS SYMPTOMS IN CAREGIVERS OF CHILDREN WITH CANCER

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Background: Children with newly diagnosed cancer and their caregivers experience significant psychosocial distress, particularly post-traumatic stress symptoms (PTSS). Social determinants of health (SDoH) may influence a family's ability to navigate a new childhood cancer diagnosis. The role of SDoH on PTSS in caregivers of children with cancer has not been well-studied in minoritzed populations.

Objectives: Our aim was to assess the role of SDoH on PTSS in Hispanic and non-Hispanic caregivers of children with newly diagnosed cancer.

Design/Method: Caregivers of children aged 0 to 17 years with newly diagnosed cancer (n=207) participated in this study between August 2017 and February 2022. Health literacy (HL), acculturation, sociodemographic factors and PTSS were measured using the Newest Vital Sign (NVS), Short Acculturation Scale for Hispanics (SASH), sociodemographic questionnaire, and Impact of Events Scale-Revised (IES-R), respectively. The IES-R has three sub-scales: intrusion, hyperarousal, and avoidance. Statistical analyses were conducted using Fisher's exact test, Wilcoxon rank sum test, and univariable and multivariable regression.

Results: Both Hispanics (n=115) and non-Hispanics (n=92) reported high levels of PTSS (mean IES-R for Hispanics=35 and non-Hispanics=28.5). Hispanic caregivers had significantly higher levels of avoidance (p=0.015), hyperarousal (p=0.011), and total PTSS (p=0.027) compared to non-Hispanic caregivers. Public insurance (p=0.054) and Spanish language used for medical communication (p=0.003) were associated with higher PTSS on multivariable analysis. HL, acculturation, marital status, and religion were not significantly associated with PTSS.

Conclusion: Caregivers of children with newly diagnosed cancer experience significant PTSS. Certain SDoH were associated with increased PTSS, primarily Hispanic ethnicity, public insurance, and Spanish language used for medical communication. This study informs the importance of early identification of caregivers at a higher risk for PTSS and psychosocial interventions tailored to cultural and language needs.

Poster # 618

HEART RATE VARIABILITY AS A PSYCHOSOCIAL BIOMARKER IN ADOLESCENTS AND YOUNG ADULTS WITH CANCER

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Background: Stress-related psychosocial factors can affect cancer outcomes through neuroimmune mechanisms. The sympathetic nervous system (SNS) coordinates one arm of the stress response, and SNS activity can be quantified via heart rate variability (HRV). Higher HRV indicates increased 'autonomic flexibility' and better health outcomes. Adolescents and young adults (AYAs) with cancer report high rates of psychosocial distress and have had diminished improvement in clinical outcomes compared to other patients. Identifying psychosocial biomarkers will help define the mechanisms linking the intertwined behavioral and biologic outcomes in AYA cancer.

Objectives: To describe HRV values in AYAs with cancer undergoing hematopoietic cell transplantation (HCT) and explore associations with patient-reported psychosocial symptoms.

Design/Method: Eligible patients were aged 12-24 years enrolled on a randomized trial testing a resilience intervention in AYAs receiving HCT (NCT03640325). To assess HRV, patients wore the Actiheart 5 (CamNTech, Inc) device for 24 hours at baseline, 1 month, and 3 months post-HCT. HRV was quantified using the Actiheart Software, yielding routine time domain metrics [standard deviation of normal-to-normal beats (SDNN) and root-mean-square of successive differences (RMSSD)]. For reference, normative adolescent SDNN and RMSSD median (IQR) values are 63 (48, 85) and 59 (45, 88) for males and 66 (46, 87) and 69 (49, 100) for females. Patient-reported anxiety and depression were measured with the Hospital Anxiety and Depression Scale (HADS, range 0-21, higher scores reflect increased symptoms). Correlations between baseline HRV and 1) baseline HADS scores, and 2) change in HADS score from baseline to 3 months, were assessed with Pearson correlation coefficients.

Results: A total of 39 HRV recordings were collected from n=17 patients (aged 12-21; 9 male, 7 female, 1 nonbinary) at 3 institutions. Median (IQR) SDNN and RMSSD were 27 (21, 38) and 11 (8, 22) in males and 25 (22, 27) and 13 (4, 19) in females, respectively. Patients with higher baseline HRV had fewer baseline symptoms of anxiety and depression ($r = -0.35$ for SDNN, $r=-0.47$ for RMSSD vs. anxiety; $r=-0.26$ for SDNN, $r=-0.39$ for RMSSD vs. depression). Among patients with elevated baseline anxiety symptoms (scores ≥ 5), higher baseline HRV was associated with greater improvement in anxiety scores from baseline to 3 months ($r = -0.66$ for SDNN, $r=-0.24$ for RMSSD).

Conclusion: AYAs with cancer receiving HCT may have inferior autonomic flexibility measured by HRV compared to healthy peers. Baseline HRV correlated with psychosocial outcomes in this small cohort. Larger studies of psychosocial biomarkers in AYAs will facilitate risk-adapted biobehavioral interventions.

Poster # 619

SOCIAL DETERMINANTS OF HEALTH AND PSYCHOSOCIAL OUTCOMES IN PEDIATRIC SURGICAL ONCOLOGY PATIENTS

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Background: The psychosocial functioning of pediatric surgical oncology patients is understudied. Additionally, there is limited literature examining the impact of social determinants of health (SDOH) on psychosocial outcomes such as academic accommodations and quality of life in this group.

Objectives: To investigate the associations of medically underserved area (MUA) status, health professional shortage area (HPSA) status, rurality, and Appalachian residence on psychosocial outcomes in pediatric surgical oncology patients.

Design/Method: This was a retrospective chart review of pediatric surgical oncology patients from March 2019 to December 2022 at Nationwide Children's Hospital (N=122). Parental PedsQL, school and developmental services use was collected during a clinical psychosocial assessment. Children ≥8 years old completed self-reports of the PedsQL. MUAs and HPSAs were classified by the Health Resources and Services Administration's Office of Shortage Designation. Rurality was determined using Rural Urban Commuting Areas (RUCA) scale (1-10; ≥4 indicated rurality) and Appalachian status via the Appalachian Regional Commission database.

Results: Patients were 0-20 years old (M=8.83; SD=6.33) and a plurality (27.0%, n=33) was diagnosed with a neuroblastic tumor. Twenty-two parents (18.0%) had an IEP or 504 plan for their child and 8.2% (n=10) reported school-endorsed concerns with the child's progress. One hundred two (83.6%) resided in a mental health HPSA, 38.5% (n=47) in a primary care HPSA, 36.9% (n=45) in a dental health HPSA, 25.4% (n=31) were rural, 21.3% (n=26) were Appalachian, and 18.0% (n=22) were in a MUA. HPSA, rural, Appalachian, and MUA residence did not significantly correlate with academic concerns or prevalence of an IEP/504 plan. MUA status significantly correlated with lower PedsQL scores on parental reports of 13–18-year-olds (t(35)=2.21, p=0.034). Dental health HPSA status significantly correlated with lower PedsQL scores for parental reports of 13–18-year-olds (t(35)=3.44, p=0.002) and for self-reports of 13–20-year-olds (t(37)=2.10, p=0.042). Appalachian status likewise significantly correlated with lower PedsQL scores on parental reports of 13–18-year-olds (t(35)=3.77, p<0.001) and for self-reports of 13–20-year-olds (t(37)=3.02, p=0.005). Primary care HPSA, mental health HPSA, or rural residence did not significantly correlate with PedsQL scores.

Conclusion: Residence in MUA, dental health HPSA, and Appalachian areas may be associated with lower parental and self-report PedsQL scores. Though not significantly associated with the psychosocial outcomes measured, a large majority of this sample resided in a mental health HPSA. These findings warrant further studies to help elucidate the impact that SDOH may have on psychosocial outcomes for pediatric surgical oncology patients.

Poster # 620

RESULTS FROM A MULTI-CENTER RANDOMIZED ANIMATRONIC DUCK INTERVENTION FOR REDUCING DISTRESS IN CANCER

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Background: Children with cancer frequently experience significant distress during treatment. Interventions incorporating medical play may reduce distress and improve patient experience. Our pilot work previously described acceptability of the My Special Aflac Duck (MSAD) intervention and provided rationale for longitudinally testing effectiveness of the MSAD in a large, randomized clinical trial.

Objectives: To describe preliminary results of a multi-institutional randomized study that evaluated impacts of the MSAD on parent-, patient-, and child life specialist (CLS)-reported quality of life (QOL) and satisfaction outcomes.

Design/Method: Eight hospitals were randomized to either receive MSAD (MSAD) or standard care (control). Participants were queried regarding patient distress, QOL, and adverse events at baseline, 1 week, 1 month, and 3 months. Those who received the MSAD completed satisfaction questionnaires. Between group univariate comparisons were conducted at each timepoint and over time. Preliminary hierarchical models controlling for patient, time, group, and site were conducted. Statistically significant ($p<0.05$) differences are presented.

Results: The study enrolled 160 patients (MSAD: n=78, control: n=82); 68 (43%) were female, 103 (65%) were white, 13 (8.1%) were Hispanic, and 86 (54%) were diagnosed with leukemia/lymphoma. The median (IQR) age at enrollment was 5.2 (4.2, 7.3) years. There were no significant differences in diagnoses or other demographics between groups.

Findings varied by reporter and time point. Both parents and CLS reported lower global distress scores among MSAD patients at 3 months, with CLS reporting greater decreases over time. Similar reductions were reported in nausea (parent report) at 1 week and procedural (parent and patient report) and treatment anxiety (parent report) at 3 months. Significantly lower frequencies and severity of pain were reported by CLS at 3 months and over time. Finally, MSAD parents rated their own anxiety (at 3 months) and depression (over time) as significantly lower.

Parents, patients, and CLS consistently reported high satisfaction with MSAD over time. Patients used the MSAD for 26-40 minutes per day throughout the 3 months with touch and medical play as the most utilized features.

Conclusion: Preliminary findings suggest patients in the MSAD condition experienced reductions in distress, nausea, pain, and treatment and procedural anxiety relative to controls, while reporting high intervention satisfaction and engagement. These results warrant inclusion of the MSAD in the CLS toolbox as an evidence-based intervention for reducing adverse psychological outcomes among young children undergoing cancer therapy. Future analyses will include multivariate modeling, which will consider sociodemographic, clinical, and treatment factors influencing outcomes.

Study supported by Aflac, Inc.

Poster # 621

NON-TRANSPLANT ASSOCIATED HEPATIC VENO-OCCLUSIVE DISEASE: A SINGLE INSTITUTION EXPERIENCE

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Background: Hepatic veno-occlusive disease (VOD) is a potentially fatal and underrecognized complication in oncology patients receiving chemotherapy outside of hematopoietic stem cell transplantation (HSCT). Various VOD diagnostic criteria exist for HSCT patients but have not been validated in the non-transplant setting.

Objectives: To 1) characterize general oncology patients clinically diagnosed with VOD and 2) evaluate the validity of HSCT VOD diagnostic criteria including pediatric EBMT (pEBMT) criteria in the non-transplant setting.

Design/Method: This retrospective review included patients aged 0-21 years diagnosed by a clinician with VOD after receiving non-transplant associated chemotherapy between 1/1/2010 and 10/1/2023. Patients were identified by team surveys and interrogation of the electronic medical record for the terms “veno-occlusive disease” and “sinusoidal obstruction syndrome.” Chemotherapy administered between day one of the current cycle and the date of VOD diagnosis was recorded. Data was collected until 10/1/2023 or to last follow up, whichever was sooner. Patients with incomplete records were excluded, including patients diagnosed at an outside institution or prior to our institution’s migration to an electronic medical record.

Results: Thirty patients met inclusion criteria. Four patients were excluded for inadequate clinical documentation. The most common chemotherapies were vincristine (20 patients, 77%) and cyclophosphamide (17 patients, 65%); the most common regimen was vincristine/6TG/cyclophosphamide/cytarabine during delayed intensification for acute lymphoblastic leukemia (eight patients, 31%). The median time from day one of the current chemotherapy cycle to clinical diagnosis of VOD was 14 days (range 3-70 days). HSCT diagnostic criteria were met on average prior to clinician diagnosis (pEBMT 1.846 days, Baltimore 0.6471 days, Seattle 1.5 days). Baltimore criteria were not met in nine patients (35%); Seattle and pEBMT criteria were met in all patients. PEBMT criteria were met prior to clinician diagnosis in 14 patients (54%) and simultaneously with or before meeting Seattle criteria in 21 patients (81%) and Baltimore criteria in 16 patients (62%). Twenty patients (77%) received diuretics, 12 patients (46%) received defibrotide, and 14 patients (54%) required critical care interventions. Eight patients died (31%); VOD was the cause of death in one patient (13%).

Conclusion: The pEBMT criteria accurately diagnosed general oncology patients with VOD and may promote earlier recognition of VOD. Though VOD-associated mortality was limited, late recognition and limited use of defibrotide may have increased patient morbidity including length of hospital stay and need for critical care intervention. General oncology patients at high risk of VOD should be identified for more intensive clinical monitoring while receiving outpatient chemotherapy.

Poster # 622

CLINICAL SIGNIFICANCE OF MASSIVE PERICARDIAL EFFUSION IN PEDIATRIC ONCOLOGY PATIENTS

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Background: Massive pericardial effusion (mPE) can be life threatening should it cause cardiac tamponade. The underlying pathogenesis in oncology patients is complex and can occur during or after cancer treatment. The prognostic significance of mPE in cancer patients remains elusive.

Objectives: To analyze the clinical presentation, treatment status, and prognosis of oncology patients who developed mPE.

Design/Method: A retrospective review of pediatric oncology patients who underwent invasive pericardial drainage for mPE diagnosed by echocardiogram from 2009 to 2022 was conducted. Patients were divided into three groups: primary disease related (PD), treatment-related (TR), and miscellaneous (M). Data are presented as mean ±standard deviation.

Results: Fifteen patients were analyzed (male 8, age 9.9 ± 6.6 years) including 4 PD, 9 TR, and 2 M. Primary malignancies were variable: acute myeloblastic leukemia (3), acute lymphoblastic leukemia (ALL) (3), osteosarcoma (2), myelodysplastic syndrome (2), malignant lymphoma (2), and others (4). Ten patients were in remission whereas five had active disease (onset or relapse). Ten patients (67%, 1 PD and 9 TR) were recipients of hematopoietic stem cell transplant (HSCT). The most common presenting symptoms were tachycardia or respiratory distress, but 3 patients were asymptomatic. None died from direct hemodynamic instability from mPE or tamponade. By linear regression analysis, younger patients tend to show longer drainage duration ($p = 0.047$), but no significant difference was noted between age and effusion volume or effusion volume and drainage duration. Drainage duration was 8.8 ± 9.6 days, and there was no recurrence. Patients after HSCT were significantly younger than others (7.0 ± 5.9 vs. 15.8 ± 2.7 years, $p = 0.009$). Average follow up duration after mPE was 3.8 ± 3.3 years. A high incidence of mortality was noted in the PD group (n = 4, 100%; two with metastatic osteosarcoma, one with malignant lymphoma with mediastinal involvement, and one with relapsed Pre-B cell ALL) compared with the TR group (n = 3, 33%) ($p = 0.011$). All four PD patients died within 35 months after mPE. Mortality was higher in patients with relapsed or refractory disease (n = 5, 100%) compared with those in remission (n = 1, 12.5%).

Conclusion: Most patients who developed mPE presented with nonspecific symptoms with high incidence in HSCT recipients. Younger patients tended to have longer drainage duration. Malignant mPE had a higher incidence of mortality. Occurrence of mPE may indicate prognostic significance in children with malignancy.

Poster # 623

INTERVENTIONS TO REDUCE PEDIATRIC CANCER TREATMENT ABANDONMENT IN LMICS: A SCOPING REVIEW

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Background: Pediatric cancer outcomes in low- and middle-income countries (LMICs) significantly lag behind those in high-income countries. One reason for this disparity is high treatment abandonment rates, defined as a failure to start or choosing not to complete curative-intent therapy after a cancer diagnosis. Although factors that cause treatment abandonment are well described, no systematic examination of interventions to reduce treatment abandonment has been conducted.

Objectives: We conducted a scoping review to describe interventions to reduce treatment abandonment in pediatric cancer patients in LMICs and to evaluate their impact on treatment abandonment outcomes.

Design/Method: A comprehensive literature search was conducted on October 21, 2022, across multiple databases, including MEDLINE Ovid, Embase, Web of Science, CINAHL, and Cochrane. The search, guided by MeSH terms and keywords, focused on LMICs, pediatric oncology, and treatment adherence. Studies were included if they met the following inclusion criteria: (a) included patients ≤18 years of age; (b) conducted in LMICs as defined by the World Bank income classification; (c) contained pre- and post-intervention measures of treatment abandonment. Two reviewers independently screened the eligible publications and extracted the data. Interventions were categorized as focusing on socioeconomic support, education/psychosocial support, and clinical care improvements.

Results: Among the 1,808 articles identified in the search, 24 studies met eligibility criteria: four from the African region, nine from the Americas, eight from the South-East Asian, and three from the Western Pacific Region (based on World Health Organization regions). Six (25%) focused exclusively on socioeconomic support, five (21%) on improving clinical care, and five (21%) on improving education/psychosocial support. Four (17%) were a mixture of two categories, and four interventions (17%) were a mixture all three. All studies demonstrated a decrease in treatment abandonment after the intervention. The median absolute risk reduction (ARR) was 16% (minimum 1%, maximum 55%). The median relative risk reduction was 40% (minimum 24%, maximum 100%). Interventions with the largest ARR values included components of socioeconomic support, psychosocial support, and clinic care improvements. Fourteen (58%) studies reported survival outcomes, and survival generally improved in the studies that reported.

Conclusion: Our scoping review describes interventions that were associated with reduced pediatric cancer treatment abandonment in LMICs. Interventions that combined socioeconomic support, psychosocial support, and clinic care improvements yielded the largest reductions. Survival outcomes also improved in many studies. These findings suggest that treatment abandonment can be effectively reduced and survival outcomes improved in LMICs with targeted interventions aimed at augmenting clinical care and patient support.

Poster # 625

IMPACT OF A FORMALIZED PEDIATRIC SURGICAL ONCOLOGY PROGRAM ON MEDICAL ONCOLOGY PROVIDER SATISFACTION

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Background: A formal Surgical Oncology Program (SOP) was established in Fall 2021 to provide comprehensive care for pediatric oncology patients. The program consists of a dedicated advanced practice provider (APP) with significant experience in pediatric medical oncology, three surgeons with diverse surgical training including pediatric urology/urologic oncology, pediatric surgery, transplant surgery, and pediatric oncofertility, a professional research assistant and a dedicated administrative service coordinator. The goal of this program was to create a more seamless transition between the surgical and medical teams for patients during their oncologic care.

Objectives: To evaluate the impact of a formalized Surgical Oncology Program on medical oncology provider and staff satisfaction.

Design/Method: We performed an electronic survey study of medical oncology providers and staff actively involved in the Center for Cancer and Blood Disorders (CCBD) in Fall 2023. The survey collected provider/staff information including clinical practice details, length of service, and if they had worked in the CCBD prior to the implementation of a formalized SOP. Those who were present prior to the SOP were asked to compare their experience pre- and post- implementation of the SOP using a five-point rating scale. Descriptive statistics were used to report provider details. Bivariate comparisons were performed using Chi-square.

Results: The survey was completed by 47 out of 80 CCBD providers/staff (58.7% response rate). Twenty-nine (61.7 %) respondents worked in CCBD prior to the SOP. There was significant improvement in excellent/good responses after implementation of the SOP for care coordination (24.1% vs 100%, $p<0.001$), communication between teams (27.6% vs 100%, $p<0.001$), ease of interaction between teams (20.7% vs 93.1%, $p<0.001$), combining multiple procedures under one sedation (31% vs 93.1% $p<0.001$), oncology provider perception of family satisfaction (17.2% vs 86.2%, $p< 0.001$), quality of pre-operative care (48.3% vs 100%, $p <0.001$) and quality of post-operative care (34.5% vs 96.6%, p, 0.001). For all survey respondents, the most valuable aspects of the SOP were reported to be a dedicated APP (91.8%) and dedicated surgeons (61.0%).

Conclusion: There was significantly improved CCBD provider/staff satisfaction with care coordination and communication, ease of interaction between medical and surgical teams and perioperative care leading to perceived improvements in patient outcomes and experiences. Future research will include evaluation of the impact of the SOP on patient/family experience.

Poster # 626

FAMILY CENTERED ROUND'S IMPACT ON COMMUNICATION AND ROUNDING EFFICIENCY FOR CHEMOTHERAPY SERVICE

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Background: To streamline patients receiving chemotherapy inpatient care and expedite discharges, the Chemotherapy Service was initiated at St Jude Children's Research Hospital in May 2018. Adhering to institutional practice, sit-down patient rounds followed by walking rounds were conducted by the Chemotherapy Service (CS), an attending, clinical pharmacist and advanced practice provider (APP), without a registered nurse (RN). To resolve communication concerns, Family-Centered Rounds (FCR), an established interdisciplinary rounding process that improves communication and patient safety, was introduced.

Objectives: To optimize staff communication and increase rounding efficiency, a standardized FCR process for CS was established. Our SMART aim was to increase CS and RN communication measured as shared understanding of patients' care plans from 70% to 90% as well as monitor rounding time to assess efficiency.

Design/Method: Quantitative and qualitative questionnaires were sent to CS and RN email groups 3-weeks prior to FCR starting, 6-weeks after starting and 1-year post FCR start. Completion was incentivized with an existing institutional recognition system reward. Initial survey data informed PDSA cycle 1: FCR process education, focus on team format. Follow-up surveys measured FCR impact on team communication, efficiency and feedback on process. PDSA cycle 2 utilized survey feedback to streamline RN presentation and schedule rounding times.
APPs manually tracked start and stop time of rounds and number of FCR patients, with a 3-month hiatus due to implementation of a new electronic medical record (EMR).

Results: There were 23 survey responses 3-weeks prior, 28 responses at 6-week post, and 31 responses at 1-year post. Prior to FCR, 74% of RNs and CS members agreed that there was a shared understanding of daily care plans. At 6-weeks post FCR implementation, this increased to 100% and maintained at 97% 1-year post. 6-weeks after implementation, 71% of respondents affirmed FCR improved communication and patient care which increased to 90% in 1 year.
Median weekly rounding time decreased from 10.5 minutes at 3 months post FCR start to 9.4 minutes after the addition of the new EMR and maintained with PDSA cycle 2. At 1 year, 82% of CS members endorsed that FCR increased their efficiency.

Conclusion: Moving to standardized FCR for chemotherapy service patients has improved provider and RN communication, which will lead to improved patient care and fewer adverse patient events. Refinement of the FCR process will continue to increase the balance measure of efficiency for all team members.

Poster # 627

TRACHEOSTOMIES IN CHILDREN WITH MALIGNANCIES – A SINGLE CENTER STUDY

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Background: Children with cancer have a high risk of complications during therapy including prolonged mechanical ventilation requiring tracheostomies. While tracheostomies have been shown to be a safe procedure, there is little literature on what factors predict positive and negative outcomes for patients

with pediatric cancer.

Objectives: The objective of this study was to characterize the patients with pediatric cancer who have undergone tracheostomies and their outcomes.

Design/Method: A single-center, retrospective chart review was performed of all patients with pediatric cancer who received tracheostomies from 2004 to 2023. Univariate analysis was performed on variables collected.

Results: 68 patients with pediatric cancer who had undergone tracheostomies were identified. The most common indications for tracheostomy were facilitation of ventilation due to respiratory failure (31/68; 46%), elective airway management for surgical local control (14/68; 21%), and airway protection due to inability to manage secretions (10/68; 15%). The most likely tumor types to achieve decannulation were head and neck tumors (14/15; 93%), followed by hematological malignancies (5/14; 36%), other solid tumors (6/21; 29%), and central nervous system tumors (5/18; 28%). The best 5-year survival after tracheostomy placement was amongst head and neck tumors (15/15; 100%), followed by central nervous system tumors (12/18; 67%), other solid tumors (12/21; 57%), and hematological malignancies (5/14; 36%). When comparing patients who underwent early tracheostomy (< 30 days of mechanical ventilation) or late tracheostomy ($\geq$ 30 days), there was no statistical difference in decannulation rates (26% vs 38%, p = 0.45) or mortality (48% vs 63%, p=0.37). The common causes of death were progression of disease (9/27; 33%), multifactorial (8/27; 30%), and infection (3/27; 11%). None were due to a tracheostomy complication.

Conclusion: The most common indications for tracheostomies for patients with pediatric cancer were facilitation of ventilation due to respiratory failure, elective airway management for surgical resection, and airway protection due to inability to manage secretions. Children with head and neck tumors had the best outcomes while hematological malignancies had the poorest. The timing of tracheostomy after mechanical ventilation did not significantly affect rates of decannulation or mortality. No deaths were due to a tracheostomy complication.

Poster # 628

THE IMPACT OF COVID-19 AND TELEHEALTH ON PEDIATRIC ONCOLOGY SOCIAL WORK PSYCHOSOCIAL ASSESSMENTS

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Background:
The COVID-19 pandemic prompted the rapid adoption of telehealth in fields like pediatric hematology, oncology, and bone marrow transplant (BMT). These diagnoses are emotionally challenging for patients and families, with social workers and medical interpreters playing vital roles in providing psychosocial support. However, the impact of this shift to telehealth on their ability to offer effective care has not been explored.

Objectives: This study aims to investigate how the COVID-19 pandemic and the increased use of telehealth services affected University of California Health System social workers and medical

interpreters in Northern California in conducting psychosocial assessments for pediatric hematology, oncology, and BMT families.

Design/Method:
We employed a mixed-methods qualitative study using an anonymous 13-question electronic Qualtrics survey and virtual semi-structured Zoom interviews. The survey collected demographic data and assessed changes in telehealth practices during the pandemic. Participants were contacted using email listservs for social workers and medical interpreters. Subsequently, social workers and medical interpreters who completed the survey were invited to participate in individual semi-structured interviews. Transcripts from these interviews were created using Descript software and independently coded and analyzed by two researchers using the Framework Analysis method and Dedoose coding software.

Results: Twenty participants completed the survey and 11 were interviewed. Survey results indicated a shift from less than 25% telehealth visits pre-pandemic to 75% during the pandemic, stabilizing at 50% post-pandemic. About 25% of appointments required medical interpretation. Comparing in-person appointments and telehealth visits, medical interpreters highlighted advantages like convenience and access, while social workers cited patient cost reduction, improved care quality in multidisciplinary settings, and an improved ability to effectively screen and refer families for necessary resources. However, both groups identified challenges in building patient and physician rapport and issues with families' technology access and literacy. Social workers also highlighted a decline in interpretation quality.

Conclusion: Telehealth has brought notable benefits to these health departments, including convenience, access, and cost saving. However, it has also posed challenges such as maintaining patient rapport and ensuring interpretation quality. This study lays the groundwork for developing telehealth best practices to enhance the support provided by social workers and medical interpreters to patients and their families.

Poster # 629

EXTENDED FLUSHING INTERVAL FOR TOTALLY IMPLANTABLE VASCULAR DEVICES IN CANCER PATIENTS

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Background: Patients with cancer need stable venous access using totally implantable vascular access port (TIVAP). Numerous flushing protocols exist including different frequencies for catheter locking to maintain catheter patency.

Objectives: We evaluated the safety and feasibility of extending the flushing interval beyond 4 weeks in adult cancer patients with TIVAP.

Design/Method: The clinical data of cancer patients who underwent TIVAP implantation at our institution between January 2018 and December 2023 were reviewed. Based on the inclusion and exclusion criteria, 337 patients were enrolled and categorized into three groups according to the length of the flushing interval: group 1 (4 weeks, n = 68), group 2 (8 weeks, n = 93), and group 3 (≥ 12 weeks, n

= 286). The basic characteristics of patients in each group and TIVAP-related complications (infection and occlusion) were analyzed.

Results: Of 337 patients, males were 186 and the median age at the placement of TIVAP was 63 years (range, 24-88). The median heparin flushing interval of a total of 337 patients was 67 days (range, 28-196 days). No significant intergroup differences were observed in terms of gender, age, time elapsed after port insertion, time after chemotherapy completion and use of anticoagulant. Of 337 patients from all three groups, TIVAP-related complications (5 infections and 1 occlusion) occurred in 5 patients (group 1: infection and occlusion in 1 each, group 2: infections in 1, group 3: infection in 1). The cumulative incidence of infection or occlusion with this extending flushing interval was 3.4%. There was no statistically significant difference in TIVAP-related complications among the three groups ($P > 0.05$).

Conclusion: Extending flushing interval for the TIVAP beyond three months in adult patients with cancer is safe and feasible without an increase of TIVAP-related complications. Given the feasibility of extended flushing in adults, we are planning to conduct further study to verify this finding in children and adolescents.

Poster # 630

THE USE OF TOPICAL ANALGESIC CREAM FOR LOCAL PAIN CONTROL IN PEDIATRIC ONCOLOGY PATIENTS

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Background: Pain is a common symptom in the pediatric oncology patient population, which could be due to the disease itself and/or diagnostic or therapeutic interventions. Uncontrolled pain is a significant cause of distress and decreased quality of life for both pediatric patients and their parents, thus adequate pain relief is of prime importance. Topical analgesic agents have bene studied extensively in adult patients, however, the data remains scarce in pediatrics. A topical compounded cream containing amitriptyline, ketamine, and lidocaine (AKL cream) could provide neuropathic pain relief and benefit to pediatric oncology patients.

Objectives: Assess the efficacy of compounded ketamine, amitriptyline, and lidocaine for control of neuropathic pain in pediatric oncology patients using pain assessments compared between baseline and up to ten days post the start of treatment.

Design/Method: Through a retrospective chart review of patients at MD Anderson Children's Cancer Center aged 0-24 years who received topical AKL cream over a span of 5 years, we evaluated pain scores at baseline compared to post AKL cream administration for 10 days. Other clinical information included in the study were demographics, oncologic diagnosis, duration of therapy, other analgesic adjuvants, opioid use, and side effects. A mixed effect model related pain score to discrete study day and age with change from baseline assessed by contrasts with Dunnett-adjusted p-values.

Results: A total of 70 patients were included in this study, with 44% being female and 56% male. Average age of patients studied was 18.4 years. The most common oncologic diagnosis categories were leukemia/lymphoma and non-neural solid tumors. All patients analyzed received AKL cream at least

once. Pain scores were recorded for 10 days post administration for 51.4% of patients. Pain scores were significantly lower than at baseline on study days 3-5 and 7-10. Independently, pain scores increased linearly by 0.19 for each additional year of age ($p<0.0001$).

Conclusion: Lower pain scores were achieved in patients using topical amitriptyline, ketamine, lidocaine cream over the study period. Topical compounded cream can serve as a potential therapeutic adjuvant for cancer related neuropathic pain in the pediatric population.

Poster # 631

UNDER RECOGNITION OF ABNORMAL BLOOD PRESSURE IN ONCOLOGY PATIENTS

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Background: The prevalence of elevated blood pressure (BP) and hypertension in the general pediatric population is an increasing concern, with risk factors such as family history and obesity playing a significant role. Among survivors of pediatric childhood cancer, the estimated prevalence of hypertension is 37%, a 2.5-fold increase compared to the general population. Pediatric cancer survivors face a unique set of risk factors that amplify their susceptibility to hypertension, including cytotoxic drugs, corticosteroids, radiation, and acute kidney injury. The ramifications of hypertension in these patients include accelerated vascular aging, damage to vital organs and an elevated risk of heart failure.

Objectives: Obtain baseline data to establish intuitional prevalence of abnormal BP in oncology patients.

Design/Method: Baseline data obtained with retrospective chart review. Using SlicerDicer we captured a population of oncology patients actively receiving chemotherapy at Connecticut Children's. Using this patient population, we assessed outpatient clinic visits. We reviewed patient demographics, oncology diagnosis, vital signs, documentation of abnormal BP, inclusion of abnormal BP on problem list as well as historic mention of abnormal BP. BP's entered in the electronic health record (EHR) were compared with standard norms as established by American Academy of Pediatrics (AAP) Clinical Practice Guidelines (CPG).

Results: Baseline data revealed 36% of patients met AAP CPG criteria for abnormal BP. Of this population, only 9% had abnormal BP documented on the problem list in the EHR and only 4% referenced abnormal BP in clinical documentation.
Chart review and audit also revealed inconsistency between EHR identification of abnormal BPs as compared to AAP CPG, exposing that the cutoffs to flag BPs as out-of-range in the EHR are not specific to patients' age, gender or height. Current EHR ranges under identify abnormal BPs likely contributing to decreased provider recognition, assessment and treatment.

Conclusion: Despite the prevalence and notable consequences associated with hypertension in oncology patients, it is an under-recognized and therefore undertreated condition in many patients. We believe by adjusting EHR alerts we will be able to better capture abnormal BPs which are specific to patients age, gender and height (using AAP CPG standards). In addition to better capture of abnormal values, we expect that establishing a standardized workflow for the recognition, documentation, follow up and management of elevated BP and HTN will help patients receive appropriate therapy.

Poster # 632

BEWARE OF THE CUTANEOUS LESION: COULD IT BE PEDIATRIC CANCER?

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Background: Cutaneous manifestations of malignancies are rare, span all types of pediatric cancer, and can present as a solitary nodule or papule, leading to a clinical diagnosis of a benign skin lesion, delaying time to definitive diagnosis. Pediatric melanoma often does not present with typical ABCDE (Asymmetry, Border irregularity, Color variation, Diameter >6mm, Evolution) detection criteria and can resemble nonmelanocytic lesions. However, nonmelanocytic tumors with primary cutaneous presentations can also present with ambiguous clinical findings, thus a high degree of clinical suspicion is needed when evaluating a child with a persistent primary cutaneous lesion.

Objectives: Elucidate features of cutaneous manifestations of pediatric tumors; evaluate time to diagnosis, and number of provider visits prior to recommendation of biopsy.

Design/Method: Retrospective study of children (≤ 18 years old) with a diagnosis of a unique malignancy that presented with a primary solitary cutaneous lesion at the University of Pittsburgh. Lesion clinical descriptions included primary morphology, color, and location. Primary endpoints were time from first presentation to care to biopsy, and number of provider visits prior to diagnostic biopsy.

Results: Herein, we present 11 patient cases where a solitary cutaneous papule or nodule was the initial clinical finding of a primary malignancy. Tumors were categorized as nonmelanocytic vs. melanocytic. Nonmelanocytic tumors included neurothekeoma, CIC-DUX4 rearranged sarcoma, LCH, dermatofibrosarcoma protuberans (DFSP), rhabdomyosarcoma, angiomatoid fibrous histiocytoma, B-cell lymphoblastic lymphoma, and alveolar soft part sarcoma. Melanocytic tumors consisted of Spitz melanoma, BAP1 inactivated melanocytic tumor (BAPoma), and nodular BRAF V600K mutant melanoma. Three (27%) lesions were described as erythematous papule/nodule of nose, abdomen, and leg; three (27%) as flesh-colored mass of back or leg; five (45%) as pink/brown papule/nodule of head and neck, trunk and leg locations. Five (45%) lesions were described as rapidly growing and three (27%) as clinically ulcerated. Average time from presentation to care to definitive diagnosis was 7 months (range 1-36 months), with average of three provider visits prior to recommendation of biopsy. All patients underwent complete surgical excision, 8 (73%) required additional surgery following initial biopsy/ surgical excision method. Six (55%) patients received systemic treatment for malignancy.

Conclusion: Cutaneous lesions with lack of response to initial clinical management strategies, rapid growth, or ulceration, may represent childhood malignancy, despite clinically benign appearance. Patients experience significant delays of care, which can negatively influence prognosis. Increased clinical suspicion is needed to diagnosis pediatric malignancy presenting as a solidary cutaneous nodule/papule.

Poster # 633

ELECTROCARDIOGRAM MONITORING FOR PEDIATRIC ONCOLOGY PATIENTS RECEIVING QTC-PROLONGING MEDICATIONS

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Background: Pediatric oncology patients frequently receive medications with the potential to prolong the QTc interval. QTc prolongation poses a risk for the development of clinically significant arrhythmias, especially torsade de pointes. There are no established guidelines regarding frequency of ECG monitoring for pediatric oncology patients receiving QTc-prolonging medications.

Objectives: We sought to establish standard guidelines for QTc monitoring in patients receiving QTc-prolonging medications.

Design/Method: An interdisciplinary team composed of pediatric oncology fellows, attending physicians, pharmacists, nurses, and electrophysiologists designed a guideline to determine what patients qualify for ECG monitoring and at what frequency. The recommendations were based on previous literature and expert opinion. QTc-prolonging medications were stratified as high, moderate, or low risk. QTc interval was defined as normal (≤ 450 ms), prolonged (>460 ms in males and >470 ms in females), and borderline prolonged (>450 ms but less than prolonged). The algorithm was as follows. Obtain a baseline ECG if receiving: 1) One high risk medication; or 2) Three or more low to moderate risk medications; and 3) if expected to receive these medications for at least seven days. If the baseline QTc is ≤ 450 ms, monitor with weekly ECGs. If it is borderline prolonged, discontinue QTc-prolonging medications as able and monitor ECG twice per week. If QTc is prolonged in an asymptomatic patient, discontinue QTc-prolonging medications, optimize serum electrolytes, and monitor ECG twice per week. If QTc is prolonged in a symptomatic patient, or QTc >500 ms, consult cardiology, discontinue QTc-prolonging medications, optimize serum electrolytes, and consider telemetry monitoring. We collected baseline data in patients admitted to the pediatric oncology unit from five randomly selected days within an 8-week timeframe to evaluate how often patients qualify for ECG monitoring based on the guideline.

Results: Fifteen patients met eligibility criteria. Thirteen (87%) were receiving 3 or more low to moderate risk medications, 1 (7%) receiving a high-risk medication, and 1 (7%) was receiving a high-risk and 3 or more low to moderate risk medications. A baseline ECG was obtained in 12 patients (80%). Weekly ECG monitoring was obtained in 8 patients (53%). One patient (7%) had a borderline prolonged QTc. There were no clinically significant arrhythmias.

Conclusion: Baseline data demonstrates there is a gap between patients who would qualify for regular ECG monitoring and those who receive it, suggesting there is a need for improvement on establishing QTc monitoring guidelines for pediatric oncology patients.

Poster # 634

SINUSOIDAL OBSTRUCTION SYNDROME UNRELATED TO HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Sinusoidal obstruction syndrome (SOS), formerly known as veno-occlusive disease, is a well-known complication following hematopoietic stem cell transplant (HSCT) caused by damage to the hepatic sinusoidal endothelium. Although clear guidelines exist for the diagnosis and management of SOS in pediatric HSCT patients, a paucity of literature exists in non-HSCT pediatric oncology patients who develop SOS secondary to chemotherapy unrelated to HSCT conditioning.

Objectives: Review our center's experience with pediatric oncology patients diagnosed with SOS unrelated to HSCT.

Design/Method: Retrospective chart review from 2016 to 2023.

Results: Seven patients diagnosed with SOS unrelated to HSCT were identified on chart review. Diagnoses included B-cell acute lymphoblastic leukemia (B-ALL) (N=6) and testicular rhabdomyosarcoma (RMS) (N=1). Median age at time of diagnosis was 8 years (range 2-15 yrs). For B-ALL patients, five had recently received thioguanine (60mg/m2/dose daily for 14 days) and were diagnosed on or after day 43 of delayed intensification (DI). One patient with B-ALL relapsed immediately prior to DI and was treated with inotuzumab (0.5mg/m2/dose) prior to developing SOS. The RMS patient received dactinomycin as part of standard treatment. Three patients were transferred to us from non-HSCT pediatric oncology centers. All patients were diagnosed with SOS following abdominal ultrasound and sluggish or full reversal of flow was seen in five patients' initial imaging at our center. Other findings included hepatomegaly, gallbladder wall thickening and ascites. All patients were treated with Defibrotide (6.25mg/kg q 6hrs) with a median duration of 14 days (range 10-17 days). Five patients required escalation to pediatric ICU level care. Six patients were successfully treated and are still living. Unfortunately, the patient with relapsed B-ALL had refractory leukemia and developed bleeding on defibrotide requiring cessation of treatment. She died at home under hospice care.

Conclusion: Diagnosis of SOS unrelated to HSCT in pediatric oncology patients is important for successful treatment. Patients who have recently received thioguanine or dactinomycin need special attention to any abnormal weight gain, refractory thrombocytopenia, right upper quadrant pain, hyperbilirubinemia or ascites. Use of defibrotide for treatment of SOS was safe and effective in our non-HSCT patient population with careful monitoring following transfusion and coagulation parameters utilized by our HSCT clinical team.

Poster # 635

CAN QUALITY RT UNDER ANETHESIA BE SAFELY DELIVERED AT A PRIVATE CLINIC OUTSIDE OF THE HOSPITAL?

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Background: Valley Children's Hospital (VCH) is a 358-bed hospital in central California with no on-site RT department. While children requiring RT were typically transferred to local hospitals, RT under anesthesia required long-distance travel to far-distant Universities. cCARE, a privately-owned cancer center in Fresno, California, was the first local facility to provide RT under anesthesia for VCH's patients. VCH contracted with cCARE to provide RT both with and without anesthesia. Professional MD services were provided by board-certified cCARE radiation oncologists. Treatment planning, medical physics and treatment delivery was provided by licensed, cCARE staff. Anesthesia consisted of conscious sedation delivered by VCH anesthesiologists supported by 2 VCH RNs.

Objectives: This paper represents a safety and feasibility review. We attempted to determine whether RT delivered under anesthesia was conducted safely and without untoward complications.

Design/Method: Ninety children from VCH received RT at cCARE. Of these, 28 were treated under anesthesia. Twelve of the children were female and 16 male. The median age was 7 y/o (range, 3-13). Histology consisted of Wilms's tumor (13), Neuroblastoma (6), CNS tumors (5) and Sarcoma (4). Twenty-four of the 28 children received concurrent or sequential chemotherapy. Twenty were treated definitively and eight for palliation.

Results: Fifteen children were treated with IMRT, 15 with 3DCRT, 1 with Electrons, and 1 with single-fraction SBRT. Median RT course was 12 fractions (range, 2-30). Median duration of therapy was 16 days (range, 2-47). One child received two courses of RT, and five were treated to >1 site. Twenty-seven of the 28 children completed their RT courses. Five experienced an RT break (range, 2-21 days). Three of these breaks were for fever and/or neutropenia. Two were for infection (RSV and/or COVID+). There were no recorded anesthesia complications or Grade 3-4 RT toxicities.

Conclusion: In our study, RT under anesthesia was successfully delivered in a local, community-based, private clinic. This represented a significant benefit to the children's continuity of care as well as greatly reducing their and their family's stress and inconvenience.

Poster # 636

IMMUNOTHERAPY IN PEDIATRICS

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Background: Immunotherapy has emerged as a promising treatment approach, specifically designed to boost the response of the immune system to target tumor cells while sparing non tumor tissue. This treatment not only holds potential for enhanced efficacy but also translates into reduced adverse effects on patients, while improving outcomes. Despite its early success, the application of immunotherapy has largely been confined among adults, with slow adoption noted in the treatment of pediatric malignancies.

Objectives: Here the objective is to demonstrate a single institution's experience with immunotherapy in pediatric oncology, in order to further the exploration of these treatment modalities in the treatment of children with cancer.

Design/Method: In our review, we studied a database of 48 pediatric patients out of 226, expressing programmed death ligand 1 (PD-L1), of which 7 have undergone immunotherapy. In this project we studied various tumor types in which immunotherapy found its utilization. We also noted adverse effects associated with this particular therapy as well as efficacy. We believe immunotherapy is poised to deliver a positive impact in the realm of pediatric patients.

Results: 7 pediatric patients with positive expression of PD-L1 received immunotherapy, involving nivolumab alone or in combination with ipilimumab or brentuximab. Hodgkin lymphoma (n=2), metastatic melanoma (n=2), histiocytic sarcoma (n=1), rectal carcinoma in the context of constitutional mismatch repair deficiency (cMMRD) (n=1), epithelioid and spindle cell hemangioma (n=1) comprised the diagnoses. Patients received between 4 and 18 cycles of immunotherapy. Out of all patients who had completed their immunotherapy regimens (n=5) or remained on treatment (n=2), 6 achieved remission or had stabilized disease. The diagnoses responding to treatment included Hodgkin lymphoma (n=2), metastatic melanoma (n=2), rectal carcinoma due to cMMRD (n=1), and epithelioid and spindle cell hemangioma (n=1). Unfortunately, after 13 months in remission, the patient suffering from a histiocytic sarcoma experienced reoccurrence in the duodenum. Immune-related adverse events included mild allergic reaction, prodromal symptoms, anemia and neutropenia, transaminitis, endocrinopathies, and self-limiting neuritis.

Conclusion: This report highlights the positive impact immunotherapy can have in the realm of pediatric malignancies, with the possibility of tumor regression or stabilizing disease. Further research is needed to accurately identify pediatric oncology patients that could benefit from immunotherapy.

Poster # 637

SCREENING PEDIATRIC ONCOLOGY PATIENTS WITH ELECTROLYTE ABNORMALITIES FOR CONGENITAL LONG QT SYNDROME

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Background: Electrolyte abnormalities in the pediatric oncology population are commonly due to renal dysfunction from chemotherapy agents and anti-microbials such as antifungal medications. Chemotherapy-induced nausea and vomiting (CINV) worsens electrolyte derangements. Severe hypomagnesemia and hypokalemia in combination with medications that directly prolong the QT interval can increase the risk of ventricular tachycardia (torsades de pointes), particularly in patients with congenital long QT syndrome (LQTS).

Objectives: To describe the benefit of genetic screening for congenital LQTS in managing pediatric oncology patients whose clinical course is complicated by electrolyte abnormalities in the setting of antifungal medications, CINV, and QTc prolonging medications.

Design/Method: Case Report

Results: A 19-year-old male with B-cell acute lymphoblastic leukemia in delayed intensification was admitted for febrile neutropenia with severe chemotherapy-induced pancytopenia. On presentation, he

complained of perirectal pain and was empirically treated with cefepime and metronidazole, and palonosetron for CINV. On hospital day (HD) 5, he developed left-sided mouth, jaw, and facial pain. Given the persistence of fever > 5 days, he had imaging studies to evaluate for invasive fungal sinusitis (IFS). Computed tomography of the sinuses demonstrated paranasal sinusitis worse in the left maxillary sinus with heterogeneous attenuation of the left maxillary sinus, and erosion of the medial wall. Nasal endoscopy revealed necrotic left inferior turbinate. He was started on broad antifungal coverage with amphotericin B and posaconazole. Biopsy confirmed *Fusarium solani* sinusitis. On HD 7, total parental nutrition was initiated for poor nutrition and electrolyte derangement due to amphotericin B; specifically potassium and magnesium. He had a cardiac arrest on HD 17 with pulseless polymorphic ventricular tachycardia (torsades de pointes) requiring chest compressions, cardioversion, and epinephrine. Labs were significant for potassium of 2.1 mmol/L and magnesium of 2.42 mg/dL. Electrocardiograms (EKG) post-cardiac arrest showed prolonged QTc intervals of 550 and 650 milliseconds. Genetic panel identified a pathogenic variant in KCNQ1 c.1893dup (p.Arg632Gln fs*20), confirming a diagnosis of congenital LQTS, type 1. He was started on nadolol and mexiletine, and QTc-prolonging medications such as anti-emetics were discontinued.

Conclusion: Electrolyte derangements and QTc-prolonging medications such as anti-emetics routinely used in patients undergoing chemotherapy can lead to cardiac arrhythmias, especially in patients with an underlying disorder. Evaluation of QTc interval by EKG in patients with hypokalemia and/or hypomagnesemia can help identify patients at risk for arrhythmias, and genetic testing for LQTS may be indicated in patients with evidence of persistent prolonged QT interval.

Poster # 638/Late Breaking Abstract

REDUCED HYDRATION FLUIDS ARE SAFE AFTER HIGH DOSE METHOTREXATE IN PEDIATRIC PATIENTS

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Background: Hydration and urine alkalinization are the mainstays for prevention of methotrexate-induced nephrotoxicity. Current oncology protocols recommend young patients with leukemia who are administered high dose methotrexate 5 grams/m2 (HDMTX) to be aggressively hydrated with an alkaline solution at a rate of 125 to 200 mL/m^2/hour. Over-hydration with the current standard post hydration recommendation can be detrimental to patients. We describe a comparison of standard post hydration after HDMTX to 50% of the current post hydration recommendation to avoid potential adverse effects.

Objectives: This pilot study sought to determine whether reduced post hydration in pediatric patients results in equal methotrexate clearance without increasing adverse events.

Design/Method: A prospective randomized controlled crossover study design of pediatric acute lymphoblastic leukemia patients was performed. Patients were randomized to begin with standard or reduced volume intravenous fluids. Over the course of 4 cycles of HDMTX, patients alternated between standard rate of 125 mL/m^2/hour and reduced volume rate of 62.5 mL/m^2/hour. Urine parameters and leucovorin administration remained consistent.

Results: Data from 37 HDMTX courses were analyzed in 10 patients aged 1 to 17 years (standard rate n = 18 vs. reduced rate n= 19). There was no difference in the median time to methotrexate clearance

based on post hydration strategy (71.7 hours (60.8-115.6) vs. 72.9 hours (59.9-132)). When viewed by age, there were no differences in mean time to methotrexate clearance between younger 74.6 hours (61.9, 87.2) and older patients 86.3 hours (73.4, 99.2), p-value = 0.1935. There was no statistical evidence of a difference in the percent change from baseline to maximum creatinine values (10% vs. 18.9%, p -value = 0.6566), maximum weight gain (0.7 kg vs. 0.4 kg, p-value = 0.0967), or rates of severe mucositis between groups. The numeric incidence of CTCAE grade 1 or higher edema was double in the standard vs. reduced post hydration strategy.

Conclusion: Reduced post hydration was safe and provided similar time to HDMTX clearance in pediatric patients. A limitation to our study is the small sample size. Larger prospective studies are needed to determine optimal post hydration for pediatric patients receiving HDMTX.

Poster # 639

DEMOGRAPHIC AND CLINICAL FEATURES OF PATIENTS REQUIRING GLUCARPIDASE AFTER HIGH DOSE METHOTREXATE

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Background: High-dose (HD) methotrexate (MTX), defined as ≥500 mg/m2, is a mainstay of treatment for acute lymphoblastic leukemia (ALL), non-Hodgkin's lymphoma (NHL), and osteosarcoma (OS). Glucarpidase is an antidote for toxic MTX levels, however there are no clear guidelines on its use, and clinicians lack standardized recommendations regarding subsequent administration of HDMTX following glucarpidase.

Objectives: To evaluate the demographic and clinical characteristics of patients who received glucarpidase and describe re-treatment patterns with HDMTX.

Design/Method: This multi-center retrospective cohort included data from patients aged 0-32 years treated at Children's Healthcare of Atlanta, Texas Children's Hospital, or Cincinnati Children's Hospital Medical Center from January 2010 through December 2020 who received at least one dose of HDMTX. Demographics (age at diagnosis, sex, race, ethnicity) and clinical factors (timing of glucarpidase, MTX clearance, body mass index [BMI]) were abstracted from the electronic health record. Descriptive statistics were calculated using R.

Results: Among 1755 patients who received HDMTX, 33 (1.9%) received glucarpidase (23 patients with ALL, 4 with NHL, and 6 with OS). Of these, 13 (39%) were female, 18 (55%) were Hispanic, median age was 11.9 years (IQR: 9.3, 17.2), and 16 (48%) were overweight or obese. The median dose of MTX was 5000 mg/m2 (IQR: 4956 mg/m2, 5000 mg/m2) for 24-hour infusions and 12,121 mg/m2 (IQR: 10,655 mg/m2, 12,454 mg/m2) for 4-hour infusions. While 19 (58%) received glucarpidase during their first HDMTX administration, the range of receipt was from administration 1 – administration 12. The median time of glucarpidase administration was 41 hours (IQR: 36, 48); this was similar across diagnosis groups. The median duration to MTX clearance was 267 hours (IQR: 195, 339) and 218 hours (IQR: 205, 296) for 24-hour and 4-hour infusions, respectively. Among glucarpidase recipients, 16 (48.5%) received at least one subsequent dose of HDMTX (ALL: 9/23, NHL: 2/4, OS: 5/6); none required additional glucarpidase.

Of these patients, 15 (93.7%) received full dose MTX, while 1 patient with ALL received a 20% dose reduction.

Conclusion: We demonstrate that receipt of glucarpidase is rare in a diverse multi-center cohort of pediatric oncology patients. Among glucarpidase recipients, more were male and Hispanic, and overweight/obese BMI rates were high. Notably, half of the patients were able to receive additional HDMTX. Future analyses will compare renal function and toxicities between glucarpidase recipients and non-recipients by diagnosis group, and elucidate factors associated with discontinuation of HDMTX.

Poster # 640

A COST UTILITY MODEL OF PHARMACOGENOMIC TESTING IN PEDIATRIC CANCER

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Background: Adverse drug reactions (ADRs) in pediatric cancer patients can result in significant lifelong costs and a decreased quality of life. Pharmacogenetic tests have been developed to predict the likelihood of a patient experiencing a harmful and expensive ADRs.

Objectives: The objective of this study was to evaluate the estimated lifetime costs and health-related quality of life (HRQoL) outcomes with pharmacogenetic testing compared to standard care.

Design/Method: Patients were stratified into genetic risk groups developed by the Canadian Pharmacogenomics Network for Drug Safety (CPNDS). Costs and HRQoL years were estimated for all toxicities based on healthcare data in British Columbia, Canada. The cost savings and HRQoL years gained were measured using cost-utility models based on the reduction in risk of toxicity from the use of dexrazoxane for anthracycline-induced cardiotoxicity(AIC), sodium thiosulfate for cisplatin-induced ototoxicity (CIO), and dose reductive strategies for thiopurine-induced myelosuppression (TIM), compared to standard of care which includes no intervention.

Results: The cost-utility models resulted in overall cost savings per patient of $716.43 (ACT), $7,796.40 (CIO), and $983.46 (TIM). For high-risk patients receiving therapeutic interventions, average cost savings per patient were $4,214.31 (ACT), $49,344.30 (CIO), and $5,066.89 (CIO). High-risk ACT and CIO patients experienced a gain of 3.9 and 2.2 quality adjusted life years (QALY), respectively.

Conclusion: The cost-utility models produced robust evidence of the cost effectiveness and benefits to HRQoL of pharmacogenetic testing prior to treatment with anthracyclines, cisplatin, and thiopurines in pediatric cancer patients.

Poster # 641

CLINICAL RISK FACTORS FOR HDMTX-INDUCED ORAL MUCOSITIS FOLLOWING INDIVIDUALIZED DOSING

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Background: Oral mucositis affected approximately 20% of cases undergoing high-dose methotrexate (HDMTX) in childhood acute lymphoblastic leukemia (ALL), despite effective methotrexate monitoring, proper hydration, urine alkalization, and leucovorin (LCV) rescue. The personalized administration of HDMTX tailored through dose adjustment based on the kinetics and leukemia risks has notably reduced oral mucositis, primarily attributed to decreased delayed excretion. However, variations persist in the incidence of oral mucositis, even when achieving similar targeted 24-hour methotrexate levels.

Objectives: This study aims to discern the risk factors influencing the incidence of oral mucositis with the current protocol for individualizing methotrexate dosing.

Design/Method: Patients' MRNs with oral mucositis Grade II or above per CTCAE Version 4.0 were retrieved from St. Jude Children's Research Hospital TOTAL XVI clinical trial study database. Clinical data, including demographic information, ALL risk classification, immunophenotype, laboratory values, concomitant medications, were retrospectively reviewed for both cases and controls. A case was defined as the occurrence of the first oral mucositis grade II or higher during consolidation. A 1:1 random case-control matching method was used to select controls, considering age (within two-years), sex, final risk classification, immunophenotype, and methotrexate course (I-IV). Statistical comparisons between cases and controls within risk group utilized McNemar's test or Bowker's symmetry test for categorical variables and Wilcoxon signed-rank test for continuous variables. An alpha of 0.05 was considered statistically significant. Analysis and case-control matching were conducted using SAS 9.4 (Carry, NC).

Results: Skin rashes were associated with mucositis incidence (case vs control: 18% vs 0% in low-risk, $p < 0.001$; 19.7% vs 5.3% in standard-/high-risk, $p = 0.008$). More acute kidney injury (AKI) developed in cases during the MTX course (28.2% vs 5.1%, $p = 0.007$ in low-risk; 23.7% vs 9.3% in standard-/high-risk). Additionally, more delayed methotrexate elimination events were noted in low-risk (35.9% vs 10.3%, $p = 0.01$) and in standard-/high-risk (40% vs 25%, $p = 0.05$) within the case groups. Fever, neutropenia, and neutropenic fever were more prevalent in cases than controls ($p = 0.001$, 0.003 | 0.007). Statistically significant differences were observed in 42-hour MTX levels ($p < 0.05$), lowest absolute neutrophil counts ($p < 0.001$), and accumulated LCV doses ($p < 0.001$).

Conclusion: After individualized HDMTX dosing, we identified new skin rashes, AKI, delayed MTX elimination, neutropenia with or without fever during the course, and MTX 42 level are the significant clinic risk factors for HDMTX-induced oral mucositis.

Poster # 642

DISTINGUISHING METHOTREXATE-RELATED POSTERIOR REVERSIBLE ENCEPHALOPATHY FROM STROKE-LIKE SYNDROME

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Background: Stroke-like syndrome (SLS) and Posterior Reversible Encephalopathy Syndrome (PRES) are manifestations of high-dose (HD)- and/or intrathecal (IT)-methotrexate neurotoxicity in pediatric acute lymphoblastic leukemia/lymphoma (ALL/LLy) that can have overlapping clinical presentations. A consensus study proposed clinico-radiologic criteria to diagnose these conditions. However, radiologic data did not include specifics of diffusion weighted imaging (DWI). Correct diagnosis is important as management differs for both.

Objectives: To describe and compare the clinico-radiologic features of SLS and PRES.

Design/Method: We retrospectively reviewed adverse events coded as 'neurotoxicity' for patients aged 1-18 years being treated for newly diagnosed ALL/LLy at St. Jude Children's Research Hospital between September 2000 and May 2022. Patients with events suggestive of methotrexate neurotoxicity who met clinico-radiologic criteria for SLS and/or PRES were included.

Results: Of 732 events, 165 were suggestive of methotrexate neurotoxicity; 25 patients met criteria for inclusion (SLS: 10; PRES: 15). There were 8 males (80%) with SLS versus 6 (40%) with PRES ($p = 0.1$). All patients with SLS and 11 (73%) with PRES self-identified as White; most were non-Hispanic. Median age at onset of SLS was 14.5 years (interquartile range (IQR) 12.5–14.9), versus 9.6 years (IQR 8.0–14.0) for PRES. Signs/symptoms included waxing and waning hemiparesis and ataxia only in SLS; seizures, visual disturbance, and hypertension only in PRES; and dysphasia, headache, and encephalopathy in both. Median days between IT-methotrexate and SLS were 16 (IQR 7–22) versus 9 (IQR 8–10) for PRES ($p = 0.05$). Median days between HD-methotrexate (all accompanied by IT-methotrexate) and SLS were 8.5 (IQR 8–10); no cases of PRES occurred in HD-methotrexate-based consolidation. Upon rechallenge, all recurrences were in the SLS group (3 with IT-methotrexate; 1 with HD-methotrexate), and none in the PRES group.

On magnetic resonance imaging (MRI), cases with SLS had exclusive deep white matter changes, while both gray and juxtacortical white matter changes were seen with PRES ($p < 0.001$). Subcortical (corona radiata) restricted water diffusion was seen on DWI and apparent diffusion coefficient mapping in all cases with SLS and in none with PRES ($p < 0.001$). Cortical and juxtacortical T2 and FLAIR hyperintensity was seen in all cases with PRES and in none with SLS ($p < 0.001$).

Conclusion: Despite some overlap, SLS and PRES can be reliably distinguished based on clinico-radiologic features; waxing and waning neurologic deficits, areas of restricted water diffusion in corona radiata, and absence of cortical gray matter changes are observed only in SLS.

Poster # 643

AN INCREASED FAILURE RATE OF ASPARAGINASE DESENSITIZATION WITH CALASPARGASE PEGOL

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Background: In late 2022, pegaspargase (SS-PEG) became unavailable to patients younger than 22 years in the United States, leaving calaspargase pegol (SC-PEG) as the only available long-acting asparaginase formulation. SC-PEG has been compared to SS-PEG in two randomized, pediatric clinical trials and found to have similar rates of adverse events with comparable rates of event-free survival. Our institution uses

a desensitization protocol for patients who experience a hypersensitivity reaction to asparaginase. Here we review our experience with desensitization since the transition to SC-PEG from SS-PEG.

Objectives: To compare the rate of hypersensitivity reactions, success of desensitization protocols, and need for alternative asparaginase preparations between patients receiving SC-PEG and SS-PEG at our institution.

Design/Method: This is a retrospective, single center study of pediatric patients who received at least 2 doses of SC-PEG between November 2022 and December 2023.

Results: We report on 26 patients with acute lymphoblastic leukemia and lymphoblastic lymphoma who received at least two doses of SC-PEG. The frequency of a grade 2 or higher clinical hypersensitivity reaction in those who received SC-PEG was 42.3% (n=11). Silent inactivation, defined as serum asparaginase activity (SAA) <0.1 IU/mL measured seven days following dosing, occurred in an additional 7.8% (n=2). Ten patients underwent SC-PEG desensitization using a protocol that was identical to our previously published protocol using SS-PEG (August, et al., Ped Blood Cancer, 2020). In the desensitization protocol, patients were premedicated with prednisone, cetirizine, famotidine, and montelukast. SC-PEG 2500 IU/m^2 was divided into three fractions of 1:100, 1:10, and 1:1 dilution. Each fraction was infused over approximately 60 minutes, increasing the rate every 15 minutes. Desensitization was tolerated with appropriate SAA levels (0.1 IU/mL) in 30% (n=3) of patients, 60% tolerated the infusion but had inappropriately low AA levels (n=6), and one patient did not complete the infusion due to an adverse event. Six patients received Rylaze following SC-PEG hypersensitivity, silent inactivation, or unsuccessful desensitization. Compared to our prior experience with SS-PEG desensitization where 17 out of 21 attempts were successful with appropriate SAA levels (August, et al., ASH, 2022), our success rate using SC-PEG (7 failures out of 10 attempts) is significantly less (p=0.013), leading to an increase in the use of an alternative asparaginase preparation.

Conclusion: Our single institution experience with SC-PEG shows a high rate of hypersensitivity reactions, a high likelihood of failure of asparaginase desensitization compared to our historical experience, and the frequent need to switch to an alternative asparaginase preparation.

Poster # 644

ASPARAGINASE HYPERSENSITIVITY: A COMPARISON OF CAL-PEG AND PEG AT A SINGLE INSTITUTION

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Background: Asparagine depletion through use of asparaginase products is as an essential treatment component for acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LBL). As asparaginases are derived from bacteria, they include foreign proteins with the potential to induce immunogenicity. This is often manifested through significant hypersensitivity reaction necessitating drug discontinuation. Calaspargase pegol-mknl (Cal-PEG), approved by the FDA in 2018, has now replaced pegaspargase (PEG) as the only pegylated asparaginase available for patients in the US under the age of 21.5 years. These molecules, derived from *E. coli*, are structurally similar with the primary difference being a more stable succinimidyl carbonate linker (Cal-PEG) in place of the succinimidyl succinate linker

(PEG), allowing for a prolonged half-life. Considering the intermittent asparagine depletion approach utilized within COG protocols, AALL07P4 confirmed Cal-PEG extended asparaginase activity and demonstrated a comparable toxicity profile to PEG, including similar rates of hypersensitivity. This trial was limited by a small number of patients receiving Cal-PEG, 111 patients in total, only 42 of whom received the currently recommended dose of 2500 IU/m2.

Objectives: To compare rates of hypersensitivity reactions of PEG and CalPEG administration

Design/Method: Pediatric patients at the University of Utah with newly diagnosed ALL/LBL diagnosed between 1/1/2020 and 10/31/2023 who received at least one dose of pegylated asparaginase were identified. Patients were grouped according to which asparaginase received, PEG or Cal-PEG. Pre-medication was administered based on institutional standards. Rates of hypersensitivity reactions (grade ≥3) were compared between the two groups.

Results: Between January 2020 and October 2023, 212 patients received a total of 631 doses of pegylated asparaginase (PEG=550, Cal-PEG=81). Of those, 170 patients received PEG and 42 received Cal-PEG. Rates of grade ≥3 hypersensitivity were significantly higher with administration of Cal-PEG, 38%, than with PEG, 15% ($P < 0.001$). Patients receiving Cal-Peg, were 3.4 times more likely to experience hypersensitivity (CI 95%, 1.6 to 7.2, $P < .001$).

Conclusion: Asparagine depletion is a hallmark of ALL/LBL therapy. Recent changes in drug availability have altered the landscape of asparaginase utilization. Although Cal-Peg is FDA approved for the frontline treatment of ALL/LBL, there remains a dearth of reported experience with its use. This single institution report found an increased number of clinically significant hypersensitivity reactions. Immunogenicity is highly variable with great unpredictability, and in the setting of asparaginase therapy, given the severity of these acute reactions and the resulting subsequent impacts on treatment, it is essential to expand the reported incidence of this toxicity.

Poster # 645

METHOTREXATE INDUCED CNS MANIFESTATIONS IN CHILDREN TREATED FOR ACUTE LYMPHOID MALIGNANCIES

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Background: Methotrexate-induced encephalopathy has been reported in 0.8% to 15% of patients receiving treatment for acute lymphoblastic leukemia/lymphomas (ALL).

Objectives: Review single center experience of methotrexate-induced central nervous system (CNS) manifestations in children receiving treatment for ALL.

Design/Method: We retrospectively reviewed the management of children who developed methotrexate related CNS manifestations during treatment of ALL at our institution between July 2013 and June 2023. A neuroradiologist re-reviewed all brain Magnetic Resonance Imaging (MRI).

Results: Thirteen out of 66 children with ALL during the study decade developed CNS symptoms at mean

age of 5.2 ± 2 years. Ten were Caucasian. One patient had T-cell, the rest had B-precursor ALL. Half of the patients had high risk disease. All were CNS1 at diagnosis and had negative end of consolidation minimal residual disease.

CNS manifestations were diagnosed during Induction (2); Consolidation (3); Interim Maintenance-1 (3); Delayed Intensification (3) and Maintenance (2) phases. Symptoms developed as early as after first dose of intrathecal methotrexate up to the 14th dose within an average of 16 days of administration and included raised intracranial pressure 10(77%), headache 7(54%), altered mental status ± seizures 7(54%), ataxia 4(31%) and vision changes 2(15%). Only 2 patients were severely neutropenic and 1 had severe transaminitis.

Brain MRI yielded subcortical white matter changes on T2/FLAIR MRI in 8(62%) patients. Changes were represented by regions of acute hyperintensity in diffuse bilateral cerebral hemispheres (4), parietal (2), occipital (1), and right hemisphere (1). Follow-up MRIs were performed 3 to 8 months later and were repeated up to 6 times over a course of 6 years in a patient. Earliest MRI improvement was evident in 3 months of initial imaging. Two out of the 4 patients with normal MRI had raised intracranial pressure as the only symptoms.

Interventions included acetazolamide (10), neuroprotective regimen (theophylline and dextromethorphan) (8), substitution of intrathecal methotrexate with cytarabine and hydrocortisone (5) and therapeutic drainage of CSF (10). Two patients required ventriculoperitoneal shunt. Eleven patients were successfully rechallenged with intrathecal-methotrexate, upon resolution of signs and symptoms.

Conclusion: About 20% of patients developed methotrexate-induced CNS manifestations in our cohort. Intrathecal route was believed to be the cause. Subcortical white matter changes on T2/FLAIR MRI and elevated intracranial pressure, were common findings. The latter has not been widely reported and inflammation of arachnoid villi impairing CSF drainage is the likely suspected etiology. Acetazolamide and therapeutic drainage of CSF helped prevent worsening of symptoms.

Poster # 646

REAL-WORLD ASPARAGINASE USE PATTERNS IN PATIENTS WITH ALL/LBL POST-RYLAZE APPROVAL

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Background: Recombinant *Erwinia* (Rylaze®) was approved by the United States (US) Food and Drug Administration (FDA) to treat acute lymphoblastic leukemia/lymphoblastic lymphoma (ALL/LBL) in patients ≥1 month old who developed hypersensitivity (HSR) to *E. coli*-derived asparaginase. There is currently limited published evidence of recombinant *Erwinia* use outside of clinical trials.

Objectives: To describe asparaginase use pattern in patients with ALL/LBL in the post-Rylaze approval timeframe (July 1, 2021–January 31, 2023).

Design/Method: This retrospective descriptive analysis used a US open claims dataset from Symphony Health. Index date was defined as first date of asparaginase treatment. Four asparaginases were

included, two *Erwinia*-derived — recombinant and native (Ewinaze®), and two *E. coli*-derived — pegaspargase (Oncaspar®) and calaspargase pegol-mknl (Asparlas®). Patients entered cohort A when they initiated their first asparaginase and cohort B when they started a second, different asparaginase. Patients were followed until treatment discontinuation, 365 days of follow-up, or January 31, 2023.

Results: Cohort A (n=1,495) included 1,370 (91.6%) pegaspargase, 85 (5.7%) recombinant *Erwinia*, 28 (1.9%) calaspargase, and 12 (0.8%) native *Erwinia*-treated patients. Among patients <18 years (n=1,145), 1,051 (91.8%), 57 (5.0%), 28 (2.4%), and nine (0.8%) initiated pegaspargase, recombinant *Erwinia*, calaspargase, and native *Erwinia* as the first asparaginase, respectively. Among patients who received *Erwinia* (recombinant and native, n=97, around 2/3 were <18 years old), the most common comorbidities were obesity (15.5%), liver disease (11.3%), and chronic obstructive pulmonary disease (COPD; 7.2%).

Cohort B (13.6% of cohort A, n=203) represented switching to a second asparaginase, including 168 (82.8%) recombinant *Erwinia*, 19 (9.4%) calaspargase, 13 (6.4%) native *Erwinia*, and three (1.5%) pegaspargase-treated patients. Most patients (n=172, 84.7%) switched from pegaspargase to *Erwinia*. Other treatment sequences included pegaspargase to calaspargase (n=19, 9.4%) and calaspargase to *Erwinia* (n=4, 2.0%). In patients who switched to *Erwinia*, 81.8% (n=148) were aged <18 years.

Among patients who switched from pegaspargase to recombinant *Erwinia*, a 1:6 dose replacement ratio was observed, with administrations most common on Mondays, Wednesdays, and Fridays.

Conclusion: Consistent with FDA approval, the first asparaginase was predominantly pegaspargase, with recombinant *Erwinia* as the second asparaginase in patients with ALL/LBL. However, recombinant *Erwinia* was observed as the initial treatment in 5.7% of patients. Recombinant *Erwinia* dosing usage aligned with the FDA-approved Monday/Wednesday/Friday dosing schedule. Limitations included the nature of the database used, mostly outpatient data, and the short timeframe. Future studies are needed to better describe HSR rates and real-world asparaginase use patterns in a rapidly changing landscape.

Poster # 647

PEGASPARGASE VERSUS CALASPARGASE IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA: A SINGLE INSTITUTION

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Background: Asparaginase agents are an integral component of treatment for pediatric patients with acute lymphoblastic leukemia (ALL). Pegaspargase and calaspargase pegol are asparaginase preparations developed with a longer half-life, offering a more attractive dosing regimen with pegaspargase dosed every 2 weeks and calaspargase every 3 weeks. A study conducted by the Dana Farber Cancer Institute consortium showed similar safety and efficacy between the two agents, leading to industry's discontinuation of pegaspargase. However, subjective concerns have been raised by the clinical community regarding a potential increase in toxicity observed with calaspargase as compared to pegaspargase, including hypersensitivity reactions, pancreatitis, and liver toxicity.

Objectives: To compare the incidence and severity of adverse events associated with pegaspargase versus calaspargase administration at NYU Langone Health.

Design/Method: A retrospective chart review was conducted of patients ≤ 21 years of age with ALL who received at least one dose of pegaspargase or calaspargase from October 2022 to October 2023 at NYU Langone Health. Data was collected including age, gender, type of ALL (B-cell versus T-cell), cycle and day of asparaginase administration, type of agent, and toxicity observed with associated Common Terminology Criteria for Adverse Events (CTCAE) grade. Relevant labs including liver function tests, lipase, and amylase, were collected. Groups were compared using Fisher's exact test, and analyses performed using SAS version 9.4.

Results: One hundred and eighteen patients (79 male and 39 female) were included. Median age was 8 years (ages 1-21). Fifty-one patients received pegaspargase and 67 received calaspargase. There was no statistically significant difference in the incidence and severity of hypersensitivity reactions (p-value = 1), pancreatitis (p-value = 0.925), or liver toxicity (p-value = 0.756) between the groups. Severe adverse events were rare with one patient experiencing a grade 4 event in the pegaspargase group and two patients experiencing grade 5 events in the calaspargase group. Grade 3 events occurred in 8% of the pegaspargase and 9% of the calaspargase groups. In the pegaspargase and calaspargase groups respectively, there were three (6%) and five (7.5%) hospitalizations due to asparaginase-related toxicity. Mild transaminitis was common in both groups, with no statistical difference in elevation of total bilirubin or transaminases between the two groups. Results are limited by timeframe, sample size, and retrospective design.

Conclusion: Calaspargase pegol has similar safety compared to pegaspargase in treatment of pediatric patients with ALL within our health system. The limitations of this study warrant further research in determining the safety of calaspargase pegol.

Poster # 648

PEGFILGRASTIM SAME DAY VERSUS SUBSEQUENT DAY ADMINISTRATION IN PEDATIRC CANCER PATIENTS

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Background: Severe neutropenia is a common complication of chemotherapy that increases the risk of serious, life-threatening infections which may result in delay of chemotherapy or dose reductions. Recombinant granulocyte colony-stimulating factor (G-CSF) can reduce duration of severe neutropenia and incidence of febrile neutropenia by stimulating production, maturation, and activation of neutrophils. Pegfilgrastim, a long-acting formulation of G-CSF, is recommended to be administered at least 24 hours after completion of chemotherapy due to the theoretical risk of an increase in neutrophil precursors that are susceptible to destruction by chemotherapy and a supposed increased risk of neutropenia during simultaneous administration. However, many institutions administer pegfilgrastim on the same day as chemotherapy due to patient convenience to prevent another office visit or decrease healthcare costs by decreasing length of inpatient admission. Adult studies are inconclusive with varying evidence, while pediatric data remains scarce in evaluating effect of timing on neutropenia.

Objectives: To determine whether there is a statistically significant difference in the incidence of neutropenia and febrile neutropenia based on same versus subsequent day administration of pegfilgrastim.

Design/Method: A retrospective chart review was conducted from October 2019 to December 2021 in patients < 40 years of age treated under the pediatric hematology oncology service at NYU Langone Health who received pegfilgrastim after chemotherapy. The same day group was defined as patients who received pegfilgrastim within 24 hours of chemotherapy completion and the subsequent day group was defined as patients who received pegfilgrastim after 24 hours of chemotherapy.

Results: Pegfilgrastim was administered to a total of 28 patients in 106 encounters. Median age was 15.1 years (IQR 3.8-18.3). Severe neutropenia occurred in 35.7% of all encounters in the same day group versus 35.4% in the subsequent day group (p=0.98). The incidence of profound neutropenia was 23.4% and 17.4% in the same day group and the subsequent day group, respectively (p=0.68). Febrile neutropenia occurred in 18.3% in the same day group and 17.1% in the subsequent day group (p=0.93).

Conclusion: There were no statistically significant differences in the incidence of neutropenia between the group of patients who received pegfilgrastim on the last day of chemotherapy versus those who received it the subsequent day. These findings are promising as it supports current literature in regards to pegfilgrastim administration timing in pediatric patients with cancer. This could significantly improve the quality of life of patients as well as potentially decrease healthcare costs. Future prospective randomized control trials are needed.

Poster # 649

IFOSFAMIDE-INDUCED ENCEPHALOPATHY IN PEDIATRIC PATIENTS WITH ONCOLOGIC DISORDERS

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Background: Ifosfamide is an alkylating agent used to treat a broad range of malignancies in both adults and children. A serious side effect of ifosfamide administration is ifosfamide-induced encephalopathy (IIE). There is very limited research on the characteristics of pediatric patients who develop IIE. Additionally, there are no current guidelines for continued chemotherapy with re-administration of ifosfamide in patients who experienced IIE.

Objectives: The objective of this study was to identify the clinical characteristics and treatment regimens of pediatric patients who experienced IIE to help predict IIE onset and facilitate early treatment.

Design/Method: This is a single-center IRB-approved retrospective review of patients with IIE from September 2017 – August 2023. IIE was defined by a change in mental status attributed to ifosfamide and graded based on the National Cancer Institute common toxicity criteria. Clinical characteristics of patients were recorded prior to and after the development of IIE. Treatment regimens and if re-administration occurred were also collected.

Results: Six patients with a median age of 9.5 years (range 4-18) developed IIE within 72 hours of ifosfamide administration. All patients but 1 were female. Of these patients 2 of 6 had a history of seizures prior to ifosfamide administration, 4 of 6 had an underlying renal abnormality (glomerular filtration rate <65, acute kidney injury, focal segmental glomerulosclerosis, or status post nephrectomy), and 4 of 6 had received the nephrotoxic agents cisplatin or carboplatin. All patients were treated with methylene blue and showed full neurologic recovery within 72 hours of treatment. Head imaging was normal except for patient 5 who developed central pontine myelinolysis with encephalitis noted on magnetic resonance imaging. Four patients were pre-treated with methylene blue prior to re-administration of ifosfamide and only one patient re-developed IIE which resolved with further administration of methylene blue.

Conclusion: Underlying renal dysfunction and the coadministration of nephrotoxic agents seem to play a role in the development of IIE in pediatric patients. Careful monitoring of these at-risk patients may help predict the early onset of IIE and facilitate immediate treatment. Methylene blue is an effective treatment regimen for IIE. Pre-treatment with methylene blue prior to re-administration of ifosfamide appears to be an effective management strategy in preventing the redevelopment of IIE in our cohort of patients.

Poster # 650

A PHASE 2 STUDY OF EFLAPEGRASTIM IN PEDIATRIC PATIENTS TREATED WITH MYELOSUPPRESSIVE CHEMOTHERAPY

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Background: Neutropenia is the most common dose-limiting toxicity of chemotherapy. To prevent prolonged neutropenia, ameliorate the risk of febrile neutropenia, and avoid treatment delays, myeloid growth factors such as granulocyte-colony stimulating factor (G-CSF) are used. Eflapegrastim is a long-acting novel recombinant human G-CSF covalently coupled to a human immunoglobulin G4 Fc fragment by a polyethylene glycol linker. Eflapegrastim is FDA approved for use in adult patients with non-myeloid malignancies receiving therapy associated with febrile neutropenia.

Objectives: Our primary objective was to evaluate the safety of eflapegrastim in pediatric patients. Secondary objectives evaluated the incidence of severe neutropenia (absolute neutrophil count [ANC] < $0.5x10^9$/L), time to recovery of severe neutropenia with ANC ≥$1.0×10^9$/L, the incidence of febrile neutropenia, and the pharmacokinetics of eflapegrastim in cycle 1.

Design/Method: This open label phase 2 study enrolled pediatric patients with solid tumors or lymphoma (without bone marrow involvement) receiving myelosuppressive chemotherapy. Patients in Cohort 1 (age 12 to <17 years) were administered eflapegrastim 171 µg/kg subcutaneously approximately 24 hours from the end of chemotherapy. Safety was evaluated by dose limiting toxicities and by adverse events. Additional cohorts opened, stratified by age, at a reduced dose of 137 µg/kg. When the white blood cell count recovered to ≥$1.5 x 10^9$/L, peripheral blood hematopoietic stem cell content was quantified by flow cytometric enumeration of CD34+ cells, and multi-lineage differentiation capacity was assessed with a selective colony forming units (CFU) assay. Fourteen days after co-culture

of each experimental treatment, 500 CD34+ cells were seeded in 6-well plates. Big burst forming units of erythroid (BFU-E), CFU of granulocyte and megakaryocyte (GM) and granulocyte, erythrocyte, macrophage, megakaryocyte (GEMM) were counted at one and two weeks after seeding.

Results: Eleven patients enrolled at our institution, and 10 received eflapegrastim. Twenty-seven doses were administered across all patients. The median time from last dose of chemotherapy to neutrophil recovery was 9 days. There were no grade 2 or higher non-hematologic adverse events. No patients required eflapegrastim dose reduction. The mean absolute CD34+ count in patients' samples was 57.28 cells/µL when the white blood cell count recovered to ≥1.5 x 10^9/L. On CFU analysis, mean day 7 total colonies were 24.94/10^5 cells. On day 14, the most common colony type was CFU-GM (14.17/10^5 cells), followed by BFU-E (8.72/10^5 cells) and CFU-GEMM (2.61/10^5 cells).

Conclusion: Preliminary data suggests eflapegrastim is a safe and effective long-acting myeloid growth factor in pediatric cancer treatment regimens.

Eflapegrastim was generously supplied by Assertio.

Poster # 651

DELAYED SERUM SICKNESS REACTION TO CALASPARGASE DURING TREATMENT FOR B-ALL

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Background: Asparaginase products are a cornerstone of treatment for Acute Lymphoblastic Leukemia (ALL). With recent data showing calaspargase is as effective with more sustained systemic drug levels, more patients are being transitioned to this formulation[1]. With this change, little has been reported in hypersensitivity reactions to this formulation.

Objectives: To describe an experience with a serum sickness like hypersensitivity reaction with calaspargase in a patient with National Cancer Institute (NCI) High Risk B-ALL.

Design/Method: Case Review

Results: We present a 13-year-old female with NCI high risk B-ALL. She initially had a hypersensitivity reaction during consolidation to calaspargase with chest tightness, nausea, emesis, pruritis, hives on bilateral palms along with erythema of her bilateral ears. Within an hour of stopping the calaspargase infusion, her symptoms had completed resolved. At the point of halting the infusion she had received about 20% of her intended 2500 units/m2 dose of calaspargase. Ten days post this reaction, she developed erythema, pain and edema of her right thumb. Over the following two days, she developed polyarthralgia involving bilateral wrists, left hand, bilateral feet, bilateral ankles and bilateral knees.

Her infectious work up ruled out viral infections with a negative respiratory viral panel, a negative strep throat swab, negative ASO and DNase B. Despite no celiac symptoms, she had a previous history of elevated celiac antibodies. Due to this history, during her work up she had an endoscopy which did not show any clinical signs of celiac disease. She had a normal C1q binding assay leading our diagnosis away from an autoimmune cause. With an otherwise negative work up, her presentation was most consistent

with a diagnosis of delayed serum sickness like reaction secondary (SSLR) secondary to recent calaspargase exposure.

SSLRs present with joint inflammation, rash and sometimes fevers following exposure to a drug. The underlying mechanism is not fully understood, but thought to be an immunologic reaction to the drug or their metabolites[2]. With our concern for increased inflammation secondary to her suspected SSLR, she was treated with celecoxib. Her symptoms quickly resolved with this treatment.

Conclusion: Our patient presented with suspected SSLR related to calaspargase administration. We did not find any reports of similar reactions, but suspect with the increased use of the calaspargase formulation, we will see further cases similar to ours.

Resources:
1. Angiolillo, et. al., Journal of Clinical Oncology, 2014
2. Pozzo-Magaña, et. al., Paediatr Child Health, 2021

Poster # 652

A BITTERSWEET CASE: AN UNEXPECTED ADVERSE EFFECT NOTED WITH CALASPARGASE PEGOL USE

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Background: Calaspargase pegol (SC-PEG), a novel derivative of pegylated asparaginase (SS-PEG) and Asparaginase (ASP), is used in pediatric acute lymphoblastic leukemia (ALL) and lymphoma (LLy) treatment. While hyperglycemia following SS-PEG and ASP has been frequently reported, hypoglycemia is less commonly seen. However, recent reports have discussed a cohort of patients with either SS-PEG or ASP-induced, hyperinsulinemic, hypoglycemia.[1,2] Additionally, while SC-PEG has been shown to result in hyperglycemia similarly to SS-PEG, hypoglycemia following treatment with SC-PEG has not been described in the literature.

Objectives: Describe a case of recurrent, non-hyperinsulinemic, hypoglycemia post-SC-PEG.

Design/Method: Case Report

Results: A 2-year-old female with pre-B cell ALL following the high-risk favorable arm of the Children's Oncology Group trial AALL 1732 received five SC-PEG doses (January - August, 2023). Hypoglycemia (blood glucose (BG) <70 mg/dL) with a mean of 48 mg/dL was incidentally noted on routine lab work prior to scheduled procedures after each of the first four SC-PEG doses, on an average of 17 days post-infusion (range: 6-29 days). Although episodes of hypoglycemia were recorded following overnight fasts for scheduled procedures, the patient remained asymptomatic. Of note, she fasted in preparation for other required procedures < 6 and > 42 days post-infusion of SC-PEG and was found to have normal BG levels during those encounters. Hypoglycemia following her first three doses was treated with dextrose-containing IV fluids and resolved quickly. However, following dose #4, she required admission, increased dextrose concentration and frequent monitoring for persistent hypoglycemia. Critical laboratory studies were obtained when her BG was < 50 mg/dL, demonstrating an elevated beta-hydroxy-butyrate (0.92 mmol/L) with a normal-low insulin level (1.7 mU/L). Other critical hypoglycemia labs were within normal

range. She did not have any other known condition or medication which could have contributed to hypoglycemia. In anticipation of expected hypoglycemia with administration of dose #5, she was preemptively treated with nasogastric tube feedings. To date, there have been no additional recordings of hypoglycemia.

Conclusion: This case report identifies a previously unreported adverse effect associated with SC-PEG. Our patient had hypoglycemic recordings approximately 1-4 weeks following administration of SC-PEG, but did not have hyperinsulinemic hypoglycemia, which has recently been reported in the literature following SS-PEG and ASP. Further studies are needed to explore causal association of this unexpected hypoglycemia related to SC-PEG in order to maintain glycemic control in other children receiving SC-PEG.

[1] Frederick et al, ASPHO, 2023
[2] Yi et al, Pediatric Blood Cancer, 2023

Poster # 653

RECOVERY FROM NELARABINE TOXICITY

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Background: Nelarabine is an important treatment for T-cell Acute Lymphoblastic Leukemia (ALL) but has a rare side effect of significant neurotoxicity that presents as a Guillain-Barre-like syndrome. Little is known about the mechanisms of Nelarabine induced neurotoxicity, although some have observed that severe nelarabine neurotoxicity is more common in patients with high leukemic burden. Reports are mixed as to the extent patients can recover from this neurotoxicity with some reports stating this neurotoxicity is irreversible. In this case report, we described a 16-year-old male with early T-cell precursor (ETP) ALL with induction failure, who developed severe neurotoxic side effects from nelarabine, but subsequently had significant neurologic improvement approximately 5 months after Nelarabine exposure.

Objectives: To expand our understanding and the literature on nelarabine's neurotoxic adverse effects.

Design/Method: Case Report

Results: This patient is a 16-year-old male diagnosed with ETP-ALL that started induction chemotherapy as per AALL1231. His end of induction bone marrow aspirate (BMA) revealed frank induction failure with 68% blasts. Given this, he proceeded immediately without count recovery to consolidation as per AALL0434 with nelarabine, at the standard dose of 650mg/m2/dose days 1-5. In the following weeks he developed an ascending paralysis consistent with a nelarabine induced Guillain Barre like syndrome that was accompanied by severe neuropathic pain. Peak neurologic decline was noted approximately one month after his last dose of nelarabine, at which time he had 0/5 strength in his bilateral arms and legs while maintaining 3-4/5 strength in his neck / cervical muscles. He received high-dose steroids and multiple doses of IVIG which did not have any immediate effects. After completing his first half of consolidation chemotherapy a repeat BMA remarkably had no detectable leukemia. After subsequently developing severe pancreatitis, given his cumulative toxicities he was transitioned to maintenance style

mercaptopurine and methotrexate with which he has maintained a remission. While he initially had minimal neurologic improvement in his first 3-4 months after nelarabine exposure, at approximately 4-5 months he had significant neurologic improvement to where he had 3-4 / 5 strength in all extremities.

Conclusion: Consistent with other observations, nelarabine induced Guillain Barre like syndrome occurred in this patient with significant leukemia burden, which appears to be an emerging risk factor for severe nelarabine induced neurotoxicity. In contrast to the reports of others, this patient had significant neurologic recovery, although this recovery was not observed until many months after the onset of symptoms.

Poster # 654

SAFE ADMINISTRATION OF RYLAZE IN PATIENTS WITH SYMPTOMATIC HYPERAMMONEMIA WITHOUT ENCEPHALOPATHY

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Background: Asparginase Erwinia chrysanthemi (rC-P; Rylaze) is used for treatment of acute lymphoblastic leukemia (ALL) in patients with hypersensitivity to pegaspargase. This enzyme catalyzes conversion of L-asparagine into aspartic acid and ammonia. Asparaginase-induced hyperammonemia (AIH) is reported after administration of all forms with symptoms ranging from nausea to encephalopathy. There is inconsistent association of serum ammonia levels with symptoms. Continued asparaginase administration is critical, as withholding doses is associated with decreased event-free survival.

Objectives: We report two patients developing symptomatic AIH with rC-P and subsequent management.

Design/Method: Single-center retrospective review.

Results: Case 1: Six-year-old male with T-cell ALL developed anaphylaxis to pegaspargase in consolidation as per AALL0434. At dose 4/6 of rC-P, he developed nausea and vomiting requiring admission for IV fluids, levocarnitine, and lactulose for hyperammonemia (peak level 240 umol/L; normalized at 48 hours). Additional rC-P doses for this course were withheld. Six weeks later he was re-challenged with rC-P. rC-P administered every 72 hours with empiric lactulose and scheduled ondansetron and dronabinol. Dose 4/6 accompanied by nausea and peak serum ammonia of 269 umol/L, rC-P proceeded with optimization of anti-emetics and clinical monitoring. Further courses were tolerated with this regimen.

Case 2: Eleven-year-old male with B-cell ALL developed anaphylaxis to pegaspargase in consolidation as per AALL1732. At dose 6/6 of rC-P he developed nausea and vomiting with hyperammonemia (peak level 239 umol/L; normalized at 96 hours). He required admission for IV fluids and lactulose. During next rC-P course he received seven doses 48-72 hours apart (peak ammonia 303 umol/L at dose 2/7) with scheduled scopalamine, odansetron, lorazepam, levocarnitine, lactulose, and intermittent fluid boluses. Nadir serum asparaginase activity levels were inadequate with Q72H dosing. In third rC-P course the same supportive care regimen was employed with all doses administered Q48H. Ammonia peaked at

219 umol/L at dose 2/7. However, symptoms were much milder, anti-emetics were reduced, and no dose adjustments were required. The same supportive care regimen will be used for further rC-P courses.

Conclusion: Symptomatic hyperammonemia can develop following exposure to rC-P. Importantly, symptoms do not clearly correlate with serum ammonia levels. We suggest an aggressive supportive care regimen consisting of scheduled anti-emetics and lactulose for symptomatic patients and recommend proceeding with rC-P in the absence of encephalopathy. This series highlights the need for awareness that the presentation of AIH is heterogeneous and requires prompt treatment to avoid delays in care, though safe administration is possible when encephalopathy symptoms are absent.

Poster # 655

VINCRISTINE TOXICITY REVEALED CHARCOT-MARIE-TOOTH DISEASE IN A CHILD WITH BRAIN TUMOR

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Background: The advent of genomic sequencing has increased our understanding of the impact of genetic background on cancer drug resistance, sensitivity, and side effects. Vincristine (VCR) is known for its dose-related neurotoxicity, manifesting as sensory and motor neuropathy, which includes the loss of deep tendon reflexes, neuritic pain, paresthesia, and wrist drop. Less commonly, it may lead to cranial nerve palsies, cortical blindness, jaw pain, sensorineural hearing loss, and laryngeal nerve paresis (hoarseness). Discontinuing VCR often results in the reversal of these symptoms.
Charcot-Marie-Tooth (CMT) is a common inherited peripheral neuropathy caused by mutations in multiple genes, and can be inherited in autosomal dominant, autosomal recessive, and X-linked recessive manners. In pediatric patients, it often remains asymptomatic until early adulthood. Individuals with CMT display heightened sensitivity to VCR neurotoxicity.

Objectives: To present a case of severe VCR neurotoxicity that resulted in the diagnosis of CMT in a child with medulloblastoma, thereby emphasizing the significance of pharmacogenomics in oncology.

Design/Method: Case report.

Results: A 4-year-old boy, presenting with three months of progressive ataxia and morning vomiting, was diagnosed with medulloblastoma. Treatment followed a radiation-avoiding strategy per the Children's Oncology Group protocol ACNS0334, which included VCR on day one. Within 24 hours of receiving VCR, he exhibited vocal hoarseness, bilateral jaw pain, drooling, and constipation. The rapid onset of severe side effects raised concerns about an underlying undiagnosed inherited neuropathy. Although the parents denied any family or personal history of neuropathy or CMT, genetic testing revealed two rare variants of unknown significance (VUS) in the MED25 and KIF5A genes. Subsequent genetic testing on the mother demonstrated that she was positive for the KIF5A gene mutation. KIF5A is associated with autosomal dominant CMT, while MED25 mutations are associated with autosomal recessive CMT. Because both mutations are of uncertain significance, it remains unclear if the two CMT genetic variants contributed to the severity of the patient's symptoms. However, synergistic heterozygosity has been reported in CMT, raising the possibility that the two mutations may have interacted to predispose to VCR neurotoxicity. Nevertheless, his symptoms resolved two weeks after

stopping VCR, and subsequent doses were halved, resulting in mild hoarseness without drooling.

Conclusion: This case underscores the significance of recognizing VCR neurotoxicity as the initial manifestation of an undiagnosed hereditary neuropathy, emphasizing the necessity for genetic evaluation not only with VCR but also with an increasing number of other oncology drugs.

Liu, Neurology, 2014
Nakamura, Neurogenetics, 2012
Vital, Neuromuscular Disorders, 2012

Poster # 656

TOXIC ERYTHEMA OF CHEMOTHERAPY-INDUCED MORTALITY IN 2 ADOLESCENTS: A CASE SERIES & LITERATURE REVIEW

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Background: Toxic erythema of chemotherapy (TEC) is a cutaneous reaction to chemotherapeutics characterized by painful plaques arising within 3 weeks of chemotherapy. Typical causative agents include doxorubicin, cytarabine, and gemcitabine. Commonly affected sites include intertriginous areas and palms and soles, and symptoms generally resolve within 4 weeks.

Objectives: Prolonged and mortal TEC eruptions TEC are rare, and few reports exist regarding TEC in pediatrics. We report on 2 adolescent patients with acute lymphoblastic leukemia who presented with rapidly progressive and mortal TEC after standard chemotherapy. We also review current literature regarding pediatric TEC.

Design/Method: Both cases were at Children's Hospital LA between 2019 and 2021. Literature review involved screening EMBASE database with search terms, and reviewing remaining articles.

Results: Case-1: An 18-year-old male with B-cell acute lymphoblastic leukemia received 4 drug induction chemotherapy with vincristine, prednisone, PEG-asparaginase, daunorubicin, and cytarabine and methotrexate. On day 8, patient developed a maculopapular rash on the neck and back, and perineal mucositis, and by day 10, developed skin sloughing, 10% body surface area rash, positive Nikolsky sign, and oral mucosal involvement. Histopathologic findings were consistent with TEC. By day 12, patient showed worsening dusky epidermal detachment, and received wound care and IV steroids. By day 17, the patient unfortunately expired.

Case-2: A 20-year-old male with T-cell acute lymphoblastic leukemia was admitted during interim maintenance chemotherapy for acute kidney injury and cholecystitis. The patient had received vincristine and methotrexate 3 days prior. The patient had an erythematous right thumb on day 2, and by day 4, developed rapidly progressive mucositis and swelling lesions of bilateral hands and feet. On day 6, patient had hepatotoxicity and enlarged bullae; methylprednisolone was initiated. On day 10, rash encompassed 30-40% body surface area. By day 17, patient developed multiorgan failure and unfortunately expired.

Conclusion: This case series highlights TEC-induced mortality, an outcome previously unreported in literature. Skin symptoms were initially interpreted as infections, before rapid progression of erythema and desquamation; punch biopsy aided diagnosis. Both experienced TEC-associated end organ damage, only previously reported in 1 study of older adults on methotrexate. Existing literature reports TEC cases with self-resolution and re-initiation of chemotherapy, and supportive care with antibiotics and topical steroids in extreme cases, but none treated with IV corticosteroids. Our patients' care included burn center wound care and IV methylprednisolone. These severe TEC presentations demonstrate the need for rapid recognition and preventative treatment for chemotherapy patients.

Poster # 657

OUTCOMES FOR FEVER AND NEUTROPENIA IN PEDIATRIC PATIENTS WITH VARIOUS NEUTROPHIL COUNTS ON DISCHARGE

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Background: Fever and neutropenia (FN) is a common complication of pediatric cancer treatment with goals geared towards screening and prevention of serious bacterial infection (SBI) integral to decreased mortality. The standard guideline from The International Pediatric Fever and Neutropenia Guideline Panel is that afebrile patients admitted for FN could be discharged without further antibiotic therapy if blood cultures remain negative at 48 hours and showed evidence of marrow recovery. The update in 2023 included recommendations regarding earlier discontinuation of antibiotics under certain circumstances. The definition of marrow recovery remains varied at different institutions. Our current definition at Children's Hospital of Richmond of marrow recovery is an absolute neutrophil count (ANC) of >/=200/µl.

Objectives: To determine if ANC at discharge was associated with readmissions and SBI.

Design/Method: This a retrospective study of patients admitted to CHOR between 2015 and 2022. We included patients 1-18 years of age on active therapy for diagnosed malignancy presenting with a temperature of >/=100.4 and ANC <500/µl. Excluded were high-risk patients with AML, relapsed ALL, or hematopoietic cell transplantation. We collected information on ANC, rates of readmission, SBI, multidrug resistant organisms (MDRO), and Clostridioides difficile infection (CDI) and length of admission. Multivariable analysis was performed using Chi-Square, Fisher's Exact Test, and Wilcoxon Rank-Sum Test.

Results: During that time, 227 patients were admitted for FN with 110 patients discharged with an ANC <200/µl and 117 patients discharged with an ANC >/=200/µl. Patients with an ANC <200/µl had high readmission rates (10.9% vs 0.85%, $p < 0.001$). There was not an increased risk for SBI in the ANC <200/µl group (11.8% vs 6.8%, $p = 0.14$). Only 2 patients were found to have SBI in the early discharge group ($p = 0.23$). Secondary analyses showed no difference on MDRO rates (2.37% vs 5.98%, $p = 0.3351$) and CDI rates (3.64% vs 2.56%, $p = 0.7149$). Average admission lengths for patients discharged with ANC <200/µl and ANC >/=200/µl were 2.9 (95%CI 2.6 to 3.1) days versus 4.1 (95%CI 3.5 to 4.7) days ($p < 0.01$).

Conclusion: Discharge ANC is associated with increased readmission rates but not associated with

increased SBI. There were no increased adverse outcomes between the two groups. Those who were discharged with ANC </=200/µl had significantly decreased lengths of admission.

Poster # 658

IMPROVING STANDARDIZATION OF OUTPATIENT ANTIBIOTIC ADMINISTRATION IN CHILDREN WITH CANCER AND FEVER

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Background: Febrile neutropenia (FN) is a common complication of chemotherapy that requires prompt evaluation and timely administration of empiric antibiotics. Evidence-based guidelines recommend the use of antipseudomonal monotherapy in children with cancer and FN. In our institution, there was no consensus in the initial empiric antibiotic for children with cancer and fever presenting to the outpatient clinic, given uncertainty of neutropenic status upon presentation.

Objectives: Global aim: To standardize FN management to improve clinical outcomes and antibiotic stewardship.
SMART aim: To increase the percentage of patients on chemotherapy who present for evaluation of FN in the outpatient clinic and receive empiric intravenous antipseudomonal antibiotics as the initial antibiotic from a baseline of 88% to >94% over 11 months (January-November 2023). Process measures included administration of antibiotics within 60 minutes from first vital signs and use of a nurse-initiated FN order set in the electronic health record (EHR).

Design/Method: Our QI project was conducted by an interprofessional team (pediatric oncologists, nurses, clinical informaticians, infectious diseases specialists, pharmacists). QI tools (process maps, Ishikawa, and key driver diagrams) were used and incorporated stakeholder input. Interventions included: 1) development of a standardized algorithm for antibiotic management in clinic; 2) four educational sessions with providers and nurses; 3) two adaptations to the EHR-enabled nurse-initiated FN order set based on provider feedback; and 4) regular updates on project status at division and monthly nursing meetings. Plan-Do-Study-Act (PDSA) cycles were analyzed.

Results: From January-March, 2023 (PDSA#1) the percentage of patients who received empiric intravenous antipseudomonal antibiotics as the initial antibiotic when they presented for FN in our outpatient clinic improved to 100%. These results were sustained throughout April-November, 2023 (PDSA cycles #2 and #3). We also achieved improvements in both of our process measures with antibiotic administration within 60 minutes increasing from 74% to 93% and use of the nurse-initiated FN order set improving from 30% to 86%.

Conclusion: Our inter-professional QI team surpassed and sustained our SMART aim, which is crucial for our high-risk population. Timely administration of antibiotics and use of the EHR-enabled nurse-initiated FN order set also improved. Notably, in instances where timely administration of antibiotics was not met, the nurse-initiated order set was also not utilized, which supports the use of standardized order sets being critical to streamlining processes. Next steps include implementing our standardized approach to children with cancer who present to our emergency department with fever.

Poster # 659

EFFECTIVENESS OF PROBIOTIC IN NEUTROPENIC PATIENTS COLONISED WITH MULTI DRUG RESISTANT BACTERIA

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Background: Most of pediatric malignancies are high grade, and require intensive chemotherapy. Intensive chemotherapy causes myelosuppression and breach anatomical barriers, thus make children on chemotherapy susceptible to infection. Moreover the frequent use of antibiotics causes dysbiosis of the gut flora and the emergence of multidrug resistant bacterias.We hypothesis that use of probiotics can restore gut flora and can reduce the incidence of MDR bacterial sepsis.

Objectives: The primary objective was to know, the effectiveness of probiotics in decreasing morbidity and mortality in febrile neutropenia patients. Secondary objectives were to know the prophylactic role of probiotics in FN, to assess changes in stool bacterial flora pre and post probiotics and to examine bacterial translocation from gut to blood causing sepsis.

Design/Method: This was a single center, open-label, randomized controlled trial. Patients aged 1month to 14 years, who had a malignancy and whose stool culture and sensitivity report showed multidrug resistant bacteria were included. Stool of patients was sent for culture and sensitivity before the institution of chemotherapy and then every 15 days till next 3 months or till intensive phase of chemotherapy, depending which one was earlier. Patients were randomized to test group (probiotic group) and control group. Following observation were analyzed for two groups, change in bacterial flora in stool at various time points, episodes of febrile neutropenia, need for intensive care unit, episodes of diarrhea and pneumonia.

Results: The number of patients eligible was 67. Thirty two patients received probiotics (Test group), 35/67 were in the control group who was not given probiotics. There was no statistically significant difference in stool bacterial flora in two groups when the change in flora was analyzed, there was no difference in PICU admissions, episodes of diarrhea, episodes of pneumonia and non neutropenic febrile episodes. The difference in the number of patients with febrile neutropenia (27/32) was statistically significant in the probiotic group as compared to non probiotic group (20/35) ($p<0.03$). The bacteria consumed as a probiotic was not grown in any patient whose blood culture was positive.

Conclusion: There were no advantages of giving probiotics in patients with febrile neutropenia whose stool surveillance showed multidrug resistant bacteria. Furthermore, there has been an increase in the number of patients with febrile neutropenia in the probiotic group. According to our study, probiotics should be avoided in the treatment of febrile neutropenia and more research is needed to establish their role in febrile neutropenia.

Poster # 660

SECOND COVID-19 INFECTION IN CHILDREN WITH CANCER: CLINICAL COURSE AND RISK FACTORS

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Background: Three years into COVID-19, 5-15% of individuals have been infected more than once. Children with comorbidities are particularly vulnerable to more severe disease with COVID-19. Specifically, children with cancer have higher rates of hospitalization, intensive care unit (ICU) admission, and death with COVID-19 than their peers, and often have their cancer-directed therapy changed, leading to unknown impacts on treatment outcomes (Johnston et al, JCO 2021). However, little is known about COVID-19 re-infections in children with cancer.

Objectives: We aimed to examine the support required and changes to cancer-directed therapy in COVID-19 re-infections among children with cancer, along with risk factors for re-infections.

Design/Method: We leveraged the Pediatric Oncology COVID-19 Case Report (POCC) registry, the largest US registry of children with cancer and COVID-19; >50% of US pediatric cancer programs report to POCC (104 institutions). These analyses included children with cancer who were ≤21yo when infected with COVID-19 and receiving cancer-directed therapy (or completed within 12 months prior to infection). Sites abstracted de-identified (i) sociodemographics, (ii) cancer-related clinical data, and (iii) COVID-19-related clinical data from medical records of first and second infections; all children with second infections had a first infection recorded. Using multivariable logistic regression, we modeled the odds of hospitalization, ICU admission, need for support and changes to cancer-directed therapy, adjusting for age, sex, race/ethnicity, insurance, diagnosis, blood or marrow transplant, absolute neutrophil count, presence of comorbidities, and vaccination.

Results: Examining 2,075 children reported to POCC between April 1, 2020 and December 11, 2023, the median age was 10 y (IQR 5-15), 68% had a hematologic malignancy, 52% were from non-white racial/ethnic groups, and 6% (n=125) reported a re-infection. Sociodemographics, disease status, comorbidities, and vaccination status were not different between children with first and second infections ($p \geq 0.2$), but those with second infections had hematologic malignancies more often (66.8% vs. 78.4%, $p=0.02$). Hospitalization, ICU admission, and therapy modifications were not different between first and second infections in univariable or multivariable analyses. In multivariable analyses evaluating predictors of second infections, only a hematologic malignancy was associated with a higher odds of a repeat infection (vs. solid tumor; OR=1.75, 95%CI 1.12-2.72).

Conclusion: Children with hematologic malignancies faced higher odds of COVID-19 re-infections. Children with cancer did not have a milder course with second infections. These data may inform pediatric oncology teams in counseling families regarding prevention (vaccination, mitigation strategies) and considering clinical management (inpatient/outpatient, anti-viral strategies) of children with cancer in the context of COVID-19 re-infections.

Poster # 661

PERCEPTIONS OF COVID-19 VACCINATION AMONG CAREGIVERS OF PEDIATRIC ONCOLOGY PATIENTS

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Background: Pediatric cancer patients are at increased risk for COVID-19 infection and related complications. COVID-19 vaccination is strongly recommended for these patients, yet little is known about vaccine perceptions in this population.

Objectives: Examine caregiver perceptions related to COVID-19 vaccination of their child with cancer.

Design/Method: In this cross-sectional survey study, English and Spanish-speaking caregivers were eligible to participate if their child (<18 years) had a cancer diagnosis and received care at Seattle Children's Hospital (June 2018-May 2021). Caregivers were recruited via email or regular mail to complete an online REDCap survey (March-June 2022). The survey addressed COVID-related knowledge, attitudes and experiences. Vaccine hesitancy was identified using the validated short form of the Parent Attitudes about Childhood Vaccines survey. Caregiver responses were linked with their child's electronic health record (EHR) data. The primary outcome was COVID-19 vaccine acceptance, defined as COVID-19 vaccine receipt (EHR-documented or caregiver-reported) or vaccine intention (if child ineligible). Survey responses and EHR data were summarized using descriptive statistics. Associations between survey responses and clinical data with COVID-19 vaccine acceptance were analyzed using multivariable logistic regression.

Results: Of 441 eligible caregivers, 103 (23%) completed the survey. Overall, 69% of caregivers accepted COVID-19 vaccine for their child with cancer; 57% were vaccine hesitant. Top reasons caregivers gave for vaccine acceptance were protection (68%) and return to normalcy (60%) and for vaccine declination were concerns about newness (59%) and safety (44%). In multivariable analysis, caregiver agreement that COVID-19 vaccination was important for their child's health was strongly associated with vaccine acceptance (90% vs. 4%, $p<0.001$). Vaccine hesitancy was negatively associated with acceptance (56% vs. 88%, $p<0.001$). Over half (56%) of hesitant caregivers accepted vaccine for their child. Receipt of flu vaccine in the past season was also a predictor of COVID-19 vaccine acceptance (75%, AOR: 3.6, 95% CI: 1.3-9.9).

Conclusion: This survey describes COVID-19 vaccine perceptions and decision-making among caregivers of pediatric cancer patients. Though vaccine hesitancy score identified nearly all caregivers who declined the vaccine, many hesitant caregivers accepted the vaccine. Although caregivers of pediatric cancer patients may express hesitancy, they may accept COVID-19 vaccination for their child.

Poster # 662

SCREENING AND VACCINATION PROCESS IMPROVEMENT TO ADDRESS GAPS IN FLU VACCINATION IN ONCOLOGY

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Background: Influenza (flu) is a contagious viral respiratory illness that leads to seasonal epidemics annually. Obtaining flu vaccines can reduce the risks of developing flu and its potentially serious complications. Oncology patients are a vulnerable patient population. Vaccine hesitancy has been shown to be prevalent within the immunocompromised oncology patient population and poses a barrier to high vaccination rates[1].

Objectives: We aimed to increase vaccination rates for Cancer and Blood Disorder Center patients at Seattle Children's Hospital to ≥ 90% by January 2024, with a global aim to prevent infections, hospitalizations, and mortality due to flu.

Design/Method: We created a dashboard to track vaccination statuses for all patients in our department; patient screening and vaccination statuses were monitored weekly. Providers and nursing staff were notified on vaccine availability, how to view vaccine statuses, and encouraged to offer flu vaccinations to patients. Exclusion criteria included bone marrow transplant or CAR-T cell infusion within 6 months, history of Guillain-Barré syndrome within 6 weeks of previous flu vaccination, or prior anaphylaxis to egg.
Our institution developed a flu vaccine screening tool, prompted by a best practice advisory (BPA) on the electronic medical record and administered by nurses and medical assistants to patients upon admission to the inpatient ward or during rooming in outpatient settings. If the patient or family declines, reasoning is documented. Following planning with key driver diagrams and a failure modes and effects analysis after the 2022-23 season, the BPA was modified to reappear every 30 days for patients who had declined or deferred vaccination, prompting re-screening. Flu vaccine orders changed to an institutional approval from a patient specific order in the 2023-24 season. Patient vaccination status is assessed during discharge readiness discussions and at daily clinic meetings.

Results: The implementation of monthly screening and the universal flu vaccine order was able to increase same day flu vaccination to 98% in those who demonstrated interest in receiving vaccine. We encountered screening rates at 63% in our inpatient and 44% in our outpatient settings between October and December 2023. Major drivers identified that prevent vaccination include deferral without follow-up, and limited means for direct communication from those screening to provider teams about declinations.

Conclusion: Data collection is ongoing; however, preliminary data suggests that multidisciplinary approach is effective in improving flu vaccination rates at our institution. Our efforts highlight the importance of multidisciplinary involvement in supporting this vulnerable population, as well as areas for continued improvement in communication.

Poster # 664

EFFECTS OF DIET ON CLOSTRIDIOIDES DIFFICILE INFECTIONS AND RECURRENCES IN ONCOLOGY PATIENTS

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Background: The incidence of C. difficile infections (CDI) has been rising over the past decade, with immune suppressed patients, such as oncology patients, being at particularly increased risk. We have previously found that a high-fat/low-fiber diet coupled with broad spectrum antibiotic treatment is associated with increased microbiome disturbance and increased morbidity and mortality upon exposure to C. difficile in mice.

Objectives: We are testing the effects of a diet intervention to increase fiber and decrease fat intake on CDI recurrence, colonization, and microbiome composition in an oncology cohort. We are also relating dietary information in Food Frequency Questionnaires (FFQ) to microbiome composition and CDI rates in oncology patients at high risk if CDI. We hypothesize diet will impact CDI rates and that this intervention can reduce CDI reoccurrence in human oncology patients.

Design/Method: Oncology patients greater than 9 years of age with a first or second CDI are actively recruited for the diet intervention. Patients tolerating a regular diet and consuming higher fat and lower fiber than typical diets are randomized to either receive the dietary intervention or to be part of the control arm. The dietary intervention involves meeting with dieticians to create a customized diet to the patient that significantly increases their intake of fiber and decreases their intake of saturated fat. Patients in the control arm continue with their regular diet. Stool samples are collected weekly for six weeks and the patients are monitored via chart review to assess for CDI recurrence within six months of initiating the intervention. Microbiome composition, C. difficile colonization, and metabolomics are measured as secondary outcomes. We are also recruiting oncology patients greater than 9 years of age at high risk of a first CDI case (based on history of antibiotic, cancer treatments etc) for diet evaluation (FFQ), fecal collection, and assessment of subsequent CDI development.

Results: In preliminary data analysis we have found that there was a gradual improvement over time in fecal microbiome alpha diversity following cessation of antibiotic treatment of a C. difficile infection. Variable levels of rebound in C. difficile colonization and symptoms were observed across patients. Four of 18 Individuals identified as high risk for C. difficile subsequently developed a CDI within 6 months of fecal sample/FFQ collection (so far).

Conclusion: A dietary intervention to increase fiber and decrease fat seems to be a rational, practical, inexpensive, and safe way to prevent CDI recurrence. Further investigation is needed to determine efficacy.

Poster # 665

OPTIMIZING CARE FOR NEUTROPENIC FEVER IN PEDIATRIC PATIENTS BASED ON BODY TEMPERATURE CRITERIA

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Background: Febrile neutropenia is a common and serious complication in pediatric oncology. Despite the incidence and mortality, there is no universally accepted definition for neutropenic fever. The

National Institute for Health and Care Excellence defines neutropenic fever as a temperature ≥100.4°F with an absolute neutrophil count (ANC) less than 500 cells/uL. Other definitions are adapted from the joint American Society for Clinical Oncology and Infectious Diseases Society of America guidelines, which specify a single oral temperature ≥101°F or a sustained temperature ≥100.4°F over one hour. Existing research faces a notable gap in defining optimal fever thresholds as certain cases could be managed in the outpatient setting, which would reduce unnecessary hospitalizations and minimize exposures for already immunocompromised patients. However, it is also crucial to investigate whether excluding patients with lower-grade fevers poses additional risks.

Objectives: Hospitals within Kaiser Permanente Northern California (KPNC) use varying fever thresholds. Kaiser Permanente Oakland Medical Center employs a fever threshold of 101.5°F, while other hospitals use a threshold of 100.4°F. Our goal is to assess potential risks associated with adopting a higher fever threshold, including rates of bacteremia, use of pressors, transfers to the pediatric intensive care unit (PICU), and hospital length of stay.

Design/Method: This is a retrospective cohort study of KPNC members aged 1-18 years, who were diagnosed with neutropenic fever between 2016 and 2022. This study describes patients admitted to the hospital based on Kaiser Permanente Oakland Medical Center's threshold of 101.5°F (high threshold group) and patients from other KPNC sites who were admitted using a threshold of 100.4°F (low threshold group). Patients with history of hematopoietic stem cell transplant or Down syndrome, or diagnosis of acute myeloid leukemia, were excluded.

Results: Study criteria was met by 183 patients including 73 (40%) admitted with a temperature <101.5°F, and 110 (60%) admitted with a temperature ≥101.5°F. Overall, 24 patients developed bacteremia and 24 patients required PICU transfer. One patient passed away during their admission. Between the low and high threshold groups, there was no statistically significant difference in rates of bacteremia (8.2% versus 16.4%, p=0.11), use of pressors (2.7% versus 4.6%, p=0.53), transfer to PICU (12.3% versus 13.6%, p=0.80), or length of hospitalization (7.4±8.4 days versus 8.1±15.9 days, p=0.69).

Conclusion: This hypothesis-generating study suggests that using higher fever thresholds for hospital admission for febrile neutropenia may be safe and decrease hospitalizations for the pediatric oncology population. Further higher-powered studies are needed to confirm these results.

Poster # 666

TICK-BORNE ILLNESSES LEADING TO FEBRILE NEUTROPENIA IN PEDIATRIC ONCOLOGY PATIENTS: A CASE SERIES

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Background: Febrile neutropenia is a common complication and leading cause of infectious mortality in children undergoing cancer treatment. Standard empiric treatment includes antipseudomonal coverage with cefepime or piperacillin-tazobactam, with vancomycin added if indicated. Persistent fevers in pediatric neutropenia without an identified source warrants further evaluation for less common causes of infection. Here, we describe a two-case series of Ehrlichiosis in febrile pediatric oncology patients.

Objectives: To report two cases of tick-borne disease in setting of neutropenic fever.

Design/Method: Case series and literature review

Results: 7-year-old male with standard-risk B-ALL on maintenance chemotherapy was admitted for persistent fever, emesis, and myalgias. Initial laboratory findings included mild pancytopenia and mild hyponatremia. Empiric coverage with cefepime was initiated. On day 3 of hospitalization, a worsening fever curve and positive Murphy's sign were noted. A history of tick exposure prompted investigation for tick-borne diseases endemic to our area, Ehrlichiosis (blood PCR) and Rocky Mountain Spotted Fever (serology), and initiation of doxycycline. Abdominal ultrasound showed acalculous cholecystitis, a reported complication of Ehrlichiosis, with PCR confirmation of *Ehrlichia chaffeensis* infection. Fevers resolved and abdominal pain improved within 24 hours of starting doxycycline.
15-year-old male with high-risk B-ALL in induction chemotherapy was admitted for fever and severe neutropenia, with laboratory findings notable for severe pancytopenia, mild hyponatremia and elevated hepatic transaminases. Respiratory viral panel was positive for Rhinovirus/Enterovirus. Fevers persisted despite empiric cefepime and multiple negative blood cultures. With history of tick exposure, tests for endemic tick-borne diseases were sent (see above) and empiric doxycycline initiated. Fevers resolved within 24 hours of initiation of doxycycline, with PCR confirmation of co-infection with *Ehrlichia chaffeensis* and *Ehrlichia ewingii*.

Conclusion: Recommended empiric broad-spectrum antibiotics for neutropenic fever cover clinically significant gram-positive and negative bacteria, including pseudomonas, but not obligate intracellular bacteria, such as Ehrlichia, Rickettsia, and Anaplasma, that are transmitted by ticks. Clinical symptoms including fever and unique laboratory abnormalities (cytopenias, hyponatremia, elevated hepatic transaminases) seen in infections with tick-borne pathogens overlap with those seen in oncology patients. Thus, special attention to exposure and travel history is necessary to appropriately diagnose these infections. Prompt initiation of doxycycline treatment for tick-borne infections is crucial in immunocompromised patients to improve clinical outcomes. As the geographic endemic area for tick-borne infections in the United States slowly enlarges and the incidence of infection increases, it is important to routinely consider tick-borne diseases in the differential for febrile neutropenia in children receiving chemotherapy.

Poster # 667

EXAMINING EQUITY IN FERTILITY PRESERVATION FOR ADOLESCENT AND YOUNG ADULT CANCER PATIENTS

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Background: With significant recent advancements in cancer therapy, planning for life as a cancer survivor has become integral to comprehensive oncology care for adolescent and young adult (AYA) patients. Yet, barriers to accessing fertility preservation services still exist for young cancer patients. These services are often prohibitively expensive out-of-pocket and are rarely covered by health insurance. Few studies have examined inequity in access to and use of fertility preservation services in patients who identify as members of populations who historically experience cancer disparities, such as

female-identifying, non-White, Hispanic; lesbian, gay, bisexual, transgender, queer, intersex, asexual/agender (LGBTQIA+); and underinsured patients.

Objectives: The aim of this study was to quantify differences in access to and use of fertility preservation services for patients from sociodemographic groups that historically experience cancer disparities who were enrolled in an AYA cancer navigation program during the COVID-19 pandemic.

Design/Method: We performed a secondary analysis from a 2021 survey about cancer care utilization during COVID-19 among AYAs ≥18 years who were diagnosed with cancer between 15-39 years of age. The survey included questions regarding fertility preservation, sociodemographic information, and a measure of financial toxicity (COST score, range 0-44). The primary outcome of interest was a binary (yes/no) response to the question, "Were you undergoing or considering fertility preservation prior to March 2020?". We compared differences in use of fertility preservation services across sociodemographic groups using Chi-squared and Fisher's exact test.

Results: Survey respondents (N=341) were mostly 18-29 years old (50.7%), 61.3% female, 37.4% underinsured, 8.5% LGBTQIA+, and 10.0% Hispanic. Underinsured patients were more likely to pursue fertility preservation compared to patients who were insured (23.8% vs 10.7% respectively, p-value 0.002) as were those with high financial toxicity (COST score ≤21), compared to those with low financial toxicity (22.8% vs 8.0%, p-value <0.0001). Lower utilization of fertility preservation was noted in LGBTQIA+, Hispanic, and female-identifying patients compared to their cisgender/heterosexual, White, and male-identifying counterparts but was not statistically significant.

Conclusion: A lower proportion of individuals who identified as part of a historically disadvantaged sociodemographic group pursued fertility preservation compared to their counterparts. Underinsured patients and those with high financial toxicity were more likely to have pursued fertility preservation, which suggests high out-of-pocket costs for using these services may have contributed to higher financial toxicity. Future directions for this study will include semi-structured interviews to better describe the experiences of individuals from different sociodemographic groups in navigating decisions about fertility preservation.

Poster # 668

ACCESS TO MENTAL HEALTH CARE IN ADOLESCENT AND YOUNG ADULTS WITH CANCER: THE PROVIDER PERSPECTIVE

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Background: Prevalence of anxiety and depression is increasing in Adolescent and Young Adults (AYA) with cancer, however there are limited resources to address unmet health needs. While AYAs undergo cancer treatment, they often require complex care, but systematic assessment of mental health needs is limited. Amongst the 118 guidelines published by the Children's Oncology Group, there are no supportive care guidelines on supporting mental health during and after treatment despite an increasing rate of mental health disorders.

Objectives: We explored barriers and facilitators to access to mental health care for AYAs undergoing

treatment for cancer at our institution.

Design/Method: Our research team comprised of pediatric oncologists, psychiatrists, psychologists and anthropologists adapted a 17-item survey from the Access to Tailored Autism Integrated Care (ATTAIN) instrument. Questions evaluated providers' knowledge, attitudes, and behaviors related to mental health needs in AYA with cancer and barriers and facilitators to effective access mental health care. The survey was completed via REDCAP by physicians (18), nurse practitioners (2), clinical nurses (1), mental health providers (9) and other (4).

Results: Response rate was 49% (34/69). Ninety percent of clinicians reported that >25% of their patients had significant mental health concerns, with anxiety and depression being the most common. Almost half (46%) described that they refer >25% of their patients to a mental health provider, however 78% reported they need help to determine when to refer, despite most (>90%) noting that they feel comfortable interpreting screening results. Ninety-seven percent stated that they would be more likely to use screening instruments if they were tracked in the electronic health record over time. Scheduling appointments with mental health providers was recognized as a major barrier to effective access to mental health care, with >90% of respondents expressing that patients and their families require additional help to schedule and attend mental health care appointments. They described months-long waits, insufficient resources, and healthcare fatigue as main obstacles. Ninety-four percent pointed out that a patient navigator to help schedule appointments would be a great facilitator to address mental health needs.

Conclusion: Systematic assessment of mental health needs for AYAs with cancer is lacking. Clinicians described significant barriers to patients receiving the mental health care they need. Further, clinicians observed that AYAs and their families require substantial support to effectively navigate the healthcare system and establish mental health care. These findings will inform future interventions.

Poster # 669

SEXUAL HEALTH EDUCATION INTERVENTION FOR CLINICIANS TREATING ADOLESCENTS/YOUNG ADULTS WITH CANCER

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Background: Prior research shows that Adolescent and Young Adults with cancer (AYAs) have notable sexual and reproductive health (SRH) care needs and want oncology clinicians to initiate SRH conversations through treatment and survivorship. Unfortunately, these conversations rarely take place. Clinicians report lack of knowledge as a key SRH communication barrier.

Objectives: To develop a suite of clinician-centered interactive educational modules to improve SRH communication between AYAs and oncology clinicians.

Design/Method: Potential module content was determined through literature review of AYA and clinician-reported SRH education needs. Expert input from members of the Children's Oncology Group (COG) Sexual Health Task Force, pediatric oncology clinicians (physicians and advanced practice

providers), AYA patients, and an instructional designer helped solidify the training content. Clinician participants were recruited through the Children's Oncology Group (COG) to review the content and structure of the modules and provide qualitative feedback. Feedback was analyzed after three participants completed their evaluations and the study team made modifications to the modules based on recurrent themes and recommendations. Changes were made to the modules and sent to the next three participants for review. This process continued until no further modifications were recommended.

Results: The initial training modules included: 1) a general overview of SRH for AYAs, 2) how to talk to AYAs about SRH, and 3) contraception and safe sex practices. Fourteen clinician participants reviewed the modules and provided feedback. Participants overall reported that the modules were informative and likely to facilitate practice change. Recommendations for a module focused on sexual dysfunction led to the development of a 4th module. Recurrent themes for module improvement included the ability to moderate the speed of the modules, inclusion of more interactive elements (e.g., embedded questions, case studies), and context indexes for each module. Themes for modifications were applied in the development of module 4.

Conclusion: This process resulted in a practical and efficient web-based resource for AYA SRH competency training for pediatric oncology clinicians. These educational modules are a first step in efforts to increase clinician awareness of SRH care needs of AYAs and standardized SRH conversations to improve sexual health outcomes The modules are currently undergoing pilot study to assess feasibility and acceptability across 5 diverse academic institutions.

Poster # 670

PERCEPTIONS OF CLINICAL TRIALS ARE ASSOCIATED WITH ENROLLMENT IN ADOLESCENTS AND YOUNG ADULTS

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Background: More than 100,000 Adolescents and Young Adults (AYA) are diagnosed with cancer in the United States each year. There are significant disparities in clinical trial enrollment and survival outcomes amongst the AYA population. While work describing system-level barriers to enrollment has been instrumental in improving access to care, patient-level barriers require further exploration.

Objectives: To describe the AYA population at our sites, elucidate underlying factors in patient perceptions of clinical trials, and explore the relationship between factors and trial enrollment.

Design/Method: AYAs and caregivers at St. Louis Children's Hospital (SLCH) and Siteman Cancer Center (SCC) with Washington University of St. Louis completed surveys measuring sociodemographics, clinical trial perceptions, trial enrollment, and reasons for trial declination. Exploratory factor analyses (EFA) were assessed for acceptable Kaiser-Meyer-Olkin and factor eigenvalues, high communality, and low cross loading. We conducted univariate analysis, incorporating our clinical knowledge, to identify a list of candidate factors associated with enrollment. A bootstrapping stepwise variable selection algorithm determined the final list in the multivariable logit model.

Results: 100 AYAs (median age 20yr, range 15-29) and 57 caregivers (median age 49yr, range 20-69)

were recruited. Patients were predominantly male, in contrast to caregivers (57.3 vs 17.5%, respectively). Most patients were treated at SLCH, 69.9% vs 30.1% at SCC. A clinical trial was presented to 63.1% of participants and, of those, 38.5% were not enrolled. EFA revealed three factors underlying perceptions of clinical trials: burden, mistrust, and incentive. Participants with higher incentive scores indicated that the benefits of a clinical trial would encourage their enrollment. Incentive and mistrust scores, as well as hospital (pediatric v. adult), were identified as the most important factors associated with enrollment. These variables were important independent predictors of trial enrollment in a multivariate model. Increased incentive scores were associated with higher odds of enrollment (OR 5.276, p = <.001), while increased mistrust scores and treatment at the adult site were associated with decreased odds (respectively OR 0.501, p = .0345; OR 0.114, p <.001). These relationships maintained significance when including only participants approached with a trial.

Conclusion: Factors of clinical trial enrollment at our sites included the hospital setting, the degree to which patients value the incentive of enrollment and degree of mistrust. Patient perceptions are further informed by their degree of burden avoidance. These findings highlight the importance of AYA-centered approaches to care and suggest specific areas of focus for future research in AYA clinical trial engagement.

Poster # 671

ADDRESSING SOCIAL HEALTH NEEDS OF ADOLESCENTS AND YOUNG ADULTS WITH CANCER: A NOVEL APPROACH

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Background: Despite established need, few psychosocial interventions have identified successful strategies for improving social health among adolescents and young adults (AYAs) with cancer.

Objectives: We applied the ORBIT model for behavioral treatment development to adapt an evidence-based psychosocial intervention [Promoting Resilience in Stress Management (PRISM)] to include a novel skill-based component targeting AYA social needs. Specifically, we aimed to (1) develop and iteratively refine social needs component content and (2) refine delivery strategies for the combined PRISM-Social Needs (PRISM-SN) program.

Design/Method: We purposively recruited AYA stakeholders (12-24 years-old, English-speaking) diagnosed with malignancy treated with chemotherapy and/or radiation <12 months from Seattle Children's Hospital. For Aim 1, we recruited AYAs in 2 waves to complete the component (1:1 session, in-person or videoconference) and a structured feedback interview querying acceptability, appropriateness, and suggestions for improvement. For Aim 2, we recruited AYAs to complete the 5-session PRISM-SN program [standard PRISM (4 1:1 sessions targeting stress-management, goal-setting, cognitive reframing, and meaning-making, 1-2 weeks apart, in-person or videoconference) + the social needs component]. AYAs provided feedback on program length, timing, and format. For both aims, qualitative feedback was analyzed using Rapid Assessment Process methods and integrated into program design.

Results: For Aim 1, initial social needs component design included skill-based content teaching AYAs to

identify their support network and match support provision and need. For Wave 1, 7 of 7 approached AYAs enrolled and 6 completed the component and interview (M=17 years-old, 50% female). Feedback was positive; AYAs found content acceptable (4/6) and appropriate (4/6), though some described need for additional skills for maintaining relationships and managing cancer-related conversations. Thus, for Wave 2, we revised content to add skills targeting social connectedness and illness communication. Seven of 8 approached AYAs enrolled and completed the component and interview (M=16 years-old, 43% female). Feedback was highly positive; AYAs found content acceptable (6/7) and appropriate (7/7). They perceived the session was helpful for recognizing support, maintaining relationships, and self-advocacy, with minimal suggestions for improvement. For Aim 2, 8 of 12 approached AYAs enrolled and 6 completed the PRISM-SN program and interview (M=17 years-old, 33% female). Feedback indicated that AYAs preferred to complete sessions weekly, in-person rather than virtually, and early in treatment.

Conclusion: A skill-based intervention component targeting social health is perceived as acceptable, appropriate, and helpful among AYAs newly diagnosed with cancer. The PRISM-Social Needs adapted program may be best delivered in-person and offered early in treatment. Findings inform subsequent proof-of-concept studies.

Poster # 672

AYA-O POWER: A NOVEL VIRTUAL AYA ONCOLOGY EDUCATION SERIES

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Background: Adolescents and young adults (AYAs) with cancer face disparities in their care and outcomes. Pediatric and medical oncology fellowship training programs are lacking in formal AYA oncology (AYA-O) education and curricula (Moerdler, JAYAO 2023).

Objectives: To develop a virtual curriculum to provide medical and pediatric oncology trainees with knowledge and education required to care for AYAs with cancer.

Design/Method: The AYA Education Working Group collaborated with the non-profit Elephants & Tea to develop and deliver the AYA educational series, "AYA-O POWER" (Adolescent and Young Adult Program for Oncology Workforce Education and Resources). The virtual longitudinal educational series was developed based on Kern's curriculum development model. Four sessions between August-November 2023 focused on AYA-O epidemiology and biology, disparities, sexual health, and oncofertility. Scheduled sessions for January-May 2024 include substance use and abuse, AYA-O ethics and end of life care, barriers to care, psychosocial needs of AYAs, and survivorship. Each session included a 20-30 minute live zoom lecture with time for discussion. All sessions were recorded and uploaded for on-demand viewing. Additionally, speakers were encouraged to record short 5 minute 'lightening lectures' which include clinical pearls and key points for rapid knowledge acquisition and reinforcement.

Results: A total of 399 participants have joined the four lectures, representing 265 unique attendees, ranging 82-132 participants per session. Attendees span the United States, Great Britain, Australia, Canada, and India. Multiple AYA care stakeholders have attended the lectures including pediatric/medical oncology trainees, advanced practice providers, oncology attendings, medical

students, researchers, psychologists, social workers, navigators, patient advocates, and caregivers. Forty-three percent of attendees care for children/adolescents, 36% care for both pediatric and adults, and 20% care only for adults. A total of 137 participants have accessed the on-demand lectures and 37 viewed the 'lightening lectures'. In post-session surveys participants expressed their excitement and satisfaction with the curriculum, asking for additional sessions, and reinforced the importance of the series for AYA-O care.

Conclusion: AYA-O POWER addresses a major gap in oncology education with a novel approach to teaching oncology trainees and AYA providers on the needs of and best practices in caring for AYAs with cancer. The global and interprofessional attendance and enthusiasm from the initial sessions of this virtual longitudinal curriculum has proved to be feasible and successful. Additional lectures are scheduled to complete the curriculum. Future directions include increasing adult oncology participation and further evaluation to assess the impact of the curriculum at the completion of the year.

Poster # 673

INVESTIGATING IMPACT OF AGE ON FERTILITY PRESERVATION IN ADOLESCENT AND YOUNG ADULT CANCER PATIENTS

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Background: The adolescent and young adult (AYA) population (15-39 years old) face a wide range of unique developmental challenges when diagnosed with cancer. Beyond the immediate medical issues, AYA oncology patients are often also dealing with complex decisions relating to reproductive health due to the gonadotoxic nature of many treatments. Decision making in the AYA population is a unique situation with many complex factors, including maturity level, coming into play. Despite the effectiveness and need for fertility preservation, it remains an underutilized resource.

Objectives: The goal of this study is to assess and understand the impact of age on the utilization of fertility preservation options

Design/Method: The study team conducted a retrospective cohort analysis of medical records from Westchester Medical Center and Maria-Fareri Children's Hospital to identify AYA cancer patients who received a cancer diagnosis and determined what percentage pursued fertility preservation methods such as sperm cryopreservation. For this analysis only male participants were considered due to the limited nature of female fertility preservation options. A simple logistic regression test was done using the age of the participants at diagnosis and their decision to pursue fertility preservation.

Results: Preliminary results show no increased odds for fertility preservation based on patient age (OR=0.99). Out of the 39 male participants in our study, 13 were included in the analysis and 26 were omitted due to missing information. Our predicted regression model had an overall percentage of 69.2%. The mean age at diagnosis, in months, was 218.05 (SD=37.71) and 97.4% of patients had no biological children at the time of diagnosis.

Conclusion: The preliminary findings did not support the initial hypothesized relationship between age and fertility preservation. However, due to the study's limitations, notably the relatively small sample

size contributing to low statistical power, a definitive conclusion cannot be made. Moving forward, increasing the study cohort and exploring other factors influencing fertility preservation decisions could improve further investigations. Additionally, many of the participants of the study had incomplete or missing data due to lack of adequate clinician documentation, which demonstrates the lack of communication that is one of the many issues in proper AYA fertility care. This study serves as a starting point, exploring one aspect of the nuanced dynamics surrounding fertility preservation in AYA cancer patients and laying the groundwork for more comprehensive research.

Poster # 674

INDEPENDENT, NOT ALONE: BALANCING SUPPORT & INDEPENDENCE FOR ADOLESCENTS & YOUNG ADULTS WITH SARCOMA

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Background: Adolescents and young adults (AYAs;15-39 years) with cancer have unique needs and experiences due to the developmental life-stage at which their disease presents. Compared to younger children or AYAs with other malignancies, AYAs with sarcoma have inferior survival and late effect outcomes due to the biology of these diseases and required treatments. AYAs with sarcoma suffer from disease- and treatment-related long-term disability and functional issues that can contribute to poorer mental health and reduced quality of life.

Objectives: We aim to characterize the unmet medical and non-medical needs of AYAs with sarcoma to inform strategies to improve outcomes for these patients.

Design/Method: Semi-structured focus-groups of AYAs (age 15-39) with sarcoma who were treated primarily at Dana-Farber Cancer Institute were conducted to investigate the experiences of AYA patients with sarcoma. Purposive sampling was used to ensure a diversity of perspectives including patient life stage and disease status. Focus-groups were conducted via Zoom by trained moderators, and focused on participants' experiences with treatment, decision-making, care team communication, supportive care services, and the effects of cancer on participants' daily lives. Focus-groups were audio recorded, transcribed verbatim, and thematic analysis was conducted via a team-based approach.

Results: We conducted four focus-groups with 20 participants (16-34 years). Focus-groups were assembled based on developmental stage and disease status: adolescence, emerging adult, young adult, and one group for those with recurrent/metastatic disease. Participants ultimately framed their desire for support services around maximizing their autonomy and maintaining a sense of normalcy. They described challenges at different stages of cancer treatment in the context of disrupting life-stage milestones such as education and career goals and the inability to return to normalcy. These included loss of independence, changing social relationships, treatment decision-making and side effects, and managing mobility changes and other late effects. Although participants were offered physical and psychosocial support services such as palliative care and social work, resources were not consistently introduced in a standardized manner and participants expressed a desire for services to be introduced earlier to better meet their needs and help facilitate their independence.

Conclusion: We identified a need for physical and psychosocial support, along with a desire for maintaining normalcy and control over identity and independence. Offering individualized support resources in a standardized and equitable fashion that maximizes patient autonomy is critical for improving outcomes for this population. These findings will inform comprehensive multidisciplinary care for this unique population of patients with disparate outcomes.

Poster # 675

IMPACT OF CHILDHOOD CANCER DIAGNOSIS AND TREATMENT COURSE ON AYA SURVIVORS' PSYCHOSOCIAL WELLBEING

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Background: With improved survival among adolescent and young adult (AYA) cancer patients, there is a growing population at risk for adverse psychosocial outcomes.

Objectives: The goal of this study is to identify risk factors for the development of psychological distress or post-traumatic stress (PTS) in AYA survivors.

Design/Method: In a prospective cohort study of patients diagnosed between 10-25 years and followed in the cancer survivorship clinic at Vanderbilt University Medical Center, survivors completed psychosocial surveys, including the ASEBA Youth (YSR) or Adult Self Report (ASR) assessing psychological distress and the Impact of Events Scale (IES) assessing PTS. Sociodemographics, diagnosis, age, treatment intensity, and chronic medical condition at time of survivorship visit were abstracted from the electronic health record. The primary outcome was psychological distress, operationalized as total internalizing or externalizing problems T-score ≥ 60 on either ASR or YSR. The IES was analyzed as a continuous variable, with higher scores reflective of greater PTS. Categorical variables were compared with Chi-square or Fisher's exact test. Continuous variables were compared with Wilcoxon rank-sum test.

Results: Among 55 subjects, median age at diagnosis was 15 years and median time from end of therapy was 4.4 years. 50% were male, 54% had a hematologic malignancy, and 96% were White. YSR/ASR and IES surveys were completed for 52 and 46 patients, respectively. Eight patients (16%) reported psychological distress on YSR/ASR. The median IES score was 8.5 (Quartiles: 0.0-17.8). Psychological distress was more common in those with hematologic malignancy (24.9% vs. 4.2%, p=0.05). No significant association was seen between psychological distress and gender (12% vs 19.2%, p = 0.7), therapeutic intensity (16.7% vs 17.6%, p=0.8), chronic medical condition (18.9% vs 7.2%, p=0.42), age at diagnosis (median 16 vs 14 years, p=0.09), and time off therapy (median 2.5 vs 5.4 years, p=0.18). Subjects with, as compared to those without, psychological distress had a higher median IES (19, Quartiles: 14-19 vs 3, Quartiles: 0-11, p=0.001). An elevated IES score was significantly associated with older age at diagnosis (Spearman rho (r) 0.301, p=0.037), but not therapeutic intensity (r 0.11, p=0.4), time off treatment (r -0.17, p=0.2), or chronic medical condition (median IES 1, Quartiles: 0-18 vs 10, Quartiles: 0-44, p=0.25).

Conclusion: Initial findings suggest a meaningful minority of AYA cancer survivors face psychological

distress and PTS. With further analysis in a larger AYA survivor population, we will assess risk factors for psychological distress and PTS in the survivorship period to inform timely preventive interventions.

Poster # 676

THE EFFECT OF PELVIC RADIATION ON LOWER URINARY TRACT FUNCTION IN CHILDHOOD CANCER SURVIVORS

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Background: Children and young adults with solid tumors in the pelvis often receive multi-modal cancer treatment consisting of cytotoxic chemotherapy, external beam radiation therapy (EBRT), and surgery. While a combination approach affords the best chance of cure and avoidance of morbidity of pelvic exenteration, these therapies may contribute to acute and chronic organ damage within this anatomically crowded area. Modern radiation therapy techniques have improved to limit toxicity; however there remains the potential for both acute and chronic treatment-related morbidity from lower urinary tract (LUT) exposure. Further, there are known effects on LUT function from chemotherapy, most notably cyclophosphamide and overlapping toxicities from chemotherapy and external beam radiation may compound each other. This study investigates the effect of EBRT on LUT function by comparing patient-reported outcome measures, urodynamic studies, and post-void residual bladder scans amongst childhood cancer survivors (CCS) who received pelvic radiation ("exposed group") compared to CCS who did not ("control group").

Objectives: To evaluate patient-reported urinary dysfunction and objective urinary flow parameters including uroflow testing and post-void bladder scan in CCS treated with pelvic EBRT vs control cohort.

Design/Method: This is an ongoing prospective cohort with accrual goal of 40 patients >1 year off therapy for any non-CNS solid tumor. An interim analysis was completed with 14 CCS ages 6-21. 9 CCS received radiation therapy to the pelvis and 5 did not. Research subjects completed the Dysfunctional Voiding Scoring System (DVSS) survey, uroflow testing, and post-void residual bladder scan. Statistical analysis was completed using chi-square or two-tailed t-test, where appropriate, and risk ratios were calculated.

Results: Interim analysis demonstrated that the exposed group had higher abnormal uroflow patterns (40% vs 67%) and had 1.67 times the risk of an abnormal uroflow (p-value 0.33), with varying abnormal uroflow patterns. The exposed group had a higher average PVR (36.6 mL vs 3.8 mL) and had 5.4 times the risk of having an abnormal post-void residual value from age-based norms (p-value 0.08). The exposed group also had higher rates of abnormal symptom scoring (56% vs 40%), with an RR of 1.39 (p-value 0.58).

Conclusion: Interim analysis of childhood cancer survivors receiving pelvic radiation compared to those who had not suggests potential deleterious effects of radiation on lower urinary tract function through patient-reported symptoms, urinary patterns, and post-void residual values. These effects appear to be more common in those patients that received higher EBRT doses. However, study is ongoing.

Poster # 677

WANING IMMUNITY TO CHILDHOOD VACCINES AMONG PEDIATRIC NON-TRANSPLANT CANCER SURVIVORS

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Background: Waning immunity from childhood vaccines can be enhanced in pediatric patients following chemo/immunotherapy. Furthermore, pediatric cancer survivors are at significantly increased risk for life-threatning infections and need for hospitalization for infection compared to those without a history of cancer. In 2020, we implemented an institutional protocol to assess the immune reconstitution and need for re-vaccination among pediatric non-transplant cancer survivors. Here we assess provider compliance with this protocol and describe rates of immune reconstitution, retention of immunity to hepatitis B (hepB), tetanus and pneumococcus 23 serotypes (PPSV23), and rates of booster vaccination among 66 patients who completed chemo/immunotherapy at CHRISTUS Children's from July 2019 to October 2022.

Objectives: To ensure optimal protection against vaccine-preventable infections among pediatric non-transplant cancer survivors.

Design/Method: A mitogen panel and hepB, tetanus and PPSV23 serum antibodies were obtained at six months off therapy. Booster vaccinations were recommended for those with insufficient immunity and titers were re-checked to ensure adequate response.

Results: Of the 66 patients, 59 (89%) had a mitogen panel off therapy and all were considered immune reconstituted. Of the 7 patients who did not have a mitogen panel, 1 was missed due to being lost to follow-up, 1 due to patient refusal, and 5 because the provider did not order the test. Only 1 of the 5 missed mitogen panels occurred after the second Plan-Do-Study-Act (PDSA) cycle started in May 2021.

HepB titers were obtained in 48/66 patients (72.7%) and insufficient in 38/48 (79%). Tetanus titers were obtained in 48/66 patients (73%) and insufficient in 1/48 (2%). PPSV23 titers were obtained in 49/66 patients (74%) and insufficient in 39/49 (80%). HepB, tetanus, and PPSV23 boosters were given to 29/38 (76%), 0/1 (0%), and 29/39 (74%) patients, respectively. The patient needing a tetanus booster was lost to follow-up.

Conclusion: Timing of immune reconstitution and recommendations for re-vaccination following chemo/immunotherapy for non-transplant survivors are not well described in the literature. Initial data reported here suggest that patients are immune reconstituted around six months off therapy, which is generally accepted among most pediatric oncologists. Most patients (~80%) have insufficient immunity to hepB and PPSV23, while the large majority (98%) retain tetanus immunity. These results will affect our next PDSA cycle, including consideration of the utility of lab tests such as the mitogen panel as well as reminders to providers to order booster vaccines when immune titers are insufficient.

Poster # 678

INVESTIGATING RURALITY AND ITS ASSOCIATION WITH CHILDHOOD CANCER SURVIVOR CARE

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Background: Childhood cancer survivors (CCS) are at increased risk of chronic health conditions due to their treatment. While studies have evaluated distance from survivor clinics as a factor leading to disparate survivor care, rurality has been understudied. Unlike distance from clinic, rurality accounts for population density and commuting flow to urban areas and is associated with reduced access to healthcare in the general population.

Objectives: To examine differences in survivor clinic initiation and follow up between rural and urban survivors of childhood cancer.

Design/Method: This retrospective analysis included patients followed in the Aflac Cancer and Blood Disorders Center who were diagnosed with cancer at <21 years, completed therapy between 2009-2017, and were alive at eligibility for survivor clinic (i.e., 2 years from completion of therapy). Patients who were <20 years of age at 18 months from the study end date (October 2020) were included in the follow-up analysis as patients are typically seen annually and age out of our care at 21 years. Demographics, treatment data, and dates of survivor clinic visits were abstracted from medical records. Patient zip codes at diagnosis were converted to Rural-Urban Commuting Area (RUCA) codes to determine rurality. Chi-square, logistic regression, and Kaplan-Meier analyses were performed.

Results: In our cohort of 1500 survivors, 11.1% were classified as living in a rural area. Among urban CCS, 78.5% attended an initial survivor clinic visit at a median time of 30.7 months from therapy completion compared to 71.7% of rural CCS at a median of 30.6 months. In multivariable analyses, rurality was found to be a risk factor for non-attendance of an initial survivor clinic visit [adjusted OR: 1.56 (95% CI 1.04-2.32)], along with age >10 years [11-17 years: 2.05 (1.52-2.76), >18 years: 3.29 (2.08-5.18) vs. <10 years], and black race [OR 1.73 (1.30-2.30) vs. white race]. Of 940 patients eligible for follow-up survivor visit analysis, 85.1% of urban CCS attended a first follow-up survivor visit at a median of 12.4 months from the initial visit compared to 81.2% of rural CCS at a median of 12.7 months. Rurality was not significantly associated with non-attendance of a follow-up survivor visit [adjusted OR 1.56 (0.76-3.00)].

Conclusion: Fewer rural survivors had an initial survivor clinic visit compared to urban survivors. However, rurality did not impact attendance at a follow-up survivor clinic visit. This initial analysis reveals that rural survivors may benefit from targeted intervention to improve initiation of survivor care.

Poster # 679

"HELP NAVIGATE THE PROCESS:" IMPROVING EARLY COMMUNICATION ABOUT LATE EFFECTS OF PEDIATRIC CANCER

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Background: Despite feeling overwhelmed by a new cancer diagnosis, parents of children with cancer value upfront information about potential late effects (LE) to make informed care decisions and prepare for the future. However, many parents and survivors are unaware of their LE risks and feel unprepared for survivorship. We are developing naviGATE, an electronic health communication intervention to enhance early family understanding of potential LE at diagnosis and during active treatment.

Objectives: To identify patient and parent information needs and preferences for early communication about LE and obtain feedback on a prototype communication tool (naviGATE).

Design/Method: Individual, semi-structured qualitative interviews were conducted with parents of children with cancer (on treatment and survivors) and adolescent and young adult (AYA) patients (on treatment and survivors) at the Dana-Farber/Boston Children's Cancer and Blood Disorders Center from April 2022 to April 2023. Purposeful sampling ensured diversity in diagnoses and sociodemographics. Interviews were conducted via Zoom or in-person, audio-recorded, and transcribed verbatim. Transcripts were individually coded with NVivo. Team-based iterative thematic analysis identified broad themes, and analysis was conducted within and across participant groups to identify areas of alignment and differences.

Results: Thirty-six semi-structured interviews were conducted with: parents of patients receiving treatment (N= 8), parents of survivors (N= 11), AYA patients receiving treatment (N= 7), and AYA survivors (N= 10). Participants across groups valued receiving LE information, yet perspectives varied on optimal timing, focus, and level of detail. Some valued comprehensive information at diagnosis to aid decision-making (especially regarding infertility) and set expectations for the future. Others felt early LE information compounded the emotional and informational burden of a new diagnosis. Those actively receiving treatment had mixed feelings–overwhelmed yet appreciative of receiving some LE information. Survivors and parents of survivors more uniformly valued early information and were more likely to perceive gaps in the information provided. Survivors desired more comprehensive LE information, including likelihood and impact on quality of life. When reviewing the prototype tool, participants valued a trusted source for information that conveyed likelihood of LE, screening and mitigation strategies, reflected patient experiences, and offered psychosocial and financial resources.

Conclusion: Parents and patients value LE information but have varied preferences for level of detail and timing. In survivorship, many wished they had received more comprehensive upfront information. To address these needs, naviGATE is being modified to allow for personalized interaction, allowing users to engage at their own pace and revisit over time.

Poster # 680

TRANSITIONING CHILDHOOD CANCER SURVIVORS TO ADULT CARE: BALANCING FAMILY ENGAGEMENT AND INDEPENDENCE

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Background: Families have a critical role in adolescent and young adult childhood cancer survivor's (AYA-CCS) transition from family-centered pediatric healthcare to patient-centered adult healthcare. For AYA-CCS family engagement can have both positive and negative consequences on emerging healthcare independence. Identifying how families participate in AYA-CCS healthcare as they transition from pediatric to adult care is critical to guide transition practices and foster independence.

Objectives: To describe families' participation in AYA-CCS healthcare and to explore demographic, treatment, and family factors associated with transition to adult primary care.

Design/Method: Single-institution, cross-sectional survey of families of AYA-CCS with non-central nervous system malignancies, > = age 18 years, enrolled in a longitudinal cohort study, project REACH. Questions addressed family's perception of the transition process from pediatric to adult primary care, their child's health, and ongoing engagement in their adult child's healthcare. Of 190 eligible families, 89 participated, of those 83 had AYA-CSS children > = age 18 years, median age 24 years (range 18-30), and 67/83 (80.7%) respondents were mothers.

Results: Most families (67.9%) report that their AYA-CCS had transitioned to adult primary care. AYA-CCS who transitioned were older ($p<0.001$) than those still in pediatric care. There was no statistically significant association between cancer diagnoses, treatment, or number of chronic conditions and transition to adult care. The primary reason for transition was pediatric office policy (53.7%), followed by patient's request (18.5%), and provider recommendation (16.7%). Most families report they still at least sometimes help their young adult child with medical decisions (68.3%), attend medical appointments (68.3%), schedule appointments (59.8%), provide transportation (56.1%), communicate with provider (56.1%), stay during visit with provider (56.1%), and worry about their young adult child's health (51.2%). Of note, transition to adult primary care was not associated with less family involvement or family worry. Programmatic factors identified by families as helpful to transition include help identifying an adult primary care provider and information on navigating adult healthcare systems.

Conclusion: Families of AYA-CCS remain engaged in the logistics and decision making related to their child's health even after the transition to adult care. Educating families about their supportive role in the transition process and how they can facilitate healthcare independence is a critical component of AYA-CCS transition practice and programs.

Poster # 681

METABOLIC-ASSOCIATED FATTY LIVER DISEASE IN CHILDHOOD CANCER SURVIVORS

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Background: Childhood cancer survivors (CCS) have increased morbidity and shorter life-expectancies compared to the general population. MASLD is diagnosed in patients with hepatic steatosis on radiographic imaging and at least one cardiometabolic risk factor (obesity, glucose intolerance/diabetes, hypertension, dyslipidemia).

Objectives: Estimate the prevalence of MASLD in CCS at a single institution and describe the clinical

characteristics of those CCS who met criteria for MASLD following cancer therapy.

Design/Method: We utilized the Mayo Clinic Cancer Registry to identify patients aged 18 years or less and diagnosed with cancer between 2014-2017. Data was extracted using Mayo Data Explorer and manual extraction. Variables collected included: demographics, cancer diagnosis, treatment history, BMI, blood pressure, AST, ALT, GGT, platelet count, albumin, AFP, lipid profile, HbA1c, glucose, and diagnoses including metabolic syndrome, diabetes, obesity, hyperlipidemia, hypertension. Data points were obtained at or near cancer diagnosis date and 1 year post primary cancer treatment. Descriptive statistics were utilized to describe the resultant cohort.

Results: 516 patients were identified in the registry. Patients who died within 36 months of diagnosis were removed (n=51). 139 patients had abdominal imaging by ultrasound, computed tomography, or MRI. 31 patients with imaging had steatotic liver disease documented at any time point. Seven patients lacked longitudinal data and were excluded.

In this population (n=24), the diagnostic cancer categories were solid tumor (43.5%), lymphoma (34.8%), CNS (13%) and leukemia (8.7%). 69.6% of patients received chemotherapy, including 1 allogeneic and 2 autologous stem cell transplants, and 43.5% received radiation. 8.7% of patients were diagnosed with diabetes mellitus and 21.7% with hypertension. At 1-year post-treatment, median ALT was 47 U/L, and median triglyceride was 192 mg/dL. Median anthropometric measurements percentiles were BMI 96%, systolic blood pressure 61%, and diastolic blood pressure 75%.

Thirty patients had elevated BMI and ALT at one-year post-treatment and most (63.3%) did not have abdominal imaging.

Conclusion: The preliminary prevalence of steatotic liver disease on imaging obtained for routine or directed care in this CCS population was approximately 20%. Obesity, hypertension, and diabetes mellitus co-occurred as would be expected in MASLD populations. Ongoing work is underway to estimate the true MASLD prevalence in this cohort. Importantly, 63.3% of CCS who met criteria for further evaluation for MASLD, did not undergo subsequent workup, highlighting that MASLD in CCS may be under diagnosed and there is a need to define risk factors in CCS and develop survivorship guidelines to promote long term liver health in CCS.

Poster # 682

RAISED ANXIETY IN HISPANIC CAREGIVERS AFTER DISCUSSION OF LATE EFFECTS IN PEDIATRIC CANCER SURVIVORS

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Background: According to the literature, more than half of childhood cancer survivors do not adhere to long-term follow up care and the Hispanic population may be at a higher risk. We conducted a quality improvement project to improve the knowledge regarding the need for long-term follow up in solid and brain tumor patients

Objectives: We implemented an educational intervention aiming to increase knowledge about the need for long-term follow up by 20% from baseline in solid and brain tumor patients who have completed therapy at Texas Children's Hospital.

Design/Method: We performed a survey in caregivers or survivors (>15 years old) treated with chemotherapy or radiation who were 3-24 months off therapy. The questions inquired the expected length of long-term follow up and possible late effects. We then provided subjects with the correct answers (lifelong to screen for late effects and a list of individualized late effects). We explored whether these questions triggered any anxiety and rated anxiety on a 10-point scale. We repeated the same process at two additional appointments at least three months apart. We prospectively assessed percent change from baseline of the following: correctly acknowledging need for lifelong follow up care, identifying at least two patient specific late effects, and how often anxiety is endorsed and rated > 5 out of 10-point scale. We compared changes in proportions using chi-squared or Fisher exact tests.

Results: We completed four PDSA cycles in 52 patients (mean age 12 years, 60% female, 67% solid tumor) with a baseline visit, 39 with two and 24 with three visits. From the first to the third visit (median time 9.5 months, range 6 – 16), correct responses for follow up duration increased from 29 to 88 percent (p=<0.001) and naming at least two late effects increased from 71 to 96 percent (p=0.04). Discussing late effects generated anxiety in 45 percent of the respondents at the first visit, with 54 percent rating anxiety > 5 out of 10 point scale. Both anxiety parameters remained the same over time from first to third visit. At baseline, Hispanic respondents endorsed anxiety more often (13/20, 65%) than Non-Hispanic group (11/32, 34%, p=0.04).

Conclusion: Awareness for lifelong follow up care among pediatric cancer survivors and caregivers is poor. Our intervention led to a meaningful increase in the intended knowledge while related discussion provoked significant anxiety, more often in Hispanic subjects. Anxiety directed interventions may increase long term follow up adherence.

Poster # 683

NEUROCOGNITIVE OUTCOMES IN SOLID TUMOR SURVIVORS: A SINGLE INSTITUTION RETROSPECTIVE CHART REVIEW

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Background: The childhood cancer survival rate has drastically improved since the 1970s. Survivors experience a variety of therapy related side effects including neurocognitive impairments. It is well documented that survivors of leukemia and CNS tumors have impaired memory, attention, psychosocial measures, cognitive and executive functioning. While progress is being made in understanding the neurocognitive health of patients undergoing CNS directed therapy, there is a scarcity of information regarding survivors of solid tumors.

Objectives: This study aimed to investigate the utilization of neuropsychological services and the benefit of an embedded school liaison in patients with a history of solid tumors in the survivorship clinic at a comprehensive cancer center.

Design/Method: A retrospective chart review of survivors of solid tumors followed in multidisciplinary long term follow up clinic was conducted including available neuropsychological evaluations. Participants were grouped into two categories: patients referred for neuropsychological testing (NPT) vs. patients not referred.

Results: 176 patient charts were reviewed. Fifty-six percent of the patients were male with a mean of age 8.35 years. Thirty-seven percent of patients were referred for neuropsychological testing (NPT). Referred patients were significantly younger at diagnosis with mean age of 4.91 years vs. 10.25 years ($p<0.001$). Referred patients were more likely to utilize special education ($p=0.010$), receive school accommodations ($p<0.001$) and to have been seen by the oncology school liaison ($p<0.001$). Patients referred for NPT were also more likely to endorse hearing concerns ($p<0.001$). There was no significant difference based on sex and self-reported behavioral or vision concerns between those referred and not referred. Forty-three percent of patients who underwent NPT demonstrated a formal neurocognitive deficit. Twenty-six percent of patients that were tested were diagnosed with Attention-Deficit/Hyperactivity Disorder (ADHD). On measures of intellectual functioning, tested survivors processing speed skills fell within the clinically low average range.

Conclusion: Survivors of solid tumors are at risk of neuropsychological deficits, specifically involving attention and processing speed. Survivors should be referred for and undergo neuropsychological testing as a standard of care in long-term follow up clinics for early detection of cognitive impairments and appropriate referrals. The presence of a school liaison may lead to a heightened awareness of neurocognitive difficulties and help patients access appropriate accommodations.

Poster # 684

DEVELOPING COMPUTATIONAL APPROACHES FOR GENERATING SURVIVORSHIP CARE PLANS IN THE EPIC ENVIRONMENT

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Background: Survivorship care plans (SCPs) summarize patient treatment, treatment-related health risks, and surveillance recommendations for oncology and hematopoietic stem cell transplant (HSCT) survivors. The manual generation of SCPs is error-prone and time consuming for healthcare providers (HCPs). Computational SCP generation can reduce provider burden and improve survivorship care.

Objectives: Validate diagnosis and treatment information generated by a computational approach to SCP generation.

Design/Method: We interviewed HCPs and analyzed current SCPs to map the workflow and create a table of SCP data elements. Primary diagnosis and treatment details were prioritized data elements for automation based on clinical importance and technical feasibility. We identified a cohort of patients diagnosed and treated for cancer, or who underwent HSCT for a benign condition prior to age 30 at our institution from 1/1/2011 to 12/31/2021. Demographic information, problem lists, medication administration records, clinical notes, diagnostic reports, and other cancer and HSCT-related data was obtain from our institution's Epic Clarity data warehouse. We developed a custom pipeline using Python

to ascertain the primary cancer diagnosis and anti-neoplastic medication history including lifetime doses. For a small learning cohort, we validated diagnosis and alkylator and anthracycline exposure, including dosage, using human-curated institutional clinical registry data and chart review.

Results: We extracted 2,422 patient records. In the oncology validation cohort (n=128), we correctly identified the specific cancer diagnosis for 115 patients (89.8%), a non-specific diagnosis in 11 patients (8.6%) and no diagnosis for 2 patients (1.6%). There were three anthracycline (daunorubicin, doxorubicin, mitoxantrone) and seven alkylating agents (busulfan, cyclophosphamide, ifosfamide, lomustine, melphalan, procarbazine, and thiotepa) administered in the validation cohort with 99.5% correct match for exposure to each agent. Incorrect exposure was due to ambulatory administration and administration of medications after manual data abstraction. Across validated medications, lifetime total dosages (mg/m2) were within 5% for 71.2% with discrepancies in the remaining due to: missing values of body surface area in the data extract (14.4%), dose ordering using mg/kg (9.4%), ambulatory administration (1.4%), intra-arterial administration (0.7%), and currently unknown reasons (2.9%).

Conclusion: It is feasible to extract and transform electronic health record data to support computational SCP generation. Work is ongoing to iteratively improve our single-center pipeline based on initial validation results, with plans for broader dissemination to other institutions using Epic if successful.

Poster # 685

DESIGNING A HUMAN-CENTERED INTERFACE FOR CANCER SURVIVORSHIP CARE PLANS

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Background: Survivors of pediatric cancer are at increased risk for health problems due to their cancer and/or its treatment, which may develop decades after treatment completion. Survivorship Care Plans (SCPs), which integrate treatment summaries and monitoring recommendations, are essential for guiding lifelong appropriate care for pediatric cancer survivors. However, generating SCPs can be a challenging process requiring tedious chart review and documents are often hard for families and providers to navigate.

Objectives: To design a user interface (UI) to generate provider- and patient-friendly SCPs, summarizing prior treatment, personal risk, and recommended surveillance.

Design/Method: To identify pain points in SCP generation, interviews of diverse users were recorded and reviewed to identify themes that described current limitations of the SCP. Themes were then member checked with participants during the first ideation session until consensus was reached. One additional ideation session is planned. By the time of presentation, we will have converged on a single design after creating mockups from current design ideas and conducting usability testing to determine if the new UI meets benchmarks for usability (e.g. tasks can be completed without any errors over 75% of the time) and if users perceive the newly designed UI as acceptable.

Results: Twelve interviews were conducted with pediatric oncologists (2), nurse practitioners (3), nurses (4), administrators (2), and a researcher (1) followed by one ideation session. Limitations to current SCP

generation that were identified included: labor intensive creation, error prone documents due to manual data entry/calculations, document length with high redundancy, and data storage as free text instead of structured variables. Design ideas included: ability to dynamically populate content, automatic calculations when possible, removal of redundancy, re-organization of the document, increased use of images, capture of exposures using structured data entry to allow for repopulation of screening recommendations. Additional results, including the final interactive prototype of the SCP document, will be available by April 2023.

Conclusion: Several challenges currently limit the efficiency of creating SCPs and their accuracy. Interviewees agreed that SCPs are too long, redundant, and could be more usable. SCP writers emphasized the importance of accuracy and thoroughness Design ideas included reorganization with structured data to dynamically populate content and ease future updates.

Poster # 686

MINDFULNESS-BASED MOBILE HEALTH APPLICATIONS: ADDRESSING BARRIERS OR AN ADDITIONAL BARRIER?

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Background: Adolescent and young adult childhood cancer survivors (AYA CCS) are at risk for psychological conditions such as depression, anxiety, and stress. AYAs are often lost to follow-up care and mindfulness mobile apps can be a good alternative to addressing unmet psychosocial needs in this population. Mindfulness mobile applications with mental health resources tailored specifically to the needs of AYA CCS are limited. To address this gap, we built on an already existing mindfulness mobile application built by the Illumination Institute (www.illuminationinst.org), using a community partnered approach.

Objectives: To test the acceptability and feasibility of a mindfulness mobile app intervention in a diverse group of AYA CCS.

Design/Method: A 12-week intervention, using this Mindfulness mobile app was conducted among a sample of twenty-eight AYA CCS aged 15-27 years and >2 years off therapy. Participants completed the Perceived Stress and the PROMIS Global-10 scales at baseline and at 4-week intervals. We compared cohorts who came off-study vs. those who remained on-study.

Results: Overall participants (n=28), were median age of 20, 62% female, 50% Hispanic, and the majority were leukemia/lymphoma CCS. Thirty-six percent of participants completed the intervention. Three came off study due to no longer having a mobile phone. In the off-study group 55.6% were Hispanic, 53% female, and 56% had public health insurance. Race, gender, and insurance were not statistically significant (p>1). Twelve (67%) participants in the off-study group listed another language other than English as their primary language vs. 30% in the on-study group. When further evaluating other measures of socioeconomic status, zip code was used as a proxy for home neighborhood, as income was not available. Off-study participants reside in areas where 10.6% live with incomes below the federal poverty level (FPL). Thirty-three percent of the sample lived in areas with a higher FPL compared to California's average of 12.1%. The frequencies of stress and nervousness between groups, with the

answers of “sometimes, fairly often and very often” were similar among the on-study and off-study groups (72% vs. 70%).

Conclusion: While AYA CCS in this study had similar frequencies of stress and nervousness and could benefit from mindfulness mobile app interventions, mobile apps interventions may not be generalizable to all AYA CCS. More data is needed on whether these apps can be generalized to more diverse populations, such as those from lower socioeconomic status.

Poster # 687

EXAMINING A NEUROPSYCHOLOGICAL SCREENING TOOL IN PEDIATRIC ONCOLOGY SURVIVORS

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Background: As the 5-year survival rates of pediatric oncology patients continue to increase, recognition of persistent conditions that may emerge after cancer-directed therapies gain greater importance. Neurocognitive deficits can arise as a late complication of certain malignancies and malignancy-directed therapies, including chemotherapy, surgery, and radiation therapy. Neuropsychological evaluations are often critical to guiding therapeutic interventions, educational planning, and mental health supports. However, often there is insufficient time during clinic appointments to assess these patients for neurocognitive morbidity and therefore those who may be at risk for neurocognitive deficits may not get referred.

Objectives: We will compare a parent-report screening tool developed by the Clinical Neuropsychology Collaborative for Childhood Cancers, referred to as the CNC3 Cognitive Screener (CNC3-CS), against independent clinician recommendations for referral to neuropsychology services in pediatric oncology survivors at a survivorship clinic.

Design/Method: The CNC3-CS is in active development by a consortium of neuropsychologists specializing in childhood cancers from institutions across the US and Canada. It incorporates elements from other validated screening tools, expanded to include additional symptom items organized by cognitive domain (e.g., attention, executive functions, processing speed), as well as pertinent background information (e.g., school history, sensorimotor impairment). We are administering the CNC3-CS to parents during their child’s annual survivorship visit, using proposed cutoff scores determining need for neuropsychology services; we are also asking the child’s survivorship provider how likely they are to recommend a formal neuropsychological evaluation based on their own history taking and physical exam.

Results: Data collection is ongoing. Preliminary data shows an accrual rate of 93.8%. Among 15 participants, 7 (46.7%) are female, 9 (60%) have a history of hematologic malignancy, 4 (26.7%) a history of solid tumor, and 2 (13.3%) a history of central nervous system tumor. All received chemotherapy for treatment, with 5 of 15 (33.3%) also requiring surgical excision, 4 (26.7%) requiring radiation therapy, and 4 (26.7%) with history of stem cell transplant. Results of the CNC3-CS screener recommended neuropsychological consultation for 3 (20%); more information needed for 2 (13.3%); and not needing

consultation for 10 (66.7%). Providers reported they would “definitely” consider referral in 5 (33.3%) and “maybe” consider referral in 4 (26.7%). Measures of agreement will be assessed with full recruitment.

Conclusion: The CNC3-CS may provide a more efficient means to identify pediatric cancer survivors in need of referral to neuropsychology services, which will improve their access to appropriate therapeutic and educational resources and enhance their quality of life.

Poster # 688

MULTISITE FEASIBILITY STUDY OF INTEGRATIVE/COMPLEMENTARY INTERVENTIONS AMONG CHILDREN WITH CANCER

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Background: Children with cancer suffer from intractable symptoms and report using complementary and integrative health interventions (CHI) without strong evidence. Due to the existing gap in rigorous outcomes research, feasibility of CHI with standardized outcome measures in this population must be established.

Objectives: To determine multi-site feasibility of CHI among children with and without cancer and examine preliminary efficacy to estimate effect sizes for future studies.

Design/Method: This exploratory feasibility prospective clinical trial was completed with convenience sampling at two geographically diverse academic children’s hospitals. Outcomes of quality of life and symptoms were measured with the PROMIS® Pediatric Global Health, Pediatric Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE®) and Faces Scale. Data were collected at baseline, pre/post CHI, and monthly for up to 6 months. CHI were provided by certified, credentialed practitioners for 30-60 minutes and included acupuncture, aromatherapy, creative arts, and massage therapy. *A priori* feasibility thresholds were 80% recruitment rate and 60% completion of at least two outcome measure surveys and one CHI encounter per participant.

Results: Ninety-five participants (Site 1 n=34, Site 2 n=61) were accrued over 18 months and completed 458 evaluations. Participants were aged 2-29 years (M=13.5, SD=5.6), most identified as female (66%), and 21% reported as being from underrepresented populations. About half of the participants were receiving treatment for cancer (52%, n=49) versus other serious illnesses (48%, n=45). Of the patients approached, 6% declined enrollment in the study, citing lack of interest (n= 5) or feeling too sick (n=1). Completion rate of $\geq$2 surveys and $\geq$1 intervention was 77%. CHI received were acupuncture (46%), aromatherapy (27%), creative arts (20%), massage therapy (6%) and hypnosis (1%). Acceptability of the CHI was 91% and no participants with or without cancer reported the surveys were difficult to complete. Field notes revealed the reasons for missing data were related to participant death, change in treatment phase, loss of interest, absence of research coordinator, and electronic data capture errors.

Conclusion: Prospective multi-site data collection in relationship to CHI exceeded feasibility thresholds and was acceptable to participants with and without cancer. These findings support feasibility of

rigorous collection of common data elements using standardized measures in future studies of children with cancer. Children with other serious illness comprise a potential comparison group. Next steps include preliminary efficacy analysis and estimation of effect sizes for quality of life and symptom outcomes.

Poster # 689

PSYCHOSOCIAL HEALTH AND CHRONIC HEALTH CONDITIONS AMONG BEREAVED SIBLINGS

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Background: Siblings who have lost a brother or sister to childhood cancer may be at increased risk for psychosocial health impairment and chronic health conditions (CHCs).

Objectives: To compare psychosocial health including psychological distress, health-related quality of life (HRQOL), educational attainment, employment and marital status as well as the burden of CHCs in bereaved and non-bereaved adult siblings enrolled in the Childhood Cancer Survivor Study (CCSS).

Design/Method: Siblings of 5-year survivors of childhood cancer enrolled in CCSS were evaluated for psychological distress and HRQOL were measured by Brief Symptom Inventory (BSI)-18 and Medical Outcomes Survey Short Form (SF)-36. Educational attainment, employment, marital status and CHCs were self-reported. CHCs were graded using Common Terminology Criteria for Adverse Events. Proportions representing dichotomized outcomes including elevated BSI-18 (T-score>63), low SF-36 scores (T-score<40), educational attainment (college versus vs no college), employment status (employed vs unemployed), and marital status (never married vs ever married) were compared among bereaved and non-bereaved siblings adjusted for age, sex, and race/ethnicity. A severity/burden score (accounting for frequency/grade of CHCs) was dichotomized (high/very high/medium severity vs none/low) for adjusted comparison among bereaved and non-bereaved siblings. Modified Poisson regression was used to obtain relative risk [RR] and 95% confidence intervals [CI].

Results: Siblings (n=3825) were an average of 40 years (range 18-75) of age at latest follow-up and among those who were bereaved (n=733) an average of 15 years (range 0-44) had elapsed from the time of death. In adjusted models, bereaved siblings reported similar risk of psychological distress compared to non-bereaved siblings (i.e. anxiety (RR, 0.90; 0.59-1.39) and somatization (RR, 0.99; 0.67-1.48)) but had greater depression risk ((RR, 1.44; 1.04-1.98). Bereaved siblings had a greater risk of social impairment (RR 1.35; 1.00-1.82). Bereaved siblings reported similar HRQOL compared to non-bereaved siblings in the domains of physical function, physical role, bodily pain, general health, vitality, emotional role, and mental health. Bereaved siblings were less likely to attend college (RR, 0.96; 0.92-1.00), but were similarly employed (RR, 0.98; 0.95-1.01) and ever married (RR, 0.98; 0.93-1.04) compared to non-bereaved siblings. Overall, bereaved siblings reported a similar burden of medium/high/very high severity of CHCs compared to non-bereaved siblings (RR, 1.05; 0.96-1.15).

Conclusion: Bereaved siblings appear similar to non-bereaved siblings in many ways, but endorse elevated levels of depression symptoms and social impairment along with lower levels of educational

attainment. Future studies should examine whether there are subgroups of bereaved siblings who are at risk of adverse psychosocial outcomes.

Poster # 690

FEASIBILITY/ACCEPTABILITY OF A TELEHEALTH HOSPICE-TRANSITION INTERVENTION FOR CHILDREN WITH CANCER

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Background: Telehealth presents a unique opportunity to improve care for patients with progressive cancer enrolling in hospice. Coordinated telehealth visits (triad of patient/family, hospital, and hospice teams) may improve communication, satisfaction with and interdisciplinary hospice collaboration.

Objectives: To assess the feasibility and acceptability of a coordinated telehealth hospice transition program.

Design/Method: This is a single-arm prospective pilot study of 0-29 year-old patients with cancer initiating hospice care between 2021-2023. Patients (18+ years), caregivers, oncology and palliative care providers, statewide hospice nurses and administrators were enrolled. The triad of caregiver/ hospice nurse/ hospital provider completed three telehealth visits in the first month of hospice enrollment, and all participants were surveyed about the feasibility and acceptability of telehealth (Technology Acceptance Model 2) after the first and third telehealth visits. Satisfaction was measured using the Consumer Assessment of Healthcare Providers and Systems (CAHPS) and completed by caregivers after visit 3 and at bereavement. Healthcare professionals also completed the Assessment of Interprofessional Team Collaboration Scale II (AITCS-II). Data were abstracted from the electronic health record and cancer registry. Participant survey responses were summarized and differences in scores were analyzed.

Results: Out of 40 eligible patients, 24 enrolled, 19 completed visit 1, and 13 completed visit 3. Patients who completed visit 1 were 53% male, with solid (42%) or central nervous system tumors (53%), living a median 47 miles (Range: 11-199) from the hospital, with a median age at death 15.1 years. Median time between enrollment and death was 47 days. Fourteen caregivers and two adult patients completed visit 1 surveys; nine caregivers and two adult patients completed visit 3 surveys. Using a 5-point Likert scale, most participants highly rated the acceptability of telehealth after visit 1 (Median: 4.5, IQR: 4.0-4.7) and 3 (Median: 4.4, IQR: 4.0-4.7)). Across 14 CAHPS questions (Scale 1-4), caregivers rated hospice services as highly satisfactory at visit 3 (Median: 3.1, IQR: 3.1 – 3.5) and bereavement (Median: 3.4, IQR: 3.4 – 3.6). Healthcare professionals completed 85 AITCS-II surveys (47 hospital providers, 26 hospice nurses, 12 hospice administrators) and reported excellent interprofessional collaboration (Median: 99/115 for hospital providers and 111/115 for hospice teams).

Conclusion: Patients, caregivers, and healthcare providers found coordinated telehealth visits during the first month of hospice enrollment to be feasible and acceptable, Satisfaction with hospice was high. Telehealth may be utilized as an acceptable alternative to in-person clinic visits or phone visits, and

fosters hospital-hospice collaboration.

Poster # 691

ASSOCIATION OF PATIENT AND CAREGIVER DISTRESS WITH REFERRAL TO PALLIATIVE CARE IN PEDIATRIC ONCOLOGY

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Background: Children with cancer experience significant distress throughout their disease course that impacts both patients and caregivers. Pediatric palliative care (PPC), when integrated early, can reduce these symptoms and improve quality of life. A mechanism for earlier integration is through screening tools to identify patients experiencing distress that could benefit from PPC. It is unknown if patient and caregiver distress, as measured by the Pediatric Distress Thermometer (DT), is associated with referral to outpatient PPC.

Objectives: Investigate whether overall distress and components of distress are associated with referral to a PPC clinic.

Design/Method: A single-institution retrospective case-control study was conducted comparing children ≥ 2 years of age with cancer who were referred to PPC from 2019-2021 to a matched sample of patients with cancer who were not referred. Matching occurred in a 1:2 ratio using propensity score matching and based on diagnosis, disease stage, relapse status, race, and sex. Distress was measured separately for patients and caregivers by the Pediatric DT at each clinic visit and averaged over time. Distress was categorized into low (0-4), moderate (5-7), and high (8-10), and emotional, family/social, practical, and spiritual components of distress were collected. Patient distress was measured by self-report (≥13 years) or caregiver proxy-report (2-12 years). Caregiver distress was self-reported. Demographic and disease data were collected. Descriptive statistics were performed, and conditional logistic regression was utilized to assess the association between high distress and PPC referral among patients and caregivers. Two-sample Wilcoxon rank-sum test was used to compare DT scores and DT components between the cohorts.

Results: The study population consisted of n=135 PPC-referred patients matched to n=257 non-referred patients. Average DT scores did not differ for patients (1.36 vs. 1.44; p=0.29) or caregivers (2.58 vs. 2.43; p=0.30). Patients with high distress had higher odds of PPC referral than those who never had high distress (OR 1.83, 95% CI 1.07-3.12). Emotional concerns were most common in the study population with 47.8% and 34.4% of patients feeling anxious and annoyed, respectively. Caregivers felt anxious (53.6%), afraid (25.7%), and depressed (24.9%) most commonly. There was no difference in DT components between the two cohorts.

Conclusion: While pediatric cancer causes distress in patients and families, DT scores remain low throughout their disease regardless of PPC referral. However, patients with high distress have higher odds of PPC referral. Further research is needed to identify biopsychosocial symptom clusters in children with cancer and assess if symptom clusters are associated with PPC referral.

Poster # 692

STORYTELLING TO SUPPORT LEGACY-MAKING FOR BEREAVED PARENTS OF CHILDREN WITH CANCER

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Background: The field of narrative medicine explores how attention to storytelling impacts clinicians and patients alike.[1,2] For bereaved parents, honoring their child's legacy is an essential aspect of coping and meaning-making,[3,4] yet little is known about how storytelling may function as a mechanism for legacy-making. Better understanding of the role of storytelling in legacy-creation may inform narrative-based interventions to support caregivers across the illness course and during bereavement.

Objectives: Through analysis of bereaved parent interviews focused on legacy, we aimed to identify and characterize the role and function of storytelling in the process of creating and sustaining legacy.

Design/Method: In this qualitative study, 19 parents of children who died from cancer participated in semi-structured interviews centered on their experiences around their child's legacy. As part of the discussion, parents were asked to describe their child's legacy, including the way their child directly and indirectly impacted others and their community and how their child's impact continues to be felt or perceived by others after their death. Interviews were audio-recorded, transcribed, and analyzed inductively to identify various applications and functions of storytelling, with thematic analysis conducted to recognize and classify key concepts related to legacy that were highlighted through parent stories.

Results: When asked to describe their child's legacy, nearly all bereaved parents told stories that illustrated their child's legacy (17/19). Storytelling content comprised sharing medical histories, describing personality traits, showcasing values, and highlighting specific examples of how a child impacted others during and after their lifetime. Of the 4/19 participants who felt unsure about how to describe their child's legacy or described the task as "hard," two (50%) used storytelling as a path to find their answer. Key thematic elements used to characterize a child's legacy through story included the child's cancer experience, the child's spirit and energy, and the child's relationships.

Conclusion: Inviting narrative creation and reflection about a child's legacy may offer a meaningful tool for supporting legacy-making for pediatric cancer patients and their families, both preceding and following the death of a child. Future work should focus on piloting narrative-based legacy activities across the illness course and following a child's death to explore the possible impact of storytelling on parents' perceptions of meaning-making and connection with their child.

1. Charon, R, JAMA, 2001
2. Remein, CDF, et al. *BMJ Open*, 2020.
3. Boles, JC & Jones, M.T. *Palliative Medicine*, 2021
4. Love, A. et al.*Journal of Pain and Symptom Management,* 2022

Poster # 693

DEVELOPMENT OF A PEDIATRIC PALLIATIVE CARE ROADMAP USING QUALITY METRICS AND STANDARDS OF CARE

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Background: Focused on pediatric oncology psychosocial standards of care for palliative care, bereavement, and interdisciplinary communication, our team sought to ensure adherence with quality care metrics through the development of a palliative care "roadmap". Through chart review we identified areas of growth, developed a targeted intervention (roadmap), and continue to modify and evaluate improvement over time.

Objectives: Focused on pediatric oncology psychosocial standards of care for palliative care, bereavement, and interdisciplinary communication, our pediatric palliative oncology team sought to standardize and ensure adherence with quality care metrics across the continuum of care delivery.

Design/Method: Our literature review identified fifteen quality measures to evaluate our current practice. We performed a retrospective chart review focused on end of life (EoL) for all patients who died from progressive disease. By evaluating our current practice gaps compared to quality metrics, we created a multidisciplinary group to draft a "Pediatric Oncology Palliative Care Roadmap" (PCR). The PCR is a physical document that travels in tandem with the patient's treatment roadmap. We chose the term "roadmap" to align ourselves with the oncology team members who reflexively look at treatment roadmaps. The PCR was then distributed to key stakeholders to include inpatient, outpatient, and home-based multidisciplinary teams for feedback. A second draft is currently being trialed in a pilot group of eight patients. Iterative feedback in both informal and formal focus groups are in progress. A more extended chart review to include three additional years is ongoing.

Results: Preliminary results are based on our first year of chart review, 2022. Twelve patients died due to progressive disease. From this group, we quantified each quality measures. 6(50%) reached EoL in preferred location, 10(83%) were not intubated within last 14 days, 9(75%) referred to hospice, 7(58%) legacy documented, 7(58%) DNR, 11(92%) disclosed nearing EoL, 5(42%) spiritual beliefs documented, 4(33%) EoL date documented, 3(25%) home visit documented, 8(67%) wish documented, and 1(8%) documented tumor donation. 10(83%) had at least 5 quality measures documented.

Conclusion: Based on published metrics and standards we identified areas of growth for our program, developed a customized intervention, and continue to evaluate our improvement over time through the implementation of our PCR.

Poster # 694

IMPACT OF EARLY PHASE STUDY ENROLLMENT ON SYMPTOM BURDEN AND QUALITY OF LIFE (QOL)

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Background: Pediatric patients with relapsed or refractory malignancy have few options. The quality of life (QoL) impact for enrolling in a phase I or II trial compared to those not participating is unknown. This information is invaluable to the consenting process as well as to clinical trial design.

Objectives: The primary aim was to determine if those enrolled on a phase I or II trial had lower scores on the Symptom Screening in Pediatrics Tool (SSPedi) total score compared to those not enrolled on a trial.

Design/Method: This Canadian multi-site study had nine sites open for accrual. SSPedi scores from baseline, 4 weeks and 8 weeks of those enrolled on an early phase trial were compared to those who did not enroll in such trials. Scores were compared for patient reports for 8-18 years and parent-proxy reports for 2-7 years. The total SSPedi score is the sum of 15 items' 4 Likert scale scores, score ranges from 0 to 60 (worst possible).

Results: Of the 41 patients, 20 (49%) patients were enrolled on an early phase trial and 21 (51%) patients were not enrolled in a study. For those enrolled on the study at enrollment time, 4 weeks and 8 weeks time points, the total SSPedi score for the participant mean was 11.1 (SD 8.1), 9.4 (SD 6.5) and 10.1 (8.3) respectively compared to those not enrolled on a study with mean scores at the same time points of 13.5 (SD 10.0), 13.5 (SD 10.5), and 15.7 (SD 13.3).

Conclusion: These results suggest that it is feasible to evaluate patients enrolled and not enrolled on early phase trials, and to compare their symptom experience. Further efforts will focus on more recruitment and using the PedsQL 3.0 Acute Cancer Module to further define differences in QoL.

This research is supported through granting from the C17 Council and Kindred Foundation.

Poster # 696

DIFFERENCES IN DISTRESS ACROSS DIAGNOSIS GROUPS IN CHILDREN WITH CANCER REFERRED TO PALLIATIVE CARE

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Background: Pediatric cancer causes significant distress in patients and caregivers which may be alleviated with subspecialty palliative care (PPC). Little is known about the relationship between cancer type and patient and caregiver distress prior to referral to PPC.

Objectives: To compare distress in children with cancer and their caregivers referred to PPC across leukemia/lymphoma (LL), solid tumor (ST), and brain tumor (BT) diagnoses.

Design/Method: A single center cross-sectional study was conducted with patients ≥2 years of age with cancer referred to a subspecialty PPC clinic over a 3-year period (2019-2021). Patient and caregiver

distress was assessed by the Pediatric Distress Thermometer (DT), a unidimensional 0-10 rating of distress. Patient distress was either measured by patient self-report (≥13 years) or caregiver proxy-report (2-12 years). Caregiver distress was self-reported by the caregiver. All DT scores measured prior to PPC referral were collected and compared across diagnosis groups over three intervals: 6 months, 3 months, and last visit prior to referral. Highest DT score for each patient and caregiver was collected. Patients and caregivers were compared separately. Demographic and disease data were collected. Descriptive statistics were performed, and Kruskal-Wallis test was used to compare DT scores across diagnosis groups for patients and caregivers.

Results: PPC-referred patients (n=153) with DT data included 29 (19%) LL, 56 (37%) ST, and 68 (44%) BT diagnoses with 76 (49.7%) having patient self-report DT scores and 77 (50.3%) having caregiver proxy-report DT scores. Caregiver data was available for 130 patients. Median DT scores did not differ by diagnosis group at 6 months, 3 months, or the last visit prior to referral for patients (p=0.64, 0.62, 0.39, respectively) or caregivers (p=0.78, 0.58, 0.52, respectively). In the 6 months prior to referral, there was no difference in highest DT score across diagnosis groups with DT scores of 4, 4, and 3.5 in patients and 5, 5, and 5 in caregivers of patients with LL, ST, and BT, respectively.

Conclusion: Among those referred to PPC, there was no difference across diagnosis groups in patient and caregiver distress, as measured by the Pediatric DT. Further work is needed to compare degree of distress in PPC-referred vs. non-referred patients and to explore whether physical, emotional, psychosocial, or spiritual components of distress contribute to overall distress.

Hematologic Malignancies/Histiocytic Disorders (701-782)

Poster # 701

COHESIN LOSS ENHANCES CHEMORESISTANCE IN T(8;21) AML

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Background: Acute myeloid leukemia with t(8;21) is a common cytogenetic subtype of AML in children, accounting for 15-20% of cases. Mutations within cohesin complex genes (*RAD21, SMC3, SMC1a*, and *STAG2*), which occur at low levels in most other subtypes of AML, are enriched in t(8;21) AML and occur in approximately 20% of patients. However, the impact of these mutations on disease biology is not understood. Adult studies suggest patients with both t(8;21) AML and loss of function cohesin mutations have decreased survival and increased risk of relapse. Thus, we hypothesized that cohesin loss in t(8;21) AML increases chemoresistance to standard chemotherapy agents.

Objectives: To assess the effects of cohesin loss on chemosensitivity in t(8;21) AML.

Design/Method: The human t(8;21) AML cell line, SKNO-1, was transduced with shRNA targeting cohesin genes *RAD21* or *SMC3* or a non-targeting control and labeled with GFP. We induced shRNA expression with doxycycline and sorted GFP^+ cells. For chemosensitivity assays, we treated GFP+ cells and non-transduced control with cytarabine or daunorubicin for 72 hours and measured cell proliferation via MTT and induction of apoptosis via Annexin V binding (AVB) flow cytometry assay. Cell cycle analysis was performed using Propidium Iodide.

Results: Cohesin-targeting shRNA reduced *RAD21* expression by 60-75% and *SMC3* expression by 40-60%, comparable to values expected from cohesin mutations. Cohesin-deficient cells had a significantly higher IC50 in response to both cytarabine and daunorubicin as measured by MTT and AVB compared to non-transduced controls. In addition, cohesin-deficient cells maintained 30-40% viability when subjected to >1 uM cytarabine which caused near-complete cell death in controls. In cell cycle analysis, cohesin-deficient cells had an increased proportion of cells in G0/G1 phase and decreased proportion of cells in S or G2/M phase compared to controls. This was also associated with an increased doubling time of cohesin-deficient cells compared to controls (106.6 hrs v. 76.6 hrs).

Conclusion: Loss of normal cohesin function in t(8;21) AML cell line, SKNO-1, led to decreased sensitivity to cytarabine and daunorubucin, two chemotherapy agents that are cornerstones of AML treatment. In addition, cohesin loss altered cell cycle progression likely via decreasing the proportion of cells in S phase, the phase in which these chemotherapy agents are most active. This suggests that cohesin mutations are enriched in t(8;21) AML as they provide a survival advantage to leukemia cells via decreased cell cycling and thus decreased sensitivity to cell cycle-dependent chemotherapy.

Poster # 702

THE UNCONVENTIONAL MYOSIN FAMILY PROTEIN MYO18A IS A NOVEL REGULATOR OF B CELL DEVELOPMENT

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Background: B cells develop from hematopoietic stem cells through an interplay of transcriptional networks and microenvironmental cues. Regulation of B cell development is critical for the generation of a pathogen-reactive antibody repertoire, as well as prevention of B cell malignancy and autoimmunity. Our previous studies have demonstrated that deletion of Myo18A leads to a significant increase in the number of progenitor precursors (pro and pre-B cells) and immature B cells in the Myo18A knockout mice

Objectives: To test that Myo18A deletion leads to dysregulated transcriptional networks in the bone marrow and expansion of B cell precursors and its connotation in acute lymphoblastic leukemia

Design/Method: The B cell–specific conditional knockout mice, Myo18A BKO, were obtained by crossing Myo18AFL/FL mice with Mb1Cre/+ mice, resulting in the genotype Myo18AFL/FL Mb1Cre/+. The Mb1Cre/+ mice, which have one Igα allele replaced with the gene for Cre-recombinase, were used as controls in all experiments. Flow cytometry data was acquired using FACS Symphony A1. Bioinformatic tools used for analysis were Seurat, ScCODA, Monocle, DEsingle analysis.

Results: Expression of the unconventional myosin family protein Myo18A starts in early B cell progenitors and increases continuously throughout B cell development. B cell-specific deletion of Myo18A (Myo18A BKO) leads to a significant expansion of bone marrow B cells. Pseudotime analysis of single cell RNA sequencing data in control $Mb1^{cre/+}$ and Myo18A BKO bone marrow cells revealed that the developmental path of B cells is unaffected in the absence of Myo18A. However, scCODA-based compositional analysis and flow cytometry showed expansion of small pre-B cells in Myo18A BKO bone

marrow. These data suggest that pre-B cell numbers are restricted by Myo18A. Differential gene expression analysis showed altered expression of genes encoding transcription factors, ribosomal, mitochondrial, and cytoskeletal proteins in small pre-B cells of Myo18A BKO mice. Among these genes, we found a decreased expression of the transcription factors Ebf1 and Foxp1. The haploinsufficiency of transcription factors such as Foxp1, Ikaros and Ebf1 is associated with acute lymphoblastic leukemia. Mechanistically, Myo18A BKO small pre-B cells exhibited greater migration along CXCL12 gradients.

Conclusion: These data indicate that Myo18A controls critical checkpoints in B cell development by regulating gene expression and migratory behavior, and thus establish a novel role for Myo18A in curating the developing B cell repertoire. The observed alterations in the expression of genes implicated in leukemic transformation suggest a possible association of Myo18A deletion in acute lymphoblastic leukemia that needs further investigation.

Poster # 703

TRANSCRIPTOMIC ANALYSIS OF PEDIATRIC CHRONIC MYELOID LEUKEMIA STEM CELLS

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Background: Pediatric Chronic Myeloid Leukemia (CML) accounts for 2-9% of leukemias in children. With an estimated incidence of 0.06 to 0.12 per 100,000 children per year, pediatric CML is substantially less common than adult CML. Although pediatric CML tends to have a more aggressive clinical presentation than adult CML, including higher leukocyte counts and greater splenomegaly, pediatric CML is treated in the same manner. While there have been advancements in the understanding of adult CML, very little is understood about the pathogenesis of pediatric CML.
To investigate the transcriptome of pediatric CML bone marrow stem cells and identify differentially regulated genes and pathways, bulk RNA-seq showed hierarchical clustering of pediatric and adult CML, suggesting differential transcriptomic profiles between the two groups. Pathway analysis identified differentially enriched pathways in pediatric CML compared to adult CML. The Rho pathway was significantly downregulated in pediatric CML compared to healthy controls, whereas previous studies reported the Rho pathway being hyperactivated in adult CML. We have confirmed differential expression of Rho regulators, such as *ARGHAP27, VAV2,* and *DLC1,* in pediatric CML cells compared to adult CML by RT-qPCR.[1]

Objectives: To study clonal heterogeneity and diversity of pediatric CML bone marrow CD34+ cells compared to healthy cells.

Design/Method: Single-cell RNA sequencing (scRNA-seq) was conducted using $CD34^{+}$ cells (20,000) from pediatric CML (n=7) and healthy pediatric (n=2) bone marrow samples using the Stem Pro CD34+ system (Miltenyi Biotec, Inc.) and Chromium Next GEM Single Cell 3' kit from 10X Genomics and performed by Stanford Genome Sequencing Service Center.

Results: Our preliminary data demonstrated that Human Leukocyte Antigen (HLA) class II-related genes such as HLA-DRA, HLA-DPB1, and CD74 were significantly downregulated in pediatric CML. Pathway enrichment analysis also showed downregulation of immune activation pathways and upregulation of T cell inhibitory pathways. Our preliminary data co-culturing T cells with CML cell lines of differential HLA

class II expression confirmed the scRNA-seq results, though further studies are required and being conducted on the immunogenicity of HLA class II in pediatric CML.

Conclusion: Our scRNA-seq data demonstrate that several immune-related genes and pathways are downregulated in pediatric CML compared to healthy controls. Future work will focus on characterizing 1) the role of HLA-related genes in pediatric CML stem cells and their impact on T cell response and 2) cell surface markers of pediatric CML stem cells to identify potential targets for immunotherapy.

References

1. Youn et al. Cancers, 2021.

Poster # 704

THE ROLE OF OVER-EXPRESSED B GLOBIN IN DRIVING RELAPSED B – CELL ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: The prognosis for patients with relapsed acute lymphoblastic leukemia (ALL) remains suboptimal despite intensification of treatment and immunotherapy. We have identified genetic and epigenetic alterations enriched at relapse that drive drug resistance. We discovered three novel super-enhancers (SEs) in the epigenetic landscape enriched at relapse in a majority of patients, implicating a role in clonal evolution. One SE is upstream of the β globin locus and leads to aberrant expression of hemoglobin beta subunit (*HBB*) mRNA. These findings were validated in a large meta-analysis of gene expression data from pediatric diagnosis/relapse pairs.

Objectives: Determine whether *HBB* upregulation in blasts plays a role in relapse and leads to drug tolerance and/or increased clonal potential.

Design/Method: A panel of B-ALL cell lines were transduced with lentiviral vectors overexpressing either wild-type HBB or an empty vector control. The generated cell lines were then plated for five days with varying drug concentrations (cytarabine, methotrexate, 6-mercaptopurine and prednisolone) and evaluated for differences in apoptosis using the Annexin V assay. Clonogenic growth *in vitro* was also assessed using MethoCult™ media. To determine if *HBB* could be facilitating clonal growth through an RNA-based mechanism, we genetically engineered cell lines with a mutation *in HBB* that either altered the translation start site or led to a premature stop codon.

Results: Notably we did not observe significant differences in chemosensitivity to any of the agents in cell lines upon overexpressing HBB. However, we did demonstrate increased clonal growth in methylcellulose compared to control (mean colony #: 226 vs. 31, $p<0.0001$), which was replicated in a second cell line (mean colony #: 68 vs. 38, $p=0.0028$).
While we confirmed mRNA expression, we were unable to detect protein by Western blot or immunoprecipitation. We observed increased clonal growth in mutant lines (mean colony # start mutant: 145, $p=0.0003$; stop mutant: 125, $p=0.0016$), suggesting a catalytic role for *HBB* RNA in expanding a leukemia stem cell population.

Conclusion: Increased clonal potential upon overexpression of *HBB* could be indicative of the ability to reconstitute a tumor from a small subpopulation following treatment. Our data suggests a novel hypothesis that *HBB* acts as a catalytic RNA to promote leukemia stem cell potential. We are analyzing RNAseq data to compare differential gene expression between control and *HBB* expressing cells to discover downstream pathways impacted by *HBB*. We are testing this hypothesis by performing limiting dilution analysis in an immunocompromised mouse model.

Poster # 706

CLINICAL AND GENE EXPRESSION DATA REVEAL SUBTYPES OF PEDIATRIC T-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Acute Lymphoblastic Leukemia (ALL) is a rapidly progressive cancer characterized by excessive immature leukocytes, which transform into leukemic cells and proliferate uncontrollably into lymphoblasts, blocking the production of normal cells. T-ALL constitutes 10–15% of pediatric ALL cases. Unlike B-ALL, T-ALL lacks clinically defined molecular subtypes, hindering risk assessment and treatment determination.

Objectives: In this study, we aimed to identify connections between clinical findings and gene expression in pediatric T-ALL to move towards defining more clinically meaningful subtypes of pediatric T-ALL.

Design/Method: We analyzed clinical and gene expression (bulk and single-cell RNAseq) data from eight pediatric T-ALL patients from the Children's Mercy Research Institute Biorepository. By utilizing various clinical data types (e.g., flow cytometry, FISH, microarray), we identified clinically relevant mutations and gene expression patterns. This offered further insight into characterizing individual patients and establishing related groups of patients.

Results: Our investigation revealed similarities in gene expression involving *LEF1*, *NOTCH1*, and *RUNX1* among two patients. In the same patients, we also observed T-cell receptor alpha (TRA) rearrangements with *TAL* and *TLX1*, indicating consistency between genomic and transcriptome findings. Furthermore, a patient with ETP-ALL had a high proportion of hematopoietic stem cells (HSC)-like cells, while another patient (not classified with ETP-ALL) displayed similar proportions of HSC-like cells and an elevated expression of genes including *IL-7* and *LMO2* compared to other patients. Moreover, our analysis identified differential expression of *ETV6* and *TOX* across our cohort, providing potential biomarkers for T-ALL subtyping.

Conclusion: Similarities in gene expression patterns among T-ALL patients, even within our small cohort, emphasize the need for refined classifications of distinct subtypes to improve treatment selection and outcomes. Additionally, we found that a patient without clinically defined ETP-ALL criteria shares a similar molecular profile as the patient with Early T-cell Precursor (ETP)-ALL. Patterns of gene and cell surface marker expression offer potential biomarkers for characterizing T-ALL subtypes and prognosis. Furthermore, the diverse signaling pathway activities identified through bulk and single-cell RNA analyses present potential therapeutic targets for treatment strategies. Future exploration utilizing

external gene expression datasets is planned to validate findings within the broader context of Children's Mercy's cohort of T-ALL patients and lay the foundation for more personalized approaches to diagnosing and treating pediatric T-ALL.

Poster # 707

INSULIN-INDUCED CHEMORESISTANCE TO DAUNORUBICIN IN PH-LIKE B-ALL

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Background: One in five pediatric patients with B-cell acute lymphoblastic leukemia (B-ALL) are obese at diagnosis,[1] which increases their risk of developing resistance to induction chemotherapy and for relapse.[2,3] However, the mechanisms by which obesity causes chemoresistance remain unclear. Obesity results in insulin resistance, leading to high levels of circulating insulin. Insulin induces cell signaling through insulin receptor (IR) and activates PI3K/AKT, a known chemoresistance pathway.[4-5] Philadelphia chromosome-like acute lymphoblastic leukemia (Ph-like ALL) with cytokine receptor-like factor 2 rearrangements (*CRLF2r*)[6] is a subtype that is more common in obesity-associated ALL and associated with poor prognosis, making it a good candidate to explore chemoresistance.

Objectives: We hypothesize that higher levels of circulating insulin during ALL induction therapy induces chemoresistance via PI3K/AKT activation in B-ALL. We first conducted experiments to determine whether insulin abrogates induction chemotherapy cytotoxicity.

Design/Method: The Ph-like *CRLF2r* B-ALL cell lines, MUTZ-5 and MHH-CALL-4 (provided by Sarah Tasian laboratory), were co-incubated for 48 hours with varying concentrations of dexamethasone, vincristine, asparaginase, or daunorubicin to determine their sensitivity to induction chemotherapy agents. Cell viability following drug exposure was analyzed via flow cytometry. Drugs showing cytotoxic activity were selected for further studies to determine the impact of insulin on chemotherapy sensitivity. Cells were then co-incubated with the chemotherapy agent (at the IC50 concentration) and insulin (10 ug/mL).

Results: Of the 4 induction agents, both Ph-like cell lines were resistant to asparaginase and vincristine and not tested further. MUTZ-5 was sensitive to daunorubicin (IC50 0.05 uM) and dexamethasone (IC50 1 uM, n=3 independent experiments). MHH-CALL-4 was only sensitive to daunorubicin (IC50 0.1 uM, n=4 independent experiments). Both cell lines demonstrated robust expression of IR by flow cytometry. Insulin did not affect the viability of untreated Ph-like B-ALL cells or the sensitivity of MUTZ-5 to dexamethasone. However, both cell lines treated with daunorubicin and insulin showed decreased apoptosis relative to cells treated with daunorubicin alone: 48.79 ± 15.13 vs 31.10 ± 14.53 (MUTZ-5, mean ± 2x standard error of mean) and 80.38 ± 4.68 vs 63.95 ± 13.83 (MHH-CALL-4) for daunorubicin vs daunorubicin + insulin ($P < 0.001$, paired t test, n=7 independent experiments).

Conclusion: Our data indicates that insulin induces daunorubicin chemoresistance in Ph-like B-ALL cells *in vitro*. The next step is to investigate IR and downstream PI3K/AKT signaling pathways in ALL cells from lean and obese children and adolescents using high-dimensional spectral flow cytometry to characterize the mechanisms underlying insulin effect on Ph-like ALL sensitivity to daunorubicin.

Poster # 708

CHARACTERISTICS AND OUTCOMES OF NEWLY DIAGNOSED AML WHO DEVIATED FROM STANDARD COG-BASED REGIMENS

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Background: Acute myeloid leukemia (AML) accounts for 20% of childhood leukemia. Despite progress in identifying high-risk (HR) patients, intensifying chemotherapy regimens, and including hematopoietic stem cell transplant (HSCT), the 5-year overall survival (OS) remains 60-70%, with worse outcomes for HR disease. Many AML patients switch from the standard regimen to an alternative regimen, presumably due to toxicity or persistent disease.

Objectives: We sought to determine when and why patients deviated from the standard COG-based AML therapy, what alternative treatments they received, and what their outcomes were. Our results will support future evidence-based decision-making regarding alternative up-front AML treatment options.

Design/Method: We retrospectively identified consecutive patients with newly diagnosed AML who were treated between January 2012 to December 2022 at Texas Children's Cancer Center. AML was diagnosed per standard WHO criteria. This project was approved by the Baylor College of Medicine institutional review board.

Results: 107 patients were included. 75 patients followed the standard sequence (per AAML1831 or AAML1031 trials) and 32 deviated, either because of persistent disease (28) or chemo-toxicity (4). 25% deviated after Induction I, 60% after Induction II, and 15% after Intensification I. Of the 28 patients who deviated due to persistent disease, 8 became measurable residual disease (MRD) negative after the first alternative cycle, 11 after the second alternative cycle, and 15 received HSCT in first remission. Fifteen patients received Fludarabine-Cytarabine (FLA) or its variation (FLAG, FLA-Idarubicin, or FLA-Azacitidine), 7 received epigenetic drugs, 5 received Cladribine with Idarubicin (IDA/2CDA) and 7 received high dose Cytarabine/Asparaginase for their first deviated cycle. All 8 patients who received FLAG as the first alternative cycle became MRD negative. Of those who followed the standard sequence, 25 were high risk and 50 were low risk. 14 patients remained MRD positive after Induction I, of which 93% became negative after Induction II and 77% received HSCT in first remission. The median survival for the deviated group was 992 days compared to 670 days for HR patients who did not deviate, with a hazard ratio of 0.69 (95% CI 0.34-1.43) and 5-year OS 46.2% vs 34.3%, respectively (p=0.32).

Conclusion: AML patients who transitioned to alternative regimens had comparable outcomes to HR patients who followed the standard therapy sequence. These data demonstrate the challenges in treating HR AML and the urgent need for new targeted therapies. Our data support the use of FLAG as an effective alternative regimen for patients with persistent disease after standard induction.

Poster # 709/Late Breaking Abstract

VENETOCLAX USE AS SALVAGE TREATMENT FOR POST-CAR T RELAPSE IN B-ALL

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Background: Despite high early response rates following chimeric antigen receptor T cell therapy (CAR-T) for relapsed/refractory pediatric B-cell acute lymphoblastic leukemia (B-ALL), half of responders will experience subsequent relapse. Antigen downregulation has emerged as a major challenge following both CD19 and CD22-targeted therapy, highlighting the need for novel antigen-agnostic salvage agents such as venetoclax, a pro-apoptotic B-cell lymphoma-2 (BCL-2) inhibitor.

Objectives: We aimed to determine whether venetoclax shows promise for use in the post-CAR setting.

Design/Method: We conducted a multi-site, retrospective study across patients with B-ALL from nine major pediatric oncology centers in the United States, who received CAR-T therapy followed by venetoclax. Deidentified data was extracted from the medical records and outcomes were analyzed using the statistical program R.

Results: Nineteen patients with a median age at venetoclax initiation of 16 years (range, 1-27) received venetoclax following CAR-T therapy. Six patients (32%) had received stem cell transplant (SCT) prior to CAR-T. Indication for CAR-T therapy was first relapse in 9 patients (47%), >1st relapse in 6 patients (32%), and refractory disease in 4 patients (21%). Of 12 patients with known antigen status at the time of venetoclax initiation, 11 patients (92%) had antigen downregulation (CD19/22, n=8 (67%); CD19, n=3, (25%)). In 14 patients (74%), venetoclax was given in combination with other chemotherapies. Of 19 patients, 12 (63%) achieved a complete response (CR) by morphology after venetoclax initiation, of which 9 (75%) were minimal residual disease (MRD) negative by flow cytometry. Six out of 11 patients with antigen downregulation achieved morphologic CR (55%). After venetoclax, 5 patients (26%) achieved CR followed by SCT, 7 patients (37%) achieved CR followed by relapse and went on to other therapies, 5 patients (26%) were unresponsive to venetoclax, and 2 patients (11%) received venetoclax as palliative treatment. With a median duration of follow-up of 264 days (range, 46-842) (defined by data cutoff or death), 7 (37%) remained alive at time of data collection. Of these, 3 (43%) received SCT following venetoclax. The most common side effect of venetoclax-based treatment was cytopenias, which occurred in 12/19 patients (63%), with 10 patients (53%) requiring transfusions while on treatment. Other commonly reported side effects were nausea in 8/18 patients (44%) and infections in 8/19 (42%).

Conclusion: Venetoclax was well-tolerated and effective at inducing remission in both antigen-positive and antigen-downregulated B-ALL relapse after CAR-T and served as a successful bridge to SCT in heavily pretreated subsets of patients with B-ALL.

Poster # 710

OUTCOMES IN PATIENTS WITH ETV6::RUNX1 OR HYPERDIPLOID B-ALL IN THE ST. JUDE TOTAL 15 AND 16 STUDIES

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Background: Children with *ETV6::RUNX1* or hyperdiploid B-acute lymphoblastic leukemia (B-ALL) typically have favorable outcomes. The St. Jude (SJ) classification considers these patients as provisional low-risk, regardless of their National Cancer Institute (NCI) risk, which may be upgraded for minimal residual disease (MRD) response of ≥1% on day 15 or testicular or central nervous system involvement.

Objectives: To determine survival outcomes and treatment related toxicities experienced by patients with *ETV6::RUNX1* and hyperdiploid B-ALL enrolled in the SJ Total XV and Total XVI studies, considering both SJ and NCI risk status.

Design/Method: We analyzed MRD response during induction, survival, and toxicities experienced by children (aged 1–18.99 years) diagnosed with *ETV6::RUNX1* and hyperdiploid B-ALL in the SJ Total XV and Total XVI studies (2000–2017).

Results: Patients with *ETV6::RUNX1* (n = 222) or hyperdiploid (>50 chromosomes) (n = 296) B-ALL had 5-year event-free survival (EFS) of 97.7%±1.1% and 94.7%±1.4%, respectively. For *ETV6::RUNX1*, EFS was comparable between NCI standard-risk and high-risk patients (97.8%±1.2% and 97.5%±2.6%, respectively; *P* = 0.917) and between SJ low-risk and standard-risk patients (97.4%±1.2% and 100.0%; *P* = 0.360). Notably, 37 of 40 NCI patients with high-risk *ETV6::RUNX1* who received SJ low-risk therapy had excellent EFS (97.3%±2.8%). For hyperdiploid B-ALL, EFS was worse for NCI high-risk patients compared to standard-risk patients (87.6%±4.5% and 96.4% ± 1.3%; *P* = 0.016) but did not differ significantly between SJ low-risk and standard/high-risk patients (96.1% ± 1.4% and 90.6% ± 3.6%; *P* = 0.133). Although EFS was similar for patients with NCI standard-risk and high-risk hyperdiploid ALL classified as SJ low-risk (96.0%±1.5% and 96.9%±3.2%; *P* = 0.719), EFS was worse for NCI high-risk patients than for NCI standard-risk patients receiving SJ standard/high-risk intensified therapy (77.4%±8.2% and 98.0%±2.2%; *P* = 0.004). Among patients with *ETV6::RUNX1* and hyperdiploid B-ALL, NCI high-risk patients receiving SJ low-risk therapy (n = 69) had lower rates of grades 2–4 pancreatitis and thrombotic events than those receiving SJ standard/high-risk therapy (n = 30) (4.4%±2.5% vs 20.0%±7.4%; *P* = 0.013 and 4.4%±2.5% vs 20.0%±7.4%; *P* = 0.011, respectively).

Conclusion: Contemporary MRD-directed therapy yielded excellent outcomes, except for patients with NCI high-risk hyperdiploid ALL with slow early MRD response, necessitating new treatment approaches. Among NCI high-risk patients, 93% with *ETV6::RUNX1* and 54% with hyperdiploid ALL experienced excellent survival outcomes and reduced treatment-related toxicities with a low-intensity regimen.

Poster # 711

OBSERVATION AND MANAGEMENT OF JUVENILE MYELOMONOCYTIC LEUKEMIA: A TEXAS MEDICAL CENTER EXPERIENCE

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Background: Juvenile Myelomonocytic Leukemia (JMML) is a rare and clonal hematopoietic disorder of infancy and early childhood with myeloproliferative/myelodysplastic features resulting from germline or somatic mutations in the RAS pathway. Management varies from observation to transplant. Given its rarity, treatment is not standardized.

Objectives: To describe the course of JMML and its management in a series of 22 pediatric patients to provide insight for monitoring, intervention, and transplant.

Design/Method: Retrospective review

Results: Twenty-two patients were included for analysis (median age = 9 months). Of patients with known genetic mutations and cytogenetics, 6 harbored germline mutations (4/6 *PTPN11*, 2/6 *CBL*), 12 somatic mutations (9/12 *RAS* (5 *KRAS*, 4 *NRAS*), 3/12 *PTPN11*, 3/12 other), and 9 cytogenetic abnormalities (6/9 monosomy7, 3/9 other). At diagnosis, splenomegaly was noted in 86% of patients. All bone marrows had <20% blasts. All patients had <20% peripheral blasts and absolute monocyte counts of > $1x10^9$/L. Thrombocytopenia was noted in 95%. Fetal hemoglobin was elevated in 82%.

Chemotherapy regimens were known in 20 patients. Seventy-seven percent received chemotherapy (14% 6-mercaptopurine (6MP) monotherapy, 18% azacytidine monotherapy, 4.5% 6-MP + azacytidine, 27% other). Fifty-nine percent (7 somatic mutations, 1 *CBL* germline mutation) underwent stem cell transplant (SCT), 77% received pre-transplant chemotherapy (2 unknown,1 none). Of those with germline mutations, 4/4 with *PTPN11* mutation did not require chemotherapy, whereas both patients with *CBL* mutations received 6-MP and one then underwent SCT.

Overall, 14/22 patients are alive. One of 4 patients treated with 6-MP and 5/5 patients treated with azacytidine had a reduction in mutant VAF. Among patients transplanted, 8/12 are living. Spontaneous remission occurred in one patient with somatic *NRAS* mutation and 2 with germline *PTPN11* mutations (time to remission 90, 13.3, and 41 months). Two additional germline *PTPN11* patients are in active surveillance 6 and 14 months after diagnosis. The 2 patients with germline *CBL* mutations improved substantially in hematologic parameters and splenomegaly with 6MP, despite unchanged mutant VAFs. Transformation to AML was seen in 2 patients, both harboring somatic *KRAS* mutations and one with additional somatic mutations in *PTPN11*, *JAK3*, *TERT*, and *CBL*. Relapse post-transplant occurred in 3/11 with a median time to relapse of 3.55 months.

Conclusion: This report provides real-world data on a series of patients with JMML treated at three institutions. Our work provides additional insight into expected time to spontaneous resolution in those with germline PTPN11 mutations, response to therapy, and outcome post-therapy across differing genetic subsets.

Poster # 712

SAFETY AND EFFICACY OF MITOXANTRONE LIPOSOME PLUS CYTARABINE IN NEWLY DIAGNOSED PEDIATRIC AML

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Background: Pediatric acute myeloid leukemia (AML) is a heterogeneous disease and accounts for approximately 15% of childhood acute leukemia. Although treatment programs have been improved over the past decades, it is still a kind of tumor with a high mortality rate in children and adolescents. Mitoxantrone hydrochloride liposome (Lipo-MIT) is an innovative anthracycline nano-drug, which has demonstrated favorable pharmacokinetic characteristics and shown preliminary efficacy in adult AML. However, the data of safety and efficacy study in children AML is limited.

Objectives: To observe the pharmacokinetics (PK) characteristics of Lipo-MIT combined with cytarabine in pediatric AML, and to preliminarily evaluate the safety and efficacy.

Design/Method: Patients(pts) with newly diagnosed pediatric AML were recruited in this ongoing, prospective, pharmacokinetic study (ChiCTR2300067964). Lipo-MIT was administered on day 1 at 30mg/m^2 and cytarabine was administered on days 1-7 at 200mg/m^2. Pts were treated for a maximum of 2 cycles, each cycle was defined as 28 days. The primary endpoints were PK characteristics of Lipo-MIT after the first dose. Secondary endpoints were safety, composite complete remission (CRc) rate, minimal residual disease (MRD) negative rate, overall response rate (ORR) and relapse-free survival(RFS).

Results: At data cut-off of 19 December 2023, 8 eligible pts were enrolled. The median age was 7.5 (range 5.0-15.0) years, with 75.0% were male. Two pts had extramedullary leukemia infiltration. Risk stratification based on cytogenetic and molecular abnormalities was available for 7 pts: 3 low risk, 2 intermediate risk, and 2 high risk. All pts who received treatment were included in the safety analysis. The most common grade 3/4 treatment-related adverse events (TRAEs) were hematological toxicities (100.0%), febrile neutropenia (25.0%) and soft tissue infection (25.0%). The median duration of neutrophil counts<0.5×10^9 was 30 days (range 2-34) and platelet counts<20×10^9 was 21 days (range 10-31). Seven of these pts were eligible for efficacy evaluation. The CRc rate after one cycle of treatment was 71.4% (5/7). Flow cytometric MRD assessment in the remission sample was available for 4 pts. The overall MRD negative rate was 100% (4/4), of which 2 were already negative after cycle 1 and 2 were negative after cycle 2. The lesions of 2 pts with extramedullary infiltration basically disappeared. Furthermore, there may be bias and statistical error in the study due to the small sample size.

Conclusion: Lipo-MIT plus cytarabine has a manageable safety profile and encouraging efficacy in pediatric AML. The trial is still ongoing to further clarify the PK characteristics, safety and efficacy.

Poster # 714

CLINICOPATHOLOGIC FEATURES OF B LYMPHOBLASTIC LEUKEMIA WITHOUT PERIPHERAL BLASTS

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Background: B lymphoblastic leukemia (B-ALL) may present without peripheral blood (PB) blasts, but it is unknown if this presentation is associated with distinctive clinical or molecular features.

Objectives: To characterize the clinicopathologic features of patients with B-ALL presenting with <1% peripheral blood blasts.

Design/Method: Thirteen patients with B-ALL presenting with <1%, and fifteen with 1-5%, PB lymphoblasts by flow cytometry were retrospectively identified from 2011-2023 at a single institution, along with twenty-nine patients presenting with >=5% PB blasts sequentially diagnosed from 2022-2023. Comparisons between those without (<1%; n=13) and with (>=1%; n=44) PB blasts were performed using Fisher's exact test and t-test (GraphPad Prism software v.10.1.0) for categorical and continuous variables, respectively.

Results: The median age at diagnosis within PB-negative and PB-positive cohorts was 9.1 (range: 2.9-16) and 5 (range: 2.1-21.6) years with female:male ratios of 3:10 and 21:23, respectively. The PB-negative cohort had between 0.08-0.9% (median: 0.27%) lymphoblasts in the PB by flow cytometry, and 30-95% (median: 88%) in the bone marrow. The PB-positive cohort had 1-84% (median: 18.5%) blasts in the PB and 25-97% (median: 87.5%) in the bone marrow. The median WBC at diagnosis was $6.4x10^9$/L (range: 0.9-16.3) for the PB-positive and $3.4x10^9$/L (range: 0.3-295) for the PB-negative cohort. Within the PB-positive and PB-negative groups 40.1% and 38.5% of cases were NCI high risk, respectively. At the time of diagnosis, the PB-negative group demonstrated more frequent musculoskeletal symptoms (77% vs. 30%; p=0.0035), higher hemoglobin (median: 8.9 vs. 7.6g/dL, p=0.0227), higher platelet count (median: 162 vs. 51K cells/uL, p=0.0061), higher likelihood of normal LDH (p=0.0002), and longer time from symptom onset to diagnosis (median: 41 vs. 14 days, p=0.0052). *ETV6::RUNX1* fusion or high hyperdiploidy (without *IKZF1* deletion) were enriched in cases with <5% blasts (21/28, p=0.0033) and in cases with <1% blasts (10/13, p=0.0186) compared to cases with >=5% blasts. There were no significant differences between groups in other features including WBC, lymphadenopathy, bleeding symptoms, fever, hepatomegaly, splenomegaly, CSF involvement, uric acid, or potassium.

Conclusion: Patients with B-ALL presenting with <1% peripheral blasts have a longer time from symptom onset to diagnosis and at the time of diagnosis have more frequent musculoskeletal symptoms, higher hemoglobin, higher platelet count, lower likelihood of LDH elevation, and higher likelihood of favorable cytogenetics. PB-negative B-ALL corresponds to a more indolent subgroup, frequently with a prolonged clinical presentation. High clinical suspicion and low threshold for utilizing sensitive PB flow cytometric analysis is needed for accurate and timely diagnosis.

Poster # 715

AGE AND ACUITY AND SEVERITY OF ILLNESS IN CHILDREN, ADOLESCENTS, AND YOUNG ADULTS WITH LEUKEMIA

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Background: Adolescent and Young Adult (AYA) patients (ages 15-39 years) with leukemia are at higher risk for mortality than younger patients. Acuity of illness in pediatric acute myeloid leukemia (AML) was

shown in prior data to mediate excess mortality in Black patients. Acuity and severity of illness in AYA versus younger patients have been understudied.

Objectives: To determine age's association with acuity and severity of illness in patients presenting with new diagnoses of leukemia.

Design/Method: We performed a retrospective analysis of 660 patients aged 1-21 years who presented with leukemia at Children's Healthcare of Atlanta between 2010-2018. High acuity of illness was defined as any ICU-level resource use in the first 72 hours following presentation (yes/no). High severity of illness was defined as initial white blood cell count ≥ 50,000 cells/microliter or any central nervous system disease (yes/no). Multivariable logistic regression was used to determine age's association with acuity or severity of illness, controlling for sex, race/ethnicity, insurance, and leukemia type.

Results: The median age of the cohort was 6 years (interquartile range 3-12 years, 65.9% aged 1-9 years, 34.1% aged 10-21 years), 52.9% were male, 47.4% were non-Hispanic White, and 41.7% had private insurance. Diagnoses included B-cell acute lymphoblastic leukemia (ALL) (68.9%), AML (16.5%), T-cell ALL (10.3%), and other leukemias (4.2%).

High acuity of illness was seen in 25.0% of the cohort and was more likely in older patients [Bivariate: 10-21 years: 36.0% versus 1-9 years: 19.3%, p <0.01; Multivariable: odds ratio (OR) for 10-21 years (versus 1-9 years): 1.93, 95% confidence interval (CI): 1.30-2.86].

High severity of illness was more likely in older patients in bivariate (10-21 years: 41.3% versus 1-9 years: 31.3%, p<0.01), but not multivariable analysis [OR for 10-21 years (versus 1-9 years): 1.11, 95% CI: 0.77-1.61]. In multivariable analysis, the odds of high severity of illness were significantly higher in non-Hispanic Black (versus non-Hispanic White) patients (OR 1.78; 95% CI: 1.16-2.72) and differed by diagnosis (OR for AML: 1.86, 95% CI: 1.19-2.93; OR for T-ALL: 4.10, 95% CI: 2.33-7.22; OR for other leukemia: 5.30, 95% CI: 1.18-12.32; reference: B-ALL).

Conclusion: AYAs were more likely than younger patients to have high acuity of illness, indicating a risk for elevated morbidity from the point of initial presentation. Future directions will determine the association of initial acuity and severity with mortality in this cohort. This research will inform strategies toward narrowing age disparities in leukemia outcomes.
(Winestone et al, *Am J Hematol*., 2017)

Poster # 716

INCIDENCE & OUTCOMES FOR TREATMENT-ASSOCIATED HEPATOTOXICITY DURING PEDIATRIC ALL INDUCTION THERAPY

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Background: Treatment-associated hepatotoxicity (TAH) is common during acute lymphoblastic leukemia (ALL) therapy. Severe TAH during the critical initial induction phase of therapy complicates

treatment delivery and may compromise event-free survival (EFS).

Objectives: The objectives of this study were to describe in an ethnically diverse population: 1) the incidence and contextual factors for TAH during pediatric ALL induction therapy, and 2) the association between severe TAH and EFS.

Design/Method: This retrospective cohort included patients with newly-diagnosed ALL at six treatment centers in the southwestern US. Clinical parameters (age, race, ethnicity, height, and weight) and liver function lab values during induction (aspartate transaminase [AST], alanine transaminase [ALT], total bilirubin [t.bili], and conjugated bilirubin [c.bili]) were abstracted from medical records. Severe TAH was defined as Common Terminology Criteria for Adverse Events (CTCAEv5) grade ≥3 and using the pragmatic endpoint of c.bili >3 mg/dL, the threshold for concomitant chemotherapy dose-modifications on many contemporary ALL protocols. The frequency of TAH was described and evaluated with multivariable logistic regression. Associations between TAH and EFS were evaluated with Kaplan-Meier plots and proportional hazards models.

Results: A total of 1,865 eligible patients were identified, including 1,099 Latinos, 505 non-Latino Whites, and 107 non-Latino Blacks. Most patients were males (56.5%), NCI standard risk (57.2%), B-cell ALL (88.5%), at a median age of 6.0 years (range: 1.0 - 22.3 years). Overweight/obesity was present in 39.5% at diagnosis. Hepatotoxicity with c.bili >3 mg/dL at presentation was rare (0.7%). During induction therapy, CTCAE grade ≥3 ALT was observed in 23.8% of cases, AST in 8.3%, t.bili in 6.9%, and c.bili >3 mg/dL occurred in 3.0% of patients. The incidence of TAH differed significantly ($p<0.01$) across combinations of age (<10 vs ≥10 years) and weight status (normal weight vs overweight/obese). For example, patients aged ≥10 years with overweight/obesity experienced the highest frequency of CTCAE grade ≥3 ALT (33.6%), AST (16.7%), t.bili (16.3%), and c.bili >3 mg/dL (10.8%). Among this group of older (age ≥10 years) individuals with overweight/obesity, c.bili >3 mg/dL was observed significantly more often in Latino versus NLW patients (13.5% vs <1%, $p=0.018$). Adjusted EFS was significantly poorer in patients with c.bili >3 mg/dL during induction compared to those without (5-year EFS: 75.6% vs 85.6%, $p=0.016$).

Conclusion: Severe TAH disproportionately affects patients who are adolescent, overweight/obese, and Latino. Severe TAH triggering protocol-defined key chemotherapy dose modifications, was associated with poorer EFS. Therefore, ethnic differences in TAH may contribute to disparities in ALL outcomes.

Poster # 717

HEALTHCARE UTILIZATION AMONG SR B-ALL PATIENTS RECEIVING INTERMEDIATE-DOSE MTX VS. BFM-LIKE THERAPY

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Background: Patients undergoing post-induction acute lymphoblastic leukemia (ALL) treatment are at risk of complications and unplanned admissions during consolidation and intensification phases. AALL0932 suggested that using intermediate-dose methotrexate (ID MTX) instead of an anthracycline and alkylator-containing Berlin-Frankfurt-Muenster (BFM)-like backbone could maintain excellent outcomes for low-risk patients while reducing toxicities.(1) This approach requires six admissions for

methotrexate. Families and providers must weigh this burden against possible side effects and associated healthcare utilization secondary to BFM-like therapy. Our institution currently recommends post-induction ID MTX for patients meeting AALL0932-like low-risk criteria.

Objectives: Determine differences in healthcare utilization between standard risk (SR) B-ALL patients receiving post-induction ID MTX vs. BFM-like therapy.

Design/Method: We conducted a single-center retrospective cohort study of SR B-ALL patients who received post-induction therapy from 2011-2023. Data were extracted from our institution's clinical data warehouse and charts manually reviewed for patients with incomplete data. Patients were analyzed according to treatment group independent of study enrollment (ID MTX vs. BFM-like); those receiving escalated regimens with high-dose methotrexate were excluded. Median LOS and ED visits were compared between cohorts using a Kruskal-Wallis test. ED visit rate was assessed using a Poisson regression. Descriptive statistics were used to summarize intensive care unit (ICU) admissions, bacteremia, and pancreatitis. Pancreatitis (grade 2 and above) was defined using the Common Terminology Criteria for Adverse Events (version 5).

Results: Among 172 qualifying patients, 22 were treated with ID MTX and 150 with BFM-like therapy. Median hospital days for the ID MTX cohort were 14.3 (range 7.7-56.6) vs. 2.1 (range 0-44.7) for the BFM-like cohort ($p = <0.001$). Median ED visits for the ID MTX cohort were 0 (range 0-3) vs. 1.5 (range 0-9) for the BFM-like cohort ($p = <0.001$). The ED visit rate was 59% higher in the BFM-like cohort compared to the ID MTX cohort ($p = 0.001$). No patients treated with ID MTX were admitted to the ICU or experienced bacteremia or pancreatitis. In the BFM-like cohort, 7 patients required ICU admission (4.7%) with median LOS 1.5 days (range 0.73-18.6), 3 had bacteremia (2%), and 4 had pancreatitis (2.6%).

Conclusion: Both post-induction ID MTX and BFM-like therapy for SR B-ALL are associated with relatively low healthcare utilization. ID MTX therapy was associated with a higher number of hospital days but lower rates of ED visits and complications. This utilization assessment offers useful information for providers and families weighing the risks and benefits of possible treatment regimens.

(1) Schore, Leukemia, 2023

Poster # 719

MANAGEMENT OF ACQUIRED HYPOFIBRINOGENEMIA IN CHILDREN WITH LEUKEMIA

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Background: Hypofibrinogenemia is common in children diagnosed and undergoing treatment for leukemia that increases the risk of bleeding. Cryoprecipitate stands as the primary choice for both prophylaxis and treatment of hypofibrinogenemia. There is a notable absence of comprehensive data on the utilization of cryoprecipitate in children with leukemia.

Objectives: To address the knowledge gap in using cryoprecipitate for children with leukemia.

Design/Method: We conducted a retrospective chart review of children with leukemia who received cryoprecipitate at The University of Texas MD Anderson Cancer Center between 2021 and 2022. Our analysis encompassed baseline patient information, details of cryoprecipitate usage, and assessments of changes in fibrinogen levels. We employed paired samples t-tests for comparative analysis.

Results: We identified 36 patients, aged 1 to 25 years, who received cryoprecipitate, with a male prevalence of 24 out of 36 (66.7%) and median weight of 47.6 kg (range: 8.4-136). Within this cohort, 5 of 36 (14%) were diagnosed with AML and 30 out of 36 (83%) were diagnosed with ALL and 27 out of 36 (75%) had recent exposure to asparaginase. Two out of 36 (6%) had a history of thromboembolism, and 6 out of 36 (17%) had a significant history of bleeding. Cryoprecipitate was administered for bleeding treatment (10 out of 36, 28%), bleeding prophylaxis (22 out of 36, 61%), and surgery prophylaxis (4 out of 36, 11%), often in conjunction with multiple red blood cell and platelet transfusions. Common comorbidities in patients receiving cryoprecipitate included disseminated intravascular coagulation (DIC) (10 out of 36, 28%) and sepsis (10 out of 36, 28 %). The median baseline fibrinogen level for the entire cohort was 0.86 g/L (95% CI 0.63 to 1.64). The median dose of cryoprecipitate infused was 176 mL (range: 45-5932; assume ~10 mg of fibrinogen per mL), resulting in a post-infusion median peak fibrinogen level of 1.85 g/L (95% CI 1.87 to 2.91) ($p<0.001$). No instances of allergic reactions or infectious complications were documented following cryoprecipitate infusion. However, a mild increase in weight gain was observed, with younger patients showing more pronounced changes.

Conclusion: Cryoprecipitate stands out as a commonly employed and effective intervention in children with leukemia, serving to replenish diminished fibrinogen levels and potentially mitigate the risk of bleeding complications. Further research is imperative to establish standardized guidelines for dosing, define precise thresholds, identify the most effective product, and explore alternative options including fibrinogen concentrate in fibrinogen replacement therapy among children with leukemia.

Poster # 720

AML CARE AT HOME: A PILOT IMPLEMENTATION OF OUTPATIENT ACUTE MYELOID LEUKEMIA (AML) MANAGEMENT

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Background: The Children's Oncology Group mandated inpatient recovery for AML chemotherapy cycles after treatment-related mortality approached 20% on CCG2961. However, 10-23% of patients are currently discharged prior to neutrophil recovery. Patients meeting strict clinical criteria have similar bacteremia rates and mortality whether recovering outpatient or inpatient-only.[a] We developed evidence-based "AML Care at Home" guidelines for outpatient AML management beyond Induction 1.

Objectives: Pilot implementation study of outpatient AML chemotherapy recovery at CHOP to evaluate feasibility, fidelity, and acceptability

Design/Method: We designed a tool to guide discharge eligibility decisions and outpatient management

based on our prior study and published adult recommendations: the Outpatient Neutropenia Care: Personalized Approach to Treatment at Home (ONC-PATH). Informed by the Consolidated Framework for Implementation Research-Expert Recommendations for Implementing Change, we developed hypothesized determinants, strategies, and mechanisms for implementation. Strategies included: collaborative refinement of ONC-PATH and supporting documents with clinicians, identification of multi-disciplinary champions, and educational sessions. Pre- and post-implementation focus groups identified barriers and facilitators and assessed acceptability. Fidelity was measured as proportion of cycles using ONC-PATH.

Results: Pre-implementation began in January 2022. We reviewed data supporting this approach and refined our implementation plan in iterative planning and educational sessions with the CHOP Hematologic Malignancies Program. We identified key stakeholders and champions from inpatient and outpatient nursing leadership, nurse practitioners, social workers, case managers, and physicians. Using their feedback, we developed an implementation toolkit: the ONC-PATH tool, manual of operations, caregiver introductory letter, fever letter template, and clinician "cheat sheet".

AML Care at Home was implemented as a clinical change on 11/15/2022. Focus groups with multi-disciplinary clinicians identified that additional outpatient visits were not burdensome to staff, communication was good, and clinicians reported patients/caregivers appreciated being home. They observed qualitatively less mucositis than expected, especially during Intensification cycles. Perceived barriers included needing to anticipate transfusions at satellite clinics without blood banks, burdensome clinic days for patients/caregivers, and patient/caregiver household material hardship.

The ONC-PATH tool was applied in 15/37 non-Induction 1 cycles (40.5%) and 14/16 cycles (87.5%) with early discharge. ONC-PATH forms were more likely to be incomplete or missing among discharge-ineligible patients based on chart abstraction.

Conclusion: Pilot implementation of AML Care at Home was feasible and acceptable. Fidelity to the ONC-PATH tool was poor overall but good among discharge candidates. We are currently developing a multi-institutional hybrid type II implementation study, with approaches to facilitate ONC-PATH uptake.

Funding: CHOP Healthcare Delivery Science Research Grant (Seif)

[a]Getz *JAMA Network Open* 2021

Poster # 721

CLADRIBINE USE IN PEDIATRIC RELAPSED LEUKEMIAS: THE MD ANDERSON CANCER CENTER EXPERIENCE

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Background: Relapse in pediatric acute myeloid leukemia (AML) can be seen in 33% of AML patients, leading to poor long-term outcomes. It is crucial to identify effective therapies with a favorable safety profile to improve outcomes in relapsed AML. Cladribine is linked to improved overall and event-free

survival in relapsed/refractory adult leukemia and is used in combination with other chemotherapy such as cytarabine, idarubicin, and venetoclax. Previous pediatrics studies found 11% complete remission (CR) in 18 patients who received cladribine. Subsequent phase 2 study found CR to be around 47% and hematologic toxicities were common.

Objectives: Evaluate the safety and efficacy of cladribine as salvage chemotherapy in pediatric relapsed/refractory leukemia.

Design/Method: IRB approval was obtained to conduct a retrospective analysis of patients treated at our institute between Jan 2015 to July 2023. Patients aged 1-21 years with a diagnosis of refractory or relapsed leukemia who had undergone at least one cycle of cladribine were included. Assessment of cladribine-associated toxicities adhered to the Common Terminology Criteria for Adverse Events version 5.0. Descriptive statistics were employed to present efficacy and toxicity data.

Results: A total of 161 patients were identified through the initial record search, upon thorough review, 40 patients were included, of which 26 were male. The median age was 20 years (Range= 2-21 years) and the predominant diagnosis was AML, found in 85% of the cohort. Additional diagnoses were acute lymphoblastic leukemia, lymphoma, and blastic plasmacytoid dendritic cell neoplasm. The most frequently administered cladribine dose was 5mg/m2/day but 10mg/m2/day was used as part of the preparative regimen prior to stem cell transplant (SCT).
Complete remission (CR)/ complete remission without blood count recovery (CRi) was found to be 44.7% while 21 patients had nonresponse to cladribine. Three patients received cladribine as preparative regimen prior to SCT and two of them maintained a disease-free status post transplant. In our cohort, a total of 24 patients received cellular therapy/ SCT. The primary adverse effects observed were grade 3/4 thrombocytopenia (N=7) and grade 3 febrile neutropenia (N=14). No dose adjustments were necessary for managing adverse events; however, cladribine was held in one patient due to a worsening clinical status.

Conclusion: In our preliminary results, we demonstrate the safety of cladribine in pediatrics. Cladribine can be a viable part of salvage therapy for relapsed AML. Future analysis will evaluate survival in addition examining genetic alteration, differentiating between patients who attained CR and those who exhibited NR within our cohort.

Poster # 722

PATIENTS' PATHS TO CHIMERIC ANTIGEN RECEPTOR T-CELL THERAPY IN B-ALL: NO TWO JOURNEYS ARE ALIKE

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Background: Chimeric antigen receptor (CAR) T-cell therapy for relapsed/refractory B-cell acute lymphoblastic leukemia (r/r B-ALL) has a critical role in improving outcomes. Access to CAR T-cell therapy is limited for r/r B-ALL international patients for whom standard therapies have failed, forcing many to undertake substantial travel in search of a cure. Our institution offers phase I CAR T-cell clinical

trials for pediatric, and adolescent and young adult (AYA) patients, and is one of the few that can accept patients nationally and internationally.

Objectives: This study aims to describe the prior therapy of patients with r/r B-ALL who received CAR T-cell therapy at the Pediatric Oncology Branch (POB), and their response to it.

Design/Method: This was a retrospective study of patients enrolled on a CAR T-cell trial at POB from 6/2012 through 3/2021. Variables including demographics, prior lines of therapy including immunotherapy, CAR T-cell product, was manually extracted from the electronic medical records, and analyzed using R software, version 4.3

Results: A total of 128 patients (70.3% male, 29.7% female) were included. The mean age at diagnosis was 15.3 years (SD 7.6). Sixty-two (48.4%) were enrolled for CD22, 49 (38.3%) for CD19, and 17 (13.3%) for dual CD19/CD22 directed therapy. The number of prior therapy lines ranged between 1 and 12 (mean 4.6, SD 2.2). Sixty-seven patients (52.3%) underwent at least one prior allogeneic hematopoietic stem cell transplantation (HSCT), 45 (35.2%) underwent at least one prior CAR T-cell therapy, and 62 (48.4%) had received prior immunotherapy, in particular, 43 (33.6%) received prior blinatumomab, and 18 (14.1%) had prior Inotuzumab Ozogamicin.
International patients comprised 44.5% (n=57). They had a higher average number of prior therapy lines (5.2 vs 4.1, p=0.01)), higher rates of prior allogeneic SCT (61.4% vs. 45.1%, p=0.08), comparable rates of prior CAR T-cell therapy (33.3% vs. 36.1%,p=0.71), and comparable rates of achieving complete remission (CR)(61.4% vs. 73.2%, p=0.12).

Conclusion: Although limited, our study is the largest to describe prior lines of therapy and treatment paths for pediatric and AYA patients with relapsed/refractory B-ALL undergoing CAR T-cell therapy. International patients had more prior therapy lines and lower CR rate post CAR T-cells, warranting further study of the impact of prior therapy on response . Characterizing prior therapies of this heavily treated population and understanding their paths will help inform future directions in expanding this novel immunotherapy availability and addressing access disparities.

Poster # 723

THE CHICKEN OR THE EGG: THROMBOSIS & CVL-DYSFUNCTION DURING PRIMARY ALL THERAPY

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Background: Complications of central venous lines (CVLs) during pediatric cancer therapy including thromboembolism (TE), CVL-dysfunction (CVLD), and culture-positive bloodstream infection (infection), are common. While a few retrospective studies demonstrated associations between these complications, their exact relationship is unclear. These complications are associated with increased morbidity and mortality. Hence, confirming the association and understanding their relationship is imperative.

Objectives: We undertook a province-wide prospective study to evaluate the epidemiology of CVLD and its impact on the development of symptomatic TE in pediatric cancer patients. As a secondary objective,

we evaluated infections and their relationship with CVLD and TE. This abstract reports on the findings in children with acute lymphoblastic leukemia (ALL, 53.1% of cohort).

Design/Method: Children (<18 years) in Ontario, Canada with newly diagnosed ALL (n=258; 60.1% male, median age at diagnosis 4.9y [Interquartile range 2.9-9.1]) were followed for development of TE, CVLD, or infection from first CVL insertion until the end of ALL therapy. The majority of patients (70.9%) were treated according to the Children's Oncology Group protocols and 49% were Standard Risk. We compared those with and without CVLD using parametric and non-parametric tests as indicated. Multivariate logistic regression models were built for the development of any TE, CVLD, and infection during therapy, adjusting for the other two outcome variables and age, +/- body mass index z-score (BMIz, n=216).

Results: During therapy, 41 (15.9%) participants had at least one TE, 105 (40.7%) one or more CVLD, and 79 (30.6%) at least one infection. Participants with CVLD were more likely to experience TE (χ^2 p=0.029) and receive additional CVLs inserted during therapy (χ^2 p<0.001). After adjusting for age, BMIz and infection, those with CVLD were more than twice as likely to experience TE (odds ratio [OR] 2.06 (95% confidence interval [CI] 0.96-4.43); development of TE was similarly predictive of CVLD. In a model without BMIz, increasing age (OR 1.08 95%CI 1.00-1.16), and both CVLD (OR 2.17, 95%CI 1.08-4.38) and infection (OR 2.43, 95%CI 1.21-4.86) were associated with the development of TE; no interaction was present.

Conclusion: Development of CVLD or Infection is associated with increased risk of TE and the occurrence of any of these three complications is associated with an increased risk of the other two complications during primary therapy for pediatric ALL. More research is needed to understand the time-based and causal relationship between TE, CVLD, and infection which will guide preventive strategies (e.g., prophylactic anticoagulation) to reduce the burden of these complications.

Poster # 724

INSTITUTIONAL EXPERIENCE USING CPX-351 IN CHILDREN WITH RELAPSED/REFRACTORY MYELOID MALIGNANCIES

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Background: Survival rates in pediatric acute myeloid leukemia (AML) are poor, with 40% of patients dying from leukemia or treatment-related toxicity. At relapse, AML is rarely curable, with a five-year overall survival (OS) of 30% despite hematopoietic stem cell transplantation (HSCT). The presence of minimal residual disease (MRD) prior to HSCT is a negative prognostic factor. Thus, the ability of AML salvage regimens to induce MRD-negative remissions is vital. However, there is no clear consensus regarding the optimal treatment of relapsed/refractory AML. In 2019, the Children's Oncology Group (COG) released the results of a pediatric phase I/II study (AAML1421) of CPX-351, a liposomal preparation of cytarabine and daunorubicin. This trial of AML in first relapse reported an overall response rate (ORR) of 75.6% after one cycle, similar to other published regimens for relapsed AML with the potential for reduced cardiotoxicity. Based on these results, CPX-351 is often utilized as an AML salvage regimen.

Objectives: We present our institutional experience administering CPX-351 to children with relapsed myeloid malignancies to provide a "real-world" experience that more closely recapitulates the heterogeneity of relapsed disease.

Design/Method: We performed a retrospective chart review at UCSF Benioff Children's Hospitals from January 2016 through August 2023 after institutional review board approval. We identified all patients who received CPX-351 as a salvage regimen for relapsed myeloid malignancies, including those who received CPX-351 with other targeted agents.

Results: We identified a diverse group of 11 patients with relapsed AML (n=5), myeloid neoplasm post-cytotoxic therapy (MN-pCT, formerly known as treatment-related AML) (n=3), treatment-related mixed phenotype acute leukemia (t-MPAL) (n=1), B/Myeloid MPAL (n=1) , and myelodysplasia-related AML (AML-MR) (n=1). This cohort of patients was similar in age, CNS status, and prior HSCT status to the AAML1421 cohort. While we observed a 100% ORR, only 2/11 (18%) achieved MRD negativity and OS was dismal at 18%.

Conclusion: In this heterogeneous "real world" cohort of patients with relapsed/refractory pediatric myeloid malignancies, CPX-351 was associated with a very low frequency of MRD-negative remissions and similarly discouraging OS. Acknowledging the critical limitations of small sample size and disease heterogeneity, based on our findings, CPX-351 does not appear superior to other regimens, particularly those containing venetoclax (33-48% MRD negativity rate). Further study on a larger scale and novel, targeted agents are needed to improve survival of children with relapsed and refractory myeloid malignancies.

(Gamis, J. Clin. Oncology, 2014) (Jacobsohn, Blood Marrow Transplant, 2018) (Niswander, Haematologica, 2023) (Karol, Lancet Oncology, 2020)

Poster # 725

HYPERGLYCEMIA SEVERITY AND PATIENT-REPORTED OUTCOMES DURING ACUTE LYMPHOBLASTIC LEUKEMIA INDUCTION

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Background: Children with acute lymphoblastic leukemia/lymphoma (ALL/LLy) may experience significant treatment-related adverse events (AEs). Hyperglycemia commonly develops during induction and can cause significant morbidity, including requiring additional blood testing and medication management. The impact of developing hyperglycemia on patient experience using patient-reported outcomes (PROs) has not been well described in this population.

Objectives: To describe impact of clinically significant hyperglycemia (CTCAE grade 2+) on other AEs and health-related quality of life during induction.

Design/Method: A prospective study of patients with ALL/LLy aged 1-21 years began on 2/11/2022 and

is ongoing at Children's Healthcare of Atlanta (CHOA). After consent, patients aged 5-17 years or their caregivers complete the nine-question (45-point scale) Patient-Reported Outcomes Measurement Information System (PROMIS) Global survey at diagnosis and weekly through the end of induction. Demographic and clinical data (family history of diabetes, targeted AEs presence and grade) are obtained via manual chart abstraction. Descriptive statistics were calculated for all study variables.

Results: Of the 53 patients who completed induction as of December 2023, 30 (57%) were male, 35 (66%) identified as White, 13 (25%) identified as Black, and 42 (79%) were Non-Hispanic/Latino. Median age at diagnosis was 5.1 years (1.3-18.6). Hyperglycemia was present in all participants: 41 (77%) grade 1; 12 (23%) grade 2+ (grade 2: n=7, 13%; grade 3: n=5, 9%). All grade 3 hyperglycemia required insulin administration. Patients with grade 2+ hyperglycemia were older (median 9.9 years (5.2,14.1) vs. median 4.4 years (3.0,9.6), p=0.02) and more likely to have a family history of diabetes (7/12, 53% vs. 8/41, 20%, p=0.03). Among the 12 patients with grade 2+ hyperglycemia, 6 (50%) developed ≥1 targeted grade 3+ AEs: 4 (33%) had elevated alanine aminotransferase, aspartate aminotransferase and/or hyperbilirubinemia and 3 (25%) had infection including sepsis. No significant differences in the risk of other AEs were noted when compared to patients with grade 1 hyperglycemia. Seventeen eligible patients/caregivers completed both the baseline and day 22 PROMIS surveys. Patients with grade 2+ hyperglycemia had a decline in median PROMIS scores between baseline and day 22 indicating worse health-related quality of life compared to those with grade 1 who had improvement (-2 (IQR: -8,3) vs. 3 (IQR: -1,5)), though this difference was not statistically significant.

Conclusion: Development of clinically significant hyperglycemia during induction is common and associated with older age and family history of diabetes. PROs indicate poorer quality of life associated with hyperglycemia. This will be further explored when enrollment is complete.

Poster # 726

MORBIDITY OF PANCREATITIS AND DEMOGRAPHIC FACTORS DURING PEDIATRIC ALL THERAPY

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Background: Curative therapies for acute lymphoblastic leukemia (ALL) carry the potential for significant complications, including treatment-related pancreatitis. To date there are limited data describing morbidity associated with pancreatitis, and the literature describes mixed associations between ethnicity and pancreatitis occurrence. Additionally, no data exist regarding the impact of structural inequities on pancreatitis risk as proxied through the Social Deprivation Index (SDI).

Objectives: To describe morbidity of treatment-related pancreatitis and determine if a univariate association exists between race, ethnicity, and social deprivation as measured through the SDI and risk or severity of pancreatitis during treatment for pediatric ALL.

Design/Method: This retrospective cohort study included children ages 0-21 years treated for ALL at Children's Healthcare of Atlanta between 2010 and 2022. Demographic data were extracted from the electronic health record. Data on pancreatitis occurrence, duration, severity, and management (ICU admission, oxygen, nutritional support) were abstracted following a detailed guide. Insurance carrier

and primary language were abstracted for patients with pancreatitis. SDI was determined by linking each extracted address at diagnosis to available zip code tabulation area datasets and separated into quintiles. Severe pancreatitis was defined as Common Terminology Criteria for Adverse Events (CTCAE) grade 3+. Differences in demographics and clinical factors were analyzed by pancreatitis severity using R Core Team (2021).

Results: The cohort included 904 patients. Of these, 76/904 (8.4%) developed at least one episode of pancreatitis; 25/76 (33%) had recurrent pancreatitis. These 76 patients received 392 courses of chemotherapy and experienced 109 unique episodes of pancreatitis in 98/392 (25%) courses, most commonly during maintenance. Of individuals with pancreatitis, 54/76 (71%) experienced grade 3+, with patients in 18/109 (17%) episodes requiring ICU admission, 21/109 (19%) receiving oxygen, 6/109 (5.6%) requiring vasopressors, 34/109 (31%) requiring nutritional support, and 6/109 (5.6%) developing pseudocysts. There were no deaths directly attributable to pancreatitis.
There was no statistically significant difference in pancreatitis incidence by race (p=0.13) or ethnicity (p=0.5), and no statistically significant differences in severity of pancreatitis by race (p=0.2), ethnicity (p=0.2), insurance type (p=0.7), primary language (p>0.9), or the patient's SDI at time of diagnosis (p=0.6).

Conclusion: In this large, diverse, single-institution cohort, nearly 1 in 10 children with ALL developed pancreatitis. While often severe and recurrent, pancreatitis risk was independent of race and ethnicity. Further, severity was not associated with race, ethnicity, insurance type, or SDI. Future directions include multivariate analysis to evaluate associations with additional clinical and demographic factors, including leukemia sub-type, body mass index, and chemotherapeutic regimens.

Poster # 727

FLOW CYTOMETRY IS A REPRODUCIBLE ADJUNCT TO CYTOMORPHOLOGY OF CEREBROSPINAL FLUID FOR ACUTE LEUKEMIA

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Background: Cerebrospinal fluid (CSF) involvement by acute leukemia is a mainstay of staging and disease management. Morphologic (cytospin) review for leukemic blasts has long been the gold standard for assessment. Challenges, such as variation in sample processing, staining, and observer experience, have in part driven advances in adjunct CSF assessment by flow cytometry (FCM), which has higher sensitivity than morphology but is considered technically difficult. Moreover, positive FCM (with concurrent negative morphology) may inappropriately upstage CNS status.

Objectives: We present our pediatric leukemia referral center's workflow and associated experience with CSF FCM for leukemia identification.

Design/Method: Beginning in April 2021, an additional 1-mL aliquot of CSF of all patients with acute leukemia was routinely obtained and placed in preservative (Transfix) or cell-culture media (RPMI) at lumbar puncture procedures. The aliquots were held refrigerated (4C) in the FCM Laboratory. One of two hematopathologists reviewed the concurrent cytospin slide for blasts. If blasts were clearly present or absent, the morphologic interpretation was resulted and FCM not performed. If the pathologist

considered the cytomorphology challenging, within 72 hours of CSF collection, FCM was performed on the stored sample and the results used to inform the morphologic interpretation. Notably, diagnostic CSF results were either based on cytomorphology alone or cytomorphology plus adjunct FCM, but never on FCM alone.

Results: During the first year of this workflow (04/2021-04/2022), FCM was requested on 70 CSF samples (1-2/week, estimated 5% of cytospins) from 46 patients (median age 9 years, 70% male, 63%/33%/4% CNS1/CNS2/CNS3, 83% B-lymphoblastic leukemia (B-ALL, n=38). FCM was positive (blasts present) in 30 cases (43%; FCM-negative: n=40/57%). In 83% of cases (n=58/70), FCM and cytospin results were concordant (26 positive, 32 negative). Among the 12 discordant cases, 8 FCM negative cases were called atypical/suspicious (7) or positive (1) by morphology, while 4 FCM-positive cases were atypical/suspicious (3) or negative (1) by morphology.

Conclusion: These data show that prospective collection of a preserved CSF aliquot during LPs from pediatric leukemia patients routinely yields informative adjunct data by FCM in the pathologic evaluation of CNS involvement. Although FCM is performed on a minority of collected CSF samples from leukemia patients, the high rate of definitive confirmatory FCM-positivity supporting suspicious or otherwise challenging features of cytomorphology justify continuing this practice. Ongoing studies include i) expansion of data collection (4/2022-present), ii) evaluation of FCM sample stability, viability and yield; and iii) comparison of our process with that at other pediatric centers.

Poster # 728

IMPROVING COMPLIANCE WITH ORAL CHEMOTHERAPY FOR PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS

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Background: Transitioning to maintenance chemotherapy can be an overwhelming time for families as they are now responsible for daily oral chemotherapy administration. The period of maintenance lasts about 1.5 to 2.5 years for pediatric acute lymphoblastic leukemia (ALL) patients, which is a large subset of their time undergoing treatment. Studies have also shown that a lower adherence rate to oral chemotherapy (<95%) has been correlated with an increased risk of relapse. Data also suggests that improved communication between caregivers and clinicians may prevent the most harm from medication errors and improve compliance.

Objectives: Our global aim of this project is to improve compliance of oral chemotherapy administration as well as the medication reconciliation process in pediatric ALL patients. This is in keeping with working toward our smart aim to standardize the ALL maintenance oral chemotherapy process to decrease the incidence of missed oral chemotherapy doses from a baseline of 27 errors per calendar year to 0 errors within one year.

Design/Method: Initially, a survey was provided to caregivers with children in maintenance evaluating their satisfaction with current process of maintenance medication review as well as provider communication around changes in medication dosage. Our first Plan-Do-Study-Act (PDSA) cycle included implementation of a standard maintenance calendar given to all families at all maintenance visits as well

as provider and nurse education about our new standard of care. Post-survey studies were also given to caregivers to assess their satisfaction with the new process of medication review and management. The reported missed doses and medication error rate was monitored in real time by our nursing team based on chart review.

Results: Pre-survey data showed the greatest opportunity in what to do if a child missed a dose of medication. Post-survey data showed a self-reported improvement in knowledge on what to do if a child missed the dose, from a baseline average of 7.7 (scale 1-10) to 8.75. There was also an objective improvement in compliance with a 92.8% improvement in mercaptopurine compliance, an 87.5% improvement in oral methotrexate adherence, and a 100% improvement in oral steroid adherence baseline on baseline number of missed doses.

Conclusion: The institution of standard maintenance calendars has improved communication between caregivers and providers. This has decreased medication errors as well as improved medication compliance. Further work needs to be done to continue to decrease missed medication doses as well as to improve provider satisfaction with the calendar process.

Poster # 729

FEASIBILITY OF DISPENSING ACUTE LYMPHOBLASTIC LEUKEMIA MAINTENANCE THERAPY IN ADHERENCE PACKAGING

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Background: Despite having remission rates ≥95%, about 20% of children with acute lymphoblastic leukemia (ALL) relapse within five years. Non-adherence (NA) to oral chemotherapy is common due to the complexity and duration of therapy. NA may contribute to nearly 50% of relapses. Studies show that NA varies by racial and ethnic identity, socioeconomic status, and age, contributing to disparities in outcomes. Adherence packaging (AP, in which medications are organized by date and time of dosing, e.g. blister pack) can simplify the medication regimen and may increase adherence to promote more equitable health outcomes.

Objectives: Primary - assess the feasibility of dispensing oral chemotherapy in AP in a timely manner (defined as ≥90% filled within 2 hours of prescription). Secondary – measure the burden of care for caregivers using standard prescription packaging vs. AP.

Design/Method: We enrolled ten children with ALL receiving maintenance therapy who, due to age or demographic factors, could be at a higher risk of NA. Eligibility criteria included at least one of the following risk factors: uninsured or on Medicaid, over 13 years of age, identify as Black and/or Hispanic, have a vulnerable family unit (single parent, alternate caregiver), or primarily speak a language other than English. The study followed the patients over two cycles (24 weeks) of maintenance therapy. For the first cycle, we prescribed medications in standard packaging from their pharmacy of choice and for the second cycle, we prescribed medications to be dispensed in AP from the pharmacy in the children's hospital every 4 weeks. After each cycle, caregivers completed the "Child with Cancer Burden of Care Questionnaire" to assess for changes in caring for their child after the intervention.

Results: Our primary aim was found not feasible as only 63% of the prescriptions in AP were filled within 2 hours. There was not a significant change in the caregivers' assessment of difficulty of care in giving oral medications before or after the intervention. Despite that, several caregivers verbally expressed their appreciation of the AP and requested medications be dispensed in the packaging after the study concluded.

Conclusion: Although we did not meet our feasibility goal in this pilot, the AP was well-received and we are exploring using a pharmacy which can mail out medications, improving our ability to dispense medications in AP even to those patients who live a distance from the center.

Poster # 730

A SYSTEMATIC REVIEW OF INTRACRANIAL HEMORRHAGE IN ACUTE PEDIATRIC PROMYELOCYTIC LEUKEMIA

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Background: Acute Promyelocytic Leukemia (APL) is a rare subset of myeloid leukemia associated with coagulopathy and differentiation syndrome at diagnosis or treatment onset. The most notable bleeding complication is intracranial hemorrhage (ICH). With cure rates for pediatric APL now >95%, deaths and complications from ICH are the remaining barriers to improvement of survival or quality of life for children with APL.

Objectives: 1. To identify the frequency and clinical and laboratory risk factors for ICH in acute childhood APL.
2. To examine the fatality rate due to ICH in childhood APL.

Design/Method: A literature search was performed using the PubMed search engine and the keywords "acute promyelocytic leukemia," AND "children" AND "childhood," AND "intracranial hemorrhage," and "bleeding." Full-text articles in English from 1996-2023 with available patient data on ICH were included. Only pediatric patients </= 18 years with (15:17) translocation detected by RT-PCR, FISH, or cytogenetics were included. Whenever possible individual patient data was included.

Results: Thirty-two articles out of 153 were included for analysis. Fifteen articles were clinical trial reports, 15 were retrospective cohort studies, and 2 were case reports. Four reports included less than 10 patients, 15 reports had 10-50 patients, 9 reports had 50-100 patients, and 4 reports had >100 patients. There were 1,670 diagnosed pediatric APL patients with 105 episodes of ICH. Of the reports with at least ten patients, there were 99 episodes of ICH (5.99%). The outcomes of ICH were available for 90 patients, showing a fatality rate of 75.5%. Sixteen out of 31 patients were male. For 33 patients, the median age was 13.4 years (range 2- 18 years). Of 30 patients with reported lab values, 24 had a WBC above 50×10^9/L, and 8 had a platelet count below 20×10^9/L (80% and 27%, respectively). Fourteen patients had coagulation labs. Seventy-nine percent had elevated PT (range 12.1-20.1 seconds), 29% had elevated PTT (range 23.6-52.1 seconds to clot formation) and 43% had decreased fibrinogen (range 60- 272 mg/dL).

Conclusion: We found the incidence of ICH in pediatric APL to be approximately 6%, with a case fatality

rate of 75.5%. Half of the studies were from smaller institutions worldwide. There were limited laboratory values from patients with ICH, however, in the small number of patients with data available, we observed 80% had an elevated WBC, and only 27% had severe thrombocytopenia. This data collection and analysis is currently ongoing to include additional databases.

Poster # 731

INFECTIOUS COMPLICATIONS DURING TREATMENT OF CHILDREN WITH RELAPSED ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Children with relapsed acute lymphoblastic leukemia (ALL) have higher rates of infection and treatment-related mortality than at initial diagnosis. While the role of targeted immunotherapy agents is increasing in this population, combination intensive chemotherapy remains the current standard approach. However, the risk of serious infections is high and may affect ability to proceed with consolidative treatment. We performed an in-depth review of infectious complications during re-induction for relapsed ALL in patients at our centre to better understand how to monitor for, prevent, and treat infections in this population.

Objectives: To describe the incidence and pattern of infections during re-induction in children with relapsed ALL at a single tertiary centre.

Design/Method: A retrospective chart review and descriptive analysis was performed of patients with relapsed ALL from British Columbia Children's Hospital receiving combination chemotherapy for initial re-induction therapy between 2006 to 2022.

Results: Forty-three patients (58% male) were included with median age at relapse of 10.2 years. The most common diagnosis was B-cell ALL (n=36; 84%). Most patients had isolated or combined medullary relapse (n=36; 84%). 90% of patients (n=39) received four-drug re-induction with steroids, an anthracycline, vincristine, and asparaginase. Median duration of severe neutropenia was 21 days. Twenty-two patients (51%) had hyperglycemia during reinduction.

There were 42 microbiologically or clinically confirmed infectious episodes in 22 patients (51%). Fourteen episodes (33%) were diagnosed in an outpatient and resulted in readmission to hospital (median duration 15 days). Two patients (4.8%) required admission to the pediatric intensive care unit (PICU), both for inotropic support.

Frequent sites of infection were head and neck (36%), bloodstream (29%), intraabdominal (29%), and skin/soft tissue (21%). Bacterial infections predominated (62%) over viral (21%) and fungal (17%). No patients received antibiotic prophylaxis other than for *Pneumocystis jirovecii*. 30% of patients received antifungal prophylaxis while admitted to hospital. Univariate linear regression showed a trend toward increased infection in patients with hyperglycemia and prolonged neutropenia.

At median follow up of 36 months, 29 patients (67%) were alive and disease-free. All deceased patients

had active disease at the time of death. There were no deaths due to infection.

Conclusion: Our results show high rates of infection in newly relapsed ALL patients undergoing combination chemotherapy re-induction. Given high rate of readmission in our cohort, inpatient admission for these patients may be warranted, particularly during periods of severe or prolonged neutropenia. Further studies may clarify if management of hyperglycemia helps to reduce infection risk.

Poster # 733

EBV-RELATED LYMPHOPROLIFERATIVE DISEASE IN PATIENTS WITH ALL: CASE REPORT AND LITERATURE REVIEW

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Background: A 2 y.o. girl with standard risk pre-B acute lymphoblastic leukemia (ALL) during cycle 5 of maintenance therapy presented with fever, upper respiratory symptoms, and left eye puffiness. CXR revealed multiple bilateral rounded opacities confirmed by CT. Biopsy was non-diagnostic. We treated with IVIG and discontinuation of chemotherapy. She returned 2 weeks later with increased swelling and a dark nodule in her eyelid. PET/CT showed multiple lesions in the head, neck, abdomen, and lungs. Biopsy of the eyelid lesion confirmed the diagnosis of EBV lymphoproliferative disease (LPD) polymorphic histology (EBER+ by immunohistochemistry, PCR positive for EBV in blood).

After 4 doses of rituximab she demonstrated only a partial response. Treatment was escalated to start R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone). Within 3 weeks she had improved clinically and EBV PCR was undetectable. Within 3 months she had no evidence of disease. We discontinued treatment after 6 cycles. Three years later she remains disease free. The rarity of EBV LPD in this population raises the concern of an underlying immunodeficiency.

Objectives: Report a case of pediatric ALL-associated EBV-LPD and compare the case to others in the literature to refine diagnosis and treatment options. Assess patient for underlying congenital immunodeficiency.

Design/Method: We performed a systematic review of the literature using PRISMA guidelines. We also performed comprehensive immunodeficiency assessment on this patient with an immunologist 6 months after therapy.

Results: We identified 16 cases in the literature. After our review, an article came out reviewing 52 other cases as well as 14 they had identified in the literature. In the majority of these cases, EBV-LPD developed during maintenance therapy or within 6 months. Additionally, many of these cases presented with extranodal manifestations in multiple organs, particularly the lungs, GI tract, and kidneys. Many resolved with discontinuation of chemotherapy alone or with the addition of rituximab. Our patient was in the minority that required further chemotherapy to achieve a complete response. We did a complete immunodeficiency workup in our patient 6 months off therapy which yielded no significant deficiencies including in B-cell function.

Conclusion: EBV LPD is a rare complication of the immunosuppression caused by chemotherapy for ALL

and does not necessarily indicate an underlying congenital immunodeficiency. If incomplete response to holding chemotherapy and giving rituximab, R-CHOP may be an effective treatment.

Poster # 734

PRIMARY MYELOID SARCOMA IN AN INFANT WITH AN NRAS MUTATION

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Background: Myeloid sarcoma (MS) is a rare extra-medullary tumor of immature myeloid cells. It presents concurrently with or precedes acute myeloid leukemia (AML) in 4-5% of pediatric AML cases. Only 14 cases of primary MS without an associated leukemia have been reported in the pediatric population. Little is known about the genomics of MS.

Objectives: Here, we present a case of an infant with a primary MS with an NRAS Q61K gain of function mutation.

Design/Method: Our patient presented as a five-month-old female with left eye and facial swelling. An MRI demonstrated multiple masses centered in the bilateral maxillary sinuses. These masses were PET avid with no other areas of involvement. Biopsy revealed the diagnosis of MS. The patient was enrolled on a clinical sequencing trial (PEDS-MIONCOSEQ), which demonstrated an NRAS Q61K gain-of-function mutation and KMT2A rearrangement. The bone marrow had 4% atypical cells, some with the same KMT2A rearrangement.

The patient was treated per COG protocol AAML1031 with daunorubicin, etoposide, and cytarabine (ADE), and prophylactic intrathecal chemotherapy. End of Induction 1 evaluation demonstrated a decrease in tumor size with 1.4% persistent bone marrow involvement. The patient proceeded next to Induction 2 therapy receiving ADE+ gemtuzumab ozogamicin. An MRI at the end of Induction 2 showed continued improvement with a negative PET scan, and no evidence of bone marrow involvement. Given these results, her young age, and minimal bone marrow involvement at diagnosis, a bone marrow transplant (BMT) was deferred, and the patient received a total of five cycles of AML-directed chemotherapy.

Results: An end-of-therapy MRI demonstrated two new lesions in the cerebellum with tonsillar herniation without clinical symptoms. The bone marrow remained negative and emergent radiation was initiated. Soon after completion of this treatment, a white plaque on the tongue emerged that was biopsy proven to be MS. CT demonstrated a new, diffuse leptomeningeal progression. Single agent trametinib was initiated due to the NRAS mutation identified at diagnosis. The patient passed away three days following trametinib initiation.

Conclusion: Isolated MS is rare with few reported cases. It generally responds to AML-directed therapy +/- local control (radiation/surgery) and BMT. Relapsed MS is not well described in the literature and there is no standard treatment. Information about the genomics of this rare tumor may provide opportunities to develop tailored, patient-specific treatments. This would be especially useful in the relapse setting and for those unable to obtain local control but can also be considered in up-front

therapy.

Poster # 735

INFANTILE T-CELL ALL

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Background: T-cell acute lymphoblastic leukemia (T-ALL) represents approximately 15% of pediatric cases of ALL diagnosed in the United States, however, in children less than 1 years old, T-ALL is rare (less than 1% of cases). Several studies have shown significant molecular and clinical differences between childhood T-ALL and infantile T-ALL (iT-ALL). Historically, iT-ALL confers a poor prognosis despite advances in ALL protocols. Due to its rarity, more information is needed about risk stratification and optimal treatment regimens.

Objectives: To describe a case of iT-ALL with its molecular and genetic findings, with the goal of providing insight into the disease and highlighting the need for improved therapies.

Design/Method: Case Report

Results: Our patient is a previously healthy 6 month old male presenting with 4 days of cough, congestion, and rhinorrhea. He had been diagnosed with bronchiolitis several days earlier but had acute worsening of tachypnea and vomiting, a chest x-ray obtained in the emergency department revealed a large anterior mediastinal mass measuring 10.2 cm x 6.2 cm x 8.6 cm. Peripheral smear showed t-cell leukemia with 16% blast population, bone marrow biopsy showed T-ALL with 23% blast population. Chromosomal analysis revealed normal male karyotype with normal 4, 7, and 10 chromosomes, and was negative for MLL or BCR-ABL rearrangements, ETV6-RUNX1 fusions, IgH, MYC, or TCF3 abnormalities. He was started on AALL0631/Interfant-06 for induction therapy, however his end of induction minimal residual disease (MRD) was 0.8%. He was switched to AALL15P1 for consolidation. His end of consolidation MRD was negative and he continued on interim maintenance, then to delayed intensification. His course has been complicated by Strep bacteremia and he is currently awaiting recovery from severe RSV bronchiolitis before maintenance therapy is started.

Conclusion: Less than 1% of childhood ALL is iT-ALL. Several case series have been published demonstrating remarkable variability in genetic aberrations. Interestingly, MLL gene rearrangements are the most common genetic aberrations in infantile B-ALL but are less common in iT-ALL, just as NOTCH1 mutations are the most commonly noted mutations in childhood T-ALL but are also less commonly reported in iT-ALL. These findings indicate that iT-ALL exists as a unique disease process in itself. A variety of genetic abnormalities associated with childhood leukemias have been described at low frequencies, as have cases with no known leukemic aberrations. Going forward, larger case series and genomic evaluations are needed to better clarify the pathogenesis of iT-ALL and its optimal treatment strategies.

Poster # 736

AVAPRITINIB AND DECITABINE IN AN ADOLESCENT WITH CBF SM-AML

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Background: Pediatric systemic mastocytosis associated with acute myeloid leukemia (SM-AML) is rare. Core binding factor (CBF)-AML in pediatrics is associated with a favorable prognosis; yet the prognosis remains uncertain when associated with SM. Diagnostic criteria of SM-AML include bone marrow demonstrating abnormal mast cells (MC) that express CD2, CD25, and/or CD30, presence of a *KIT* mutation, and elevated serum tryptase. CBF-AML may be characterized by the *RUNX1::RUNX1T1* translocation, its presence scantly reported in MC.

Objectives: case report highlighting a unique occurrence of SM-AML in an adolescent with negative minimal residual disease (MRD) for CBF-AML but persistence of *RUNX1::RUNX1T1* in MC. Residual mastocytosis was treated with avapritinib, a KIT inhibitor, and decitabine.

Design/Method: The chart and literature were reviewed.

Results: A 14-year-old Nigerian male was diagnosed with *KIT*-mutated CBF-AML. He presented after weeks of generalized weakness, shortness of breath, and fever. Physical exam was notable for tachycardia, coarse breath sounds, and splenomegaly. Laboratory evaluation showed WBC 35.3k/uL, 35% blasts, hemoglobin 6.8g/dL, platelets 63k/uL. Bone marrow aspirate showed 27% blasts and 10% abnormal MC; flow cytometry detected 32% blasts (CD13, CD33, CD19 (partial), CD34, CD38, CD117, myeloperoxidase positive) and 1.14% aberrant MC (CD25, CD30 positive; CD2 negative). Immunostaining detected tryptase in 10% of bone marrow cells in a scattered and interstitial pattern without clusters or aggregates. A translocation screen detected t(8;21) *RUNX1*::*RUNX1T1*. Next generation sequencing (NGS) detected *KIT (Exon 17 D816H, VAF 7.1%), ASXL2, CREBBP, KRAS, NRAS,* and *PTPN1* mutations. Conventional mutation testing did not differentiate between MC and myeloblast populations.
He was treated on study COGAAML1831. At end of induction he was MRD negative for AML and MC, *KIT* negative, but FISH showed 1.5% *RUNX1:RUNX1T1*. Treatment protocol was unaltered. End of therapy bone marrow evaluation was MRD negative for AML, but 0.22% aberrant MC, *RUNX1::RUNX1T1* detection (FISH 4.5%, RT-PCR 4.19%), and resurgence of *KIT* by NGS. Cell sorting showed that *KIT* and *RUNX1::RUNX1T1* were harbored within CD117 expressing-MC but not myeloid progenitors. He was treated with avapritinib and decitabine to target *KIT* and *RUNX1::RUNX1T1*. After 3 cycles, evaluations still showed no evidence of AML, resolution of *KIT* mutation, and normal serum tryptase. The patient experienced grade 4 neutropenia, grade 2 thrombocytopenia, and grade 1 nausea and cheilitis.

Conclusion: Mutation analysis supports a shared clonal progenitor between AML and SM. This case illustrates safe and effective management through avapritinib and decitabine for residual SM in an adolescent with *KIT*-mutated CBF-SM-AML.

Poster # 737

ADEM AS PARANEOPLASTIC SYNDROME: A RARE PRESENTATION OF PEDIATRIC B-ALL

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Background: Acute disseminated encephalomyelitis (ADEM) is a monophasic, immune mediated demyelinating disorder that is usually precipitated by a viral etiology or stress. ADEM has been reported in acute leukemia after hematopoietic stem cell transplant, but there is limited evidence associating paraneoplastic ADEM and pediatric acute leukemia.

Objectives: To discuss the unique case of paraneoplastic ADEM preceding pediatric B cell acute lymphoblastic leukemia (B-ALL)

Design/Method: Case report and review of literature

Results: A 3 year old male with a history of prematurity and multiple skeletal anomalies presented with seizure like activity, and a 2 week history of malaise and generalized weakness. On further evaluation he was noted to be severely pancytopenic. He subsequently developed shock and respiratory failure with cardiac arrest, secondary to high output cardiac failure. His workup for infectious, autoimmune, inherited bone marrow failure syndromes and lymphoproliferative etiologies were negative. Bone marrow evaluation was significant for marked hypocellularity with absent multilineage hematopoiesis, consistent with severe aplastic anemia. An MRI brain/spine was notable for patchy hyperintensities throughout subcortical white matter, consistent with ADEM. CSF studies showed elevated protein with normal cells. He was treated with IV immunoglobulin (IVIG) and a brief course of filgrastim, and his blood counts normalized in a few weeks. A repeat brain/spine MRI showed complete resolution of previously noted hyperintense patches. He was closely followed up with concern for smoldering leukemia with transient marrow aplasia and ADEM like paraneoplastic syndrome. Five months later, he presented with fever and workup was notable for bicytopenia with circulating blasts. Bone marrow evaluation was consistent with B-ALL with favorable cytogenetics. He is currently being treated per Children's Oncology Group (COG) protocol AALL0932.

Conclusion: Neurological paraneoplastic syndromes preceding ALL has been rarely reported in the literature. Paraneoplastic ADEM is mostly associated with lung or ovarian cancer or lymphoma, but its association with childhood leukemias is not well described. The clinical variation in neurological paraneoplastic syndromes is thought to be related to an aberrant antibody interaction with neuronal proteins in response to cancer antigens, however one third of patients do not have detectable antibodies. Our patient developed B-ALL 5 months after initial presentation of ADEM and transient marrow hypoplasia. His initial features of ADEM gradually improved with IVIG infusion. This case highlights the importance of recognition of ADEM as a paraneoplastic syndrome, and clinicians should perform attentive surveillance for the development of hematological malignancies, particularly in the absence of an identifiable trigger.

Poster # 738

PEDIATRIC OCULAR MYELOID SARCOMA: A RARE EXTRAMEDULLARY MANIFESTATION OF ACUTE MYELOID LEUKEMIA

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Background: Ocular myeloid sarcoma (OMS) is an exceptionally rare extramedullary manifestation of acute myeloid leukemia (AML). OMS involves infiltration of immature myeloid cells into ocular tissues, leading to localized tumor formation. While myeloid sarcoma can affect various anatomical sites, its occurrence in the ocular region is particularly uncommon.

Objectives: To present a rare case of pediatric ocular myeloid sarcoma, emphasizing clinical features, diagnostic considerations, and treatment.

Design/Method: Case Report.

Results: An 11-month-old female with presented to emergency department with pallor, tachycardia, and decreased activity for 4 days. She was previously admitted 13-days prior with similar complaints and was found to be pancytopenic. Bone marrow aspirate and biopsy at that time revealed no malignant process and rheumatologic and immunological workup was negative. Past medical history was significant for partial mosaic trisomy-18, pulmonary hypertension, hypoxic ischemic encephalopathy, and fetal hydrops at delivery. On admission, physical exam revealed a pale, fatigued infant with ecchymotic discoloration and swelling of the eyelids bilaterally and repeat laboratory studies demonstrated pancytopenia. Orbital magnetic resonance imaging (MRI) revealed a hypercellular appearance, concerning for leukemia/lymphoma or neuroblastoma versus an inflammatory/immune-mediated process. A right-sided eyelid mass biopsy revealed skeletal muscle and a diffuse abnormal infiltrate composed of large cells with pleomorphic nuclei, fine blastic chromatin, and occasionally indented nuclei. By immunohistochemistry the abnormal cells were positive for CD4 and CD43. Flow cytometry identified a blast population expressing CD33, CD13, CD34, CD45, and HLADR. Flow cytometry of peripheral blood was negative for acute leukemia, but a repeat bone marrow showed 9% blasts positive for CD34 and CD33. Overall, the findings were consistent with a malignant hematopoietic neoplasm: ocular myeloid sarcoma. Subsequent cytogenetics showed 47,XX,+r(18)(p11.32q21.1)c[21]/46,XX[9]. The patient's family consented to COG-AAML1831, induction chemotherapy was initiated, and patient achieved remission with negative MRD by flow cytometry and PET scan showed resolution of FDG avidity.

Conclusion: Ocular myeloid sarcoma is an extremely rare manifestation of AML. Here, we present a challenging diagnostic case of pediatric OMS which initially presented as fluctuating pancytopenia and new-onset bilateral eyelid swelling in an 11-month-old. Despite the initial negative bone marrow studies, OMS cannot be ruled out as a local manifestation of AML. Interdisciplinary workup with ophthalmology and oncology confirmed the diagnosis via orbital MRI and biopsy. We recommend that clinicians remain suspicious for OMS in context of negative bone marrow studies and peripheral mass findings. Future studies are needed to determine proper treatment for ocular myeloid sarcoma in varying age groups.

Poster # 739

UTILIZING PET-CT TO DETECT EMD IN PATIENTS WITH B-ALL RECEIVING CART: A PROSPECTIVE PILOT STUDY

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Background: The presence of extramedullary disease (EMD) in patients with relapsed/refractory B-cell acute lymphoblastic leukemia (B-ALL) may be associated with inferior or delayed responses to chimeric antigen receptor T (CART) cells. At relapse, estimates suggest that 15-25% of patients exhibit combined medullary/EMD, however this is likely an underestimation due to a lack of routine whole body disease assessments. We hypothesize that identification and serial monitoring of EMD utilizing 18-fludeoxyglucose positron emission tomography-computerized tomography (PET-CT) imaging may aid in predicting CART outcomes and risk of early disease progression.

Objectives: To describe the incidence of non-central nervous system (CNS) EMD in patients with relapsed/refractory B-ALL proceeding to CART and to identify risk factors associated with the presence of non-CNS EMD.

Design/Method: We obtained PET-CT in patients with relapsed/refractory B-ALL as part of pre-CART evaluation on a prospective clinical trial (NCT05969002). Participants with identified EMD underwent repeat imaging at day 28, 3 months, and beyond as indicated for disease surveillance.

Results: To date, five patients with a median age of 17.8 years (IQR: 6.9-28.6) have been enrolled. None had a prior history of non-CNS EMD, however all had prior CNS disease. 4/5 patients received prior immunotherapy (3 CART, 3 blinatumomab, 1 inotuzumab) with the most proximal being CART in three patients. 3/5 patients underwent prior hematopoietic stem cell transplant.

Two patients had pre-CART EMD detected on PET-CT. Pt-01 demonstrated FDG avidity in the kidneys bilaterally correlating with hypodensities on MRI. Bone marrow (BM) disease burden was 1.63% of mononuclear cells by flow cytometry. CD19/22 directed CART were administered and a complete response of all disease sites was attained. Pt-04 demonstrated FDG avidity at multiple sites, including extensive perinephric involvement that was biopsy confirmed B-ALL. Concurrent BM had 0.17% measurable residual disease (MRD) only. This level of EMD delayed CART infusion to facilitate cytoreduction.

Conclusion: EMD is likely underdiagnosed in refractory and heavily pretreated patients undergoing evaluation for CART. In our initial experience, PET-CT has identified EMD in 2/5 patients despite no previous history. Notably however, all had a prior history of CNS disease and exposure to immunotherapy. The lack of standardized whole-body imaging for pre-CART evaluation may represent a gap in patient assessment, especially in those with yet to be defined risk factors. This may have important implications for patient management and outcomes. Further enrollment will serve to elucidate the incidence of EMD in these patients and help identify risk factors that should prompt PET-CT evaluation for EMD.

Poster # 740

INOTUZUMAB AS A BRIDGE TO CAR-T CELL THERAPY IN A PATIENT WITH DOWN SYNDROME AND REFRACTORY ALL

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Background: Patients with Down syndrome (DS) and Acute Lymphoblastic Leukemia (ALL) have poorer outcomes and worse toxicities with chemotherapy. Treatment with Anti CD-19 Chimeric Antigen receptor T-cells (CAR-T) has shown higher remission rates in refractory ALL in patients with DS with more manageable toxicity profiles as compared to other salvage treatments. Inotuzumab ozogamicin (Anti CD22) has been successfully used as a bridge to curative treatment, especially for CAR-T therapy in children and young adults with refractory ALL but there is limited data in patients with DS.

Objectives: To report the successful use of Inotuzomab Ozogamicin as a bridge to curative CAR-T in a patient with DS and refractory Pre-B ALL.

Design/Method: Case Report with Literature review.

Results: Our patient with DS was diagnosed with Pre-B ALL, CRLF2+ positive, CNS negative at the age of 19 years when he presented with hyperleukocytosis (WBC >400 X 10^3 /uL) and received induction chemotherapy as per AALL1131. His end of induction bone marrow showed 90 % blasts categorizing him as an induction failure. He received additional chemotherapy with Vincristine and Methotrexate, the follow up bone marrow showed 60 % blasts. He underwent leukapheresis for CAR-T cell production. He then received 2 doses of Inotuzumab which he tolerated well, a bone marrow was repeated which showed 0.03 % Minimal residual disease (MRD). He received lymphodepleting chemotherapy with Fludarabine and Cyclophosphamide followed by CAR-T cell infusion. He developed mild Grade I/II Cytokine release syndrome within a week of the infusion and received a total of 2 doses of Tocilizumab and had no recurrence of symptoms. His follow up bone marrow examinations have been negative for ALL by morphology, flow and NGS and he has been in sustained remission for more than one year.

Conclusion: CAR-T therapy has recently emerged as a tolerable and curative treatment for patients with DS and refractory ALL, however, it is critical to understand the importance of using effective bridging therapies to ensure a successful outcome. There is some data about the use of Inotuzumab in pediatric and adolescent patients with relapsed/refractory ALL but there is limited data about its utility in patients with DS. Our case serves as an example of excellent efficacy with limited toxicities following the use of Inotuzumab as a bridging therapy to CAR-T and should be considered in patients with DS and refractory ALL.

Poster # 741

CONCORDANT INFANT AML IN TWINS WITH A CBFA2T3-GLIS3 FUSION TREATED PER DIFFERENT ARMS OF AAML1831

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Background: Acute myeloid leukemia (AML) accounts for 20% of childhood leukemias and a fourth of these cases occur in patients less than 2-years-old. Infant AML in monozygotic twins is rare and occurs

due to an in-utero acquired leukemic clone that arises in one twin and metastasizes to the other. The CBFA2T3-GLIS2 fusion is a translocation found in about 5% of all patients with AML, is primarily seen in children less than 5-years-old and is associated with a poor outcome.

Objectives: Describe a case of monozygotic twins with infant AML with a CBFA2T3-GLIS3 mutation, treated on different arms of AAML1831.

Design/Method: Case report

Results: Twin A: A 7-month-old female diagnosed with AML with a CBFA2T3-GLIS3 fusion. She was enrolled on Children's Oncology Group (COG) AAML1831, randomized to Arm A, and had persistent disease following Induction II (MRD 23%). Treatment for refractory disease with fludarabine, cytarabine and G-CSF was initiated; however, her disease continued to progress (MRD 52%). Given her sister's response to the experimental arm of AAML1831, she was given AAML1831, Arm B, Induction 1. Despite treatment, she continued to have progressive AML and succumbed to her disease.

Twin B: The monozygotic twin of the previous patient was evaluated shortly after her sister's diagnosis and was found to also have AML with CBFA2T3-GLIS3 fusion. The patient was enrolled on COG AAML1831, randomized to Arm B, and was in remission following Induction II (MRD negative). She then received an allogenic unrelated cord blood transplant following a myeloablative conditioning regimen using busulfan and fludarabine. However, she had medullary relapse at day +42. Despite palliative chemotherapy with azacitidine, she had AML progression and succumbed to her disease.

Conclusion: This is a case of concordant infant AML in monozygotic twins with a CBFA2T3-GLIS2 fusion treated per different treatment arms on AAML1831. Due to the poor prognosis of patients with this this fusion, currently they require high-risk treatment and use of stem-cell transplant. Despite these interventions in our patients, they did not survive. Continued research needs to be done on targeted, more effective agents for AML patients with CBFA2T3-GLIS2 fusion.

Poster # 742

A 2 YEAR OLD WITH REFRACTORY AML CBFA2T3-GLIS2 ONCOGENIC FUSION: TRIAL WITH A NOVEL TARGET THERAPY

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Background: Acute myeloid leukemia (AML) with CBFA2T3-GLIS2 oncogenic fusion (RAM phenotype) is commonly seen in young children. It is characterized by an aggressive myeloid phenotype due to the high frequency of refractory disease and cumulative incidence of relapse. In an effort to discover alternative options, target therapies have developed. FOLR1 is uniquely expressed in CBF/GLIS AML and is absent in other subtypes and in normal hematopoietic cells. Targeting FOLR1 with STRO-002 and ELU001 is a promising approach to improve outcomes in high-risk leukemia.

Objectives: We report a case of a child diagnosed with AML (CBFA2T3-GLIS2, Rham phenotype) with FOLR1 expression refractory to conventional chemotherapy and targeted therapy with STRO-002. She is currently on salvage therapy with ELU001.

Design/Method: Case Report/Literature Review

Results: A two-year -old female diagnosed with very high-risk AML harboring CBFA2T3-GLIS2 RAM phenotype. Initial diagnosis showed bone marrow aspirate with 22% involvement and core biopsy with 70% involvement, flow cytometry showed RAM phenotype and FOLR1 expression. Started on AAML1831 with suboptimal response (EOI MRD 2.5%), transitioned to induction II AAML1031; EOI II 0.9%. Given the disease progression was started on STRO-002. Weekly STRO-002 inhibitory activity assays conducted for clearance of competing free antibodies, ensuring optimal conditions for subsequent dosages. Bone marrow biopsy and aspirate after 5 cycles of STRO 002 showed MRD 0.5 with absence of FOLR1 expression. Further discussion revealed elevated STRO antibody levels ~90% prompting consideration of DV FLAG/STRO chemotherapy, in addition to Plerixafor for mobilization of leukemic cells. Due to persistent refractory disease, salvage therapy ensued with Venetoclax, Azacitidine, and Gemtuzumab Ozogamicin. Despite 7 cycles of STRO002 with Plerixafor on cycles 4-6; bone marrow evaluation showed refractory disease with FOLR1 expression on a minor subset. Given refractory high risk leukemia patient was started on ELU001 compassionate use with the end goal to proceed to bone marrow transplant.

Conclusion: In the context of high-risk AML this case explores the utilization of FOLR1-directed antibody therapy in a patient with a CBFA2T3-GLIS2 mutation. Further advacement in target therapies is needed to potentially improve outcomes for pediatric patients with high risk AML.

Poster # 743

COMPLICATIONS FROM VARICELLA IMMUNIZATION IN A PATIENT NEWLY DIAGNOSED WITH T-CELL ALL

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Background: Live vaccines, including varicella, are withheld in pediatric oncology patients due to risk of infection in an immunocompromised host. Vaccinations in this immunocompromised population can lead to systemic infections or reactivation, commonly due to the varicella (VZV) vaccine. Ophthalmic VZV involvement can cause a vast sequela of complications including dermatitis, conjunctivitis, keratitis, uveitis, and chorioretinitis. Very rarely, varicella has been reported to cause damage to the ciliary ganglion, with subsequent loss of parasympathetic innervation to the iris, causing tonic pupil dilation.

Objectives: This case demonstrates a rare complication of the varicella vaccine and its sequelae in a toddler recently diagnosed T-cell ALL.

Design/Method: Case Report

Results: A previously healthy 13-month-old female presented with hyperleukocytosis (white blood cells 803/uL), anemia (hemoglobin 3.6 g/dL), thrombocytopenia (platelets 25 $10^3/\mu L$), thirteen days after receiving her measles, mumps, rubella and varicella (MMRV) vaccination. She was diagnosed with T-cell lymphoblastic leukemia (flow cytology: 96% cells expressed CD2, CD4, CD5, CD7, CD8, CD38, CD45 dim, CD57, and CD71), and was treated with conventional chemotherapy. Within two weeks of treatment initiation, a diffuse maculopapular rash developed. By day 28 of induction, most of the lesions appeared

well-healing, however a new vesicular rash following the right cranial nerve V1 distribution appeared. Serum PCR confirmed VZV. Ten days later, she was noted to have new onset anisocoria, with the right pupil 2 mm larger than the left pupil and no constriction to light. She had mild ptosis, secondary to her preexisting dermatitis. Her extraocular motility was full, and MRI/MRA revealed no significant abnormalities, ruling out a diagnosis of third cranial nerve palsy. Dilute pilocarpine (0.1%) testing constricted the right pupil from 5.5mm to 3.5mm with no change to the left pupil at 3.5mm, confirming the diagnosis of tonic pupil. She also developed mild hypoaccommodation, which resolved after several weeks. She has completed six months of oncological treatment without obvious improvement to pupillary motility.

Conclusion: Although live-attenuated vaccination has been successful at protecting against VZV in immunocompetent patients, oncology patients should not receive vaccines during immunocompromised states, such as at diagnosis or during chemotherapy. This is a unique case of a one-year-old child who was administered vaccines just prior to her oncologic diagnosis, resulting in a diffuse rash due to VZV as well as ophthalmic involvement. Though treated promptly, the infection caused a chronic tonic pupil and secondary photophobia, a rare ophthalmic complication of the virus, which can be irreversible.

Poster # 744

THERAPY RELATED, KMT2A REARRANGED LEUKEMIA TREATED USING PALBOCICLIB AND BLINATUMOMAB

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Background: Germ cell tumor treatment regimens that include etoposide place patients at risk for therapy-related acute lymphoblastic leukemia (t-ALL). t-ALL has a poorer prognosis than de novo acute lymphoblastic leukemia (ALL) and higher frequency of high-risk features, including *KMT2A* rearrangement (*KMT2A*r). Germ cell tumors expressing cyclin-dependent kinase 4 (CDK4) may be targeted with palbociclib. Palbociclib has since been used for anti-leukemic activity against Philadelphia chromosome positive ALL and found safe in relapsed/refractory ALL. Cyclin D has also been shown to play an essential role in ALL initiation and progression, and CDK6 has been described as a direct target of *KMT2A*r. Blinatumomab may be used as consolidation therapy to target CD19 positive leukemia cells as a bridge to CD19 CAR T-cell therapy for patients with t-ALL.

Objectives: To demonstrate safety and provide an example of an effective induction and consolidative regimen combining chemotherapy, palbociclib, and blinatumomab in a patient with t-ALL.

Design/Method: Case report, a retrospective chart analysis was conducted.

Results: We describe the case of a 20-year-old female with therapy-related B-cell acute lymphoblastic leukemia (B-ALL) with *KMT2A*r (t(4;11)(q21;q23)) who had a concurrent stable mature germ cell tumor with immature features that failed prior treatment options. She had previously received bleomycin, intravenous etoposide, and cisplatin as well as oral etoposide for tumor control before presenting with hyperleukocytosis (WBC 244 k/microL) with concern for leukemia. She received a standard four drug

induction (prednisone, vincristine, daunorubicin, asparaginase) combined with palbociclib, a CDK4/6 inhibitor, to target both leukemia and her germ cell tumor. This combination induced remission with no minimal residual disease (MRD) by flow cytometry and resolution of *KMT2A*r by fluorescence-in-situ hybridization (FISH), and the germ cell tumor remained stable. However, imaging 3 months post-induction revealed teratoma-related pleural metastases progressed. Due to social concerns and no available donor, the patient was offered CD19 CAR-T cell therapy. She received Blinatumomab as a bridge to CAR T-cell therapy. Following CD19 CAR-T cell infusion, the patient remains in molecular remission.

Conclusion: Adjunct use of palbociclib should be considered for the treatment of *KMT2A*r leukemias. This case highlights the safety of palbociclib used in combination with cytotoxic induction therapy followed by blinatumomab immunotherapy in a young adult with *KMT2A*r therapy-related B-ALL who attained MRD negative disease with cytogenetic and molecular remission. This treatment strategy provides an option for *KMT2A*r ALL in the relapsed, refractory leukemia setting.

Poster # 745

DARATUMUMAB AS A TOXICITY-SPARING AGENT DURING FRONTLINE TREATMENT OF T-ALL: A CASE REPORT

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Background: T-cell acute lymphoblastic leukemia (T-ALL) accounts for 10-15% of newly diagnosed pediatric ALL cases annually. Successful treatment of T-ALL relies on the use of traditional chemotherapy agents which are associated with significant morbidity and mortality. Patients with relapsed T-ALL have a poor prognosis due to the relative lack of novel therapies. Immunotherapy, such as bispecific T-cell engagers, chimeric antigen receptor T-cells, and antibody-conjugated chemotherapy, has revolutionized treatment for B-ALL. These therapies are often well tolerated with few off-target toxicities, making them an ideal alternative for patients with severe treatment-related complications on traditional backbones. However, there are no approved immunotherapy options for T-ALL. Thus, patients with severe complications of T-ALL therapy have limited treatment options during illness recovery periods to maintain remission. Daratumumab, a monoclonal antibody against CD38, an antigen expressed on 90-100% of T-ALL, has recently been evaluated for use in relapsed T-ALL. However, its use as a toxicity-sparing agent during frontline T-ALL therapy has not been reported.

We present the case of an adolescent with T-ALL who developed severe treatment-related pancreatitis, in whom daratumumab was used as toxicity-sparing therapy during upfront treatment.

Objectives: Describe the use of daratumumab in a patient with T-ALL who was unable to tolerate cytotoxic chemotherapy as a safe and effective bridge until treatment-related complications resolved.

Design/Method: Case Report

Results: A 15-year-old male with T-ALL was treated by an institutional practice standard modeled largely off COG AALL0434 Arm B. During Delayed Intensification he developed severe asparaginase-induced pancreatitis with a pancreatic leak and pseudocyst formation. He underwent serial abdominal drain

placements with management further complicated by multiple infectious and nutritional complications that persisted while receiving modified maintenance-style chemotherapy. Due to intolerance of traditional chemotherapy, he was then treated with single-agent daratumumab as weekly infusions for two cycles, followed by every-other-week infusions for a third cycle. He tolerated daratumumab without any adverse effects. He received most infusions as an outpatient. He eventually had all abdominal drains removed without further infectious complications and resumed traditional maintenance therapy with continued remission.

Conclusion: Targeted immunotherapies have recently thrust the field of oncology forward by both improving survival and decreasing toxicity in patients with acute leukemias and other malignancies. While the specific role of daratumumab for T-ALL is still being investigated, this case demonstrates that it can be feasibly and safely used during frontline therapy as a non-cytotoxic chemotherapy option in patients experiencing severe treatment-related complications.

Poster # 746

ACUTE LYMPHOBLASTIC LEUKEMIA IN A PATIENT WITH GLYCOGEN STORAGE DISEASE TYPE 1

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Background: Glycogen storage disease type Ia (GSDIa) is an inherited disorder caused by a deficiency of glucose-6-phosphatase which cleaves glycogen to glucose leading to hypoglycemia, lactic acidosis and hepatomegaly between birth and 6 months of age. Initial laboratory findings show hypoglycemia, lactic acidosis, hyperuricemia, hypercholesterolemia and hypertriglyceridemia. Patients may develop bleeding disorders from impaired platelet function, anemia from decreased erythropoietin production due to renal failure and acute pancreatitis from severe hyperlipidemia and hypertriglyceridemia.

Objectives: We report a case of a 19 month old female with glycogen storage disease type Ia diagnosed with Pre B Acute Lymphoplastic Leukemia (Pre B ALL).

Design/Method: Case report

Results: A 19 month old female with history of GSDIa presented with a 2 month history of worsening abdominal distention, hepatomegaly, hypoglycemia, development of splenomegaly and refusal to walk. On admission she was found to have anion gap metabolic acidosis with elevated lactic acid, bicytopenia with hemoglobin (5.2g/dl), platelets (4 10K/uL) and leukocytosis (21.1 10K/uL), elevated LDH 1174IU/L and uric acid 11.5mg/dl. She was treated as GSD decompensation with close glucose monitoring, fluids and empiric antibiotic therapy. Repeat CBC 2 days after showed persistent bicytopenia with normal WBC and 17% of immature cells in the blood. She was diagnosed with Pre-B ALL. She started standard risk therapy following AALL1731. Multidisciplinary team management included genetics, endocrinology and hem/onc. In preparation for sedated procedures requiring fasting, she was started on total parenteral nutrition titrating glucose infusion rate to maintain stable glucose levels. Close glucose and electrolyte monitoring was required while she was treated with steroids. On admission patient had presented with elevated lipase (651 IU/L) and hypertriglyceridemia (337mg/dl), therefore decision was made to replace pegaspargase with asparaginase erwinia chrysanthemi (Rylaze) for better control of side effects given shorter half life. Additionally, elevated uric acid was treated less aggressively with only allopurinol

knowing the patient's baseline levels were in the upper limit of normal. Patient is now on consolidation, MRD negative.

Conclusion: The overlap of symptoms including lactic acidosis, hyperuricemia, cytopenias, hepatomegaly made the diagnosis of ALL challenging. There has been one case of GSD type 1b with AML that received G-CSF however no cases of GSDIa with ALL have been reported. In this case we highlight the value of a multidisciplinary team for individualized care taking into consideration potential side effects of standard therapy.

Poster # 747

A DIAGNOSTIC CHALLENGE: ML-DS IN A PATIENT WITH TRISOMY 21 MOSAICISM OLDER THAN 4 YEARS OF AGE

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Background: Children with Down syndrome (DS) are at increased risk of developing myeloid leukemia (ML) driven by *GATA1*, a transcription factor specific to megakaryocyte development. The pre-leukemic clone typically first presents in the neonatal period as Transient Abnormal Myelopoiesis (TAM), which usually spontaneously resolves. However, in 20% of patients, the *GATA1*-mutated clone persists and transforms into ML-DS before the age of 4. Because of increased sensitivity of ML-DS blasts to cytarabine and other agents and increased susceptibility of patients with DS to toxicity, patients with ML-DS are treated with reduced intensity treatment regimens. However, the treatment of patients ≥4 years-old on ML-DS protocols remains sparsely reported.

Objectives: Describe the presentation of an older patient with mosaic trisomy 21 in his bone marrow with ML-DS.

Design/Method: Case report

Results: A 4-year, 10-month-old boy presented with epistaxis, thrombocytopenia, and peripheral blasts. He had a history of neonatal anemia and circulating blasts which spontaneously resolved but no features of DS. FISH performed on peripheral blood during infancy showed 21% of cells with trisomy 21 (T21), but PHA-stimulated karyotype and subsequent FISH on skin biopsy were normal. He was diagnosed with TAM in the context of trisomy 21 mosaicism and followed until his 4th birthday. Flow cytometry from the current presentation was consistent with myeloid leukemia including expression of the megakaryocytic markers CD42b and CD61. With *GATA1* testing pending, the decision was made to initiate treatment as per the ML-DS protocol AAML0431. Subsequent cytogenetics and sequencing of his bone marrow revealed trisomy 21 in 30/30 examined cells, a pathogenic deletion in exon 3 of *GATA1* as well as pathogenic mutations in *CTCF*, *MPL,* and *WT1*—all known cooperating mutations in ML-DS. Minimal residual disease testing using flow cytometry after Induction I and at end of therapy showed no evidence of disease.

Conclusion: Despite a detailed understanding of the molecular drivers of ML-DS, treatment of patients is often initiated without confirmatory *GATA1* testing based on a diagnosis of constitutional trisomy 21

and age less than 4 years. In this case, the patient's older age and normal FISH after resolution of his TAM posed a diagnostic challenge. However, the history of TAM and megakaryocyte blast immunophenotype suggested a disease mechanism consistent with ML-DS and he was successfully treated as such. This case report adds to the sparse literature regarding mosaic ML-DS and documents an exceedingly rare case presenting past the age of 4.

Poster # 748

SUCCESSFUL TREATMENT OF PRECURSOR B-CELL ALL WITH IGH/MYC REARRANGEMENT

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Background: Though there are favorable survival rates for patients with both precursor B-cell acute lymphoblastic leukemia and mature-B cell or Burkitt leukemia/lymphoma, these are two distinct entities with different treatment approaches. A subset of patients have now been described who present with precursor B-ALL with MYC translocations. These patients are rarely reported and not eligible for ALL or B-NHL trials. There is a paucity of data available to guide treatment. The largest published series 14 patients with pre-B ALL and IGH-MYC translocations. Analysis of only 6 patients match the translocation and surface marker expression seen on cytogenetic analysis of the patient described here.

Objectives: We add to the available literature for patients with precursor B ALL immunophenotype and IGH-MYC rearrangements by describing the successful treatment of a 2-year-old patient with precursor B-cell ALL and negative surface immunoglobulins found to have a t(8;14) IGH/MYC translocation.

Design/Method: A 2-year-old male initially presented with one month of fevers, bruising, and pancytopenia. Bone marrow aspirate and biopsy were performed, and flow cytometry showed a large population of B lymphoblasts expressing CD19, CD10, CD20, CD22, and TdT. Blasts were negative for surface immunoglobulins. The patient was enrolled on the open COG study AALL1731 and treated with a standard three-drug induction. Day 8 peripheral blood MRD was performed and demonstrated an immature B-cell population of 0.24% of viable cells. The patient completed 15 days of induction therapy prior to FISH demonstrating a translocation between the long arms of chromosomes 8 and 14, resulting in an IGH/MYC gene rearrangement, rendering him ineligible to continue on study AALL1731.

Results: Therapy was transitioned to treatment as per ANHL1131 with two cycles of R-COPADM, two cycles of R-CYVE, and two cycles of maintenance. He generally tolerated chemotherapy well with complications of mucositis and need for nasogastric tube feeds. He also developed adrenal insufficiency that resolved after treatment. He required intermittent blood and platelet transfusion support. He completed therapy 5 months after diagnosis. End-of-treatment bone marrow aspirate and biopsy performed with high sensitivity MRD flow cytometry was negative for abnormal B-lymphoblasts. He was recently seen at 9-months off therapy and is clinically well with a normal complete blood count and no signs of relapse.

Conclusion: We describe a case of successful treatment of a patient with precursor B cell ALL and IGH/MYC rearrangement with R-COPADM and R-CYVE who is currently 9 months off therapy without evidence of relapsed disease.

Poster # 749

IS IT TIME TO CONSIDER PHILADELPHIA-LIKE (PH-LIKE) T CELL ACUTE LYMPHOBLASTIC LEUKEMIA?

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Background: Risk adapted therapy based on cytogenetic and molecular signatures of leukemic cells has led to improved outcomes in childhood leukemia. This is especially true in B lineage leukemias, where tyrosine kinase inhibitors and Janus kinase inhibitors are used. However, their use in T-cell disease is not routine.

Objectives: To describe the clinical and genomic findings of a child with high risk, refractory T-ALL

Design/Method: Case report

Results: A 3 yo male with T-ALL presented with a WBC of 350K and was CNS negative. Blast cells expressed CD3, CD2, CD7, CD5, CD56, CD1a and TDT. CD4, CD8, and CD34 were negative. Cytogenetics showed 45,XY,der(7)t(7;15)(q36;q15) ,-15[6]/46,XY[14]. Molecular diagnostics revealed 3 clinically significant variants: ETV6/JAK2 (a fusion consistent with Ph-like ALL), CDKN2A chromosome 9 copy number loss, and PTEN chromosome 10 c.1027—2A>G splice variant. He completed induction per AALL1231. End of induction MRD was 0.13%. He continued therapy per AALL0434 with nelarabine. End of consolidation MRD was 0.92% with persistent presence of ETV6/JAK2 translocation. Additional chemotherapy included induction per AALL07P1 and high dose methotrexate per interim maintenance 1 of AALL1732. MRD decreased to 0.09%. He received a fully matched sibling donor transplant with a myeloablative TBI/CY based preparative regimen. After initial engraftment, day +30 bone marrow showed relapsed disease. While awaiting enrollment in a CAR-T therapy trial he was started on re-induction with Vincristine, prednisone, doxorubicin and daratumumab (anti-CD38 monoclonal antibody). Efforts to get approval for use of ponatinib or dasatinib as targeted agents were denied. The child died 1 year post diagnosis.

Conclusion: Relapsed T-ALL has poor survival outcomes. Unlike B- lineage ALL, up-front therapy does not stratify treatment based on cytogenetic/molecular findings. Many T -ALL patients have various JAK mutations; most not associated with Ph-like ALL. There is at least one pediatric case of dasatinib responsive T-ALL with ABL1 amplification (Crombet, Pediatr Blood Cancer 2012). A number of targeted therapies, are currently being studied in relapsed T-cell ALL as well (Lato et al., 2021). In cases of T-cell disease where standard salvage therapies fall short, the stratification based on molecular diagnostics could become crucial. The clinical trajectory of this particular case raises the question of whether treatment for T-ALL should be informed by molecular diagnostic findings rather than relying solely on cell surface markers.

Poster # 750

A CASE REPORT ON NOVEL COMBINATION THERAPY IN A PEDIATRIC PATIENT WITH CLL

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Background: Chronic Lymphocytic Leukemia (CLL) is a common disorder in the adult population with an average age of incidence at 70 years. CLL commonly presents as leukocytosis, localized lymphadenopathy, and skin rash. First line therapy for symptomatic patients was previously an intensive chemotherapeutic regimen, but new targeted therapy provides remission with fewer side effects.

Objectives: To describe a case of pediatric CLL treated with combination targeted therapy.

Design/Method: A 16 y.o. previously healthy female presented to her primary care office for progressive fatigue and bilateral cervical lymphadenopathy for 2 months. She was noted to have a hemoglobin of 6.7 g/dL and extensive bilateral cervical lymphadenopathy. On admission, white blood cell count was 11.6 K/uL, hemoglobin 6.7 g/dL, and platelets 114 K/uL. Bone marrow aspiration and biopsy showed an abnormal B cell population positive for CD5, CD19 bright, and CD23 with kappa light chain restriction, negative for TdT. Chromosomal analysis was positive for 46, XX del 11 (q21,q22). Findings were consistent with CLL with bone marrow involvement. CT scan showed extensive multifocal lymphadenopathy in the neck, chest, abdomen, and pelvis. The largest conglomerate lymphadenopathy in the abdomen measured 12.9 cm x 5.9 cm x 17.4 cm. She was referred to MD Anderson due to the abnormally young age at presentation. Exam revealed diffuse macular skin rash characteristic of CLL skin infiltration, cervical lymphadenopathy and hepatosplenomegaly.

Results: Given her large disease burden, treatment was initiated with ibrutinib 420 mg daily monotherapy for debulking. Dose was lowered to 280mg daily due to joint pain and monotherapy was continued for 2 additional months. Venetoclax therapy with ramp up dosing was then initiated at 3 months in combination with ibrutinib. CT scan after 4 months of therapy showed impressive response with largest residual node in abdomen measuring 2.6 x 1.4 cm. She remains on combination therapy with venetoclax 400mg daily and ibrutinib 280mg daily with sustained response.

Conclusion: This case describes the youngest patient with CLL reported to date treated with targeted therapy. Traditional first line therapy for CLL is fludarabine-cyclophosphamide-rituximab combination, but here we report a pediatric patient treated safely and effectively with a less intensive regimen of ibrutinib-venetoclax. High index of suspicion is needed for pediatric patients presenting with CLL, and novel therapies to decrease toxicity are being investigated in adults but can be considered for pediatric patients as well.

Poster # 751

HYPERURICEMIA-INDUCED PROLONGED QTC IN A PEDIATRIC PATIENT WITH SPONTANEOUS TUMOR LYSIS SYNDROME

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Background: Acute lymphoblastic leukemia (ALL) is a common childhood malignancy. Tumor lysis syndrome is an oncologic complication that can precipitate electrolyte derangements, cardiac

arrhythmias, seizures and renal failure in children with newly diagnosed ALL. There are numerous potential reasons for a child who is experiencing tumor lysis syndrome to have cardiac conduction changes. In the setting of tumor lysis syndrome, cardiac conduction abnormalities are commonly associated with abnormal potassium or calcium levels. Anthracyclines are a cornerstone of chemotherapy and may also cause cardiac conduction abnormalities. Hyperuricemia has occasionally been associated with cardiac conduction abnormalities in adults. There are no known reports of cardiac conduction problems caused by hyperuricemia in children with ALL.

Objectives: To describe severe prolongation of the QTc interval associated with extreme hyperuricemia in a pediatric patient with ALL and spontaneous tumor lysis syndrome.

Design/Method: This is a case report of a 15 yr-old male patient with a diagnosis of T-cell ALL. Our patient's chart was reviewed. Electrocardiographic and biochemical profile data, including serum electrolytes and uric acid levels, were collected from the time of presentation to our hospital through the Induction phase of chemotherapy. Data was then organized into a run chart to determine timing of various outcomes and interventions.

Results: This teenage male presented with abdominal pain, easy bruising, and intermittent hematuria. Labs demonstrated severe acute kidney injury, thrombocytopenia, anemia, peripheral blasts, hyperuricemia, and elevated LDH. Diagnosis of T-cell ALL was confirmed. His serum uric acid level upon presentation was > 33.1 mg/dL and required renal clearance with rasburicase and dialysis. Despite normal serum potassium, magnesium, and calcium levels and lack of QTc prolonging medications, our patient was noted to have a QTc of 558 msec on his initial electrocardiogram. Anthracycline doses during Induction were decreased by 50% in an attempt to mitigate cardiac conduction risk. The QTc normalized to 411 msec over a period of 11 days, and the remaining anthracyclines were given at full dose.

Conclusion: Profound hyperuricemia resulted in severe prolongation of the QTc interval in this child with T-cell ALL. Our data provide evidence that uric acid is an important factor to consider when monitoring for cardiac dysfunction in the setting of tumor lysis syndrome and chemotherapy. Given that tumor lysis syndrome is a common complication of childhood leukemia, evaluation of cardiac conduction with ECGs in the setting of isolated severe hyperuricemia is imperative.

Poster # 752

HYPEREOSINOPHILIA AS A PRESENTING SYMPTOM IN PRE B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: B-ALL with a IGH-IL3 fusion is exceedingly rare and difficult to diagnose. We present a case of a 10 year old male who presented with hypereosinophilia and cardiogenic shock.

Objectives: To present a rare subtype in Pre B-ALL

Design/Method: case report

Results: A 10 year old male presented with a two week history of fever, abdominal pain, respiratory distress, and difficulty ambulating. He was found to be in cardiogenic shock and was admitted to the ICU for inotropic support. Initial white blood count found to be 131,000 with a predominance of 81% eosinophils (normal range is 0-5%). Initial echocardiogram showed an ejection fraction of 24% and enhancement of LV endocardium which was concerning for an infiltrative process. No immature lymphocytes were seen on hsi peripheral blood smear. Flow cytometry showed 0.5% B lymphoblasts in peripheral blood and 4.8 % B-lymphoblasts via bone marrow aspirate. Cytogenetics revealed a IGH-IL3 translocation. Patient was then treated per AALL1732. Patient unfortunately expired within 3 months after starting treatment secondary to cardiac failure.

Conclusion: B-cell leukemia presenting with hypereosinophilia is not commonly seen in children. The t(5;14)(q31;q32); IGH-IL3 fusion is an underrecognized rare subset in B-ALL that results in IL-3 overproduction which induces maturation and release of eosinophils. Blast infiltration of the bone marrow varies in patients resulting in low or undetectable peripheral blasts and normal to slightly decreased hemoglobin and platelet count which can further delay diagnosis. Eosinophilic infiltration causing cardiac dysfunction and even subsequent heart failure can be seen in these patients. Treatment response to conventional chemotherapy has been poor and morbidity can be increased in patients with organ damage.

Poster # 753

B-ALL TREATMENT FOR A CHILD WITH CORNELIA DE LANGE SYNDROME IS COMPLICATED BY VOCAL FOLD PARESIS

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Background: Cornelia de Lange Syndrome (CdLS) is an autosomal dominant condition characterized by developmental delay and characteristic dysmorphic features. Several case reports have raised questions regarding a link between CdLS and leukemia, though a genetic predisposition is not established. Vincristine, widely used in chemotherapy regimens to treat acute lymphoblastic leukemia (ALL), is associated with peripheral neuropathies and rarely vocal cord paralysis. Vocal cord paralysis can have a highly variable course and may be an indication for dose reduction or elimination of vincristine.

Objectives: To report a case of B-ALL in a child with CdLS complicated by vincristine induced vocal fold paresis causing airway compromise and respiratory distress

Design/Method: Case report and review of literature

Results: A 5-year-old with short stature and normal development presented with several weeks of easy bruising, petechiae, and musculoskeletal pain. She was diagnosed with standard risk B-ALL with an ETV6:RUNX1 fusion. Treatment was initiated per AALL1731. Features of synophrys, low set ears, low posterior hair line, thin upper lip, short stature, and velopharyngeal insufficiency, in addition to a sibling with recent CdLS diagnosis, prompted genetic evaluation. Testing confirmed CdLS (RAD21 c.193C>T p.Arg65Ter heterozygous). Day 29 bone marrow aspirate showed no detectable disease. The following day she presented with stridor, cough, tachycardia, and poor perfusion. She was treated with racemic epinephrine, dexamethasone, and high flow nasal cannula with heliox. Flexible laryngoscopy

demonstrated immobile vocal cords fixed in a paramedian position consistent with vincristine induced vocal fold paralysis. Vincristine was held during consolidation with gradual improvement of symptoms. Vincristine was reintroduced at 50% dose reduction during first interim maintenance. She again developed stridor with vocal cord paresis confirmed on laryngoscopy after a complicated sedation. Despite recurrent vocal cord paresis, vincristine was reintroduced during delayed intensification, initially dose reduced by 50% and then increased to full dose in interim maintenance, which she tolerated well. She remains on full dose vincristine during maintenance with close monitoring by oncology and otolaryngology.

Conclusion: Vincristine induced vocal cord paralysis is an infrequently reported complication of vincristine which should be considered in patients presenting with stridor. This case adds to the literature a presentation complicated by an underlying disorder known to be associated with upper airway abnormalities, CdLS. Patients with underlying upper airway anomalies may be at higher risk for developing vincristine induced vocal cord paralysis. Additionally, this case adds to the literature raising questions about cancer risk in CdLS patients.

Poster # 754

GASTROINTESTINAL MUCORMYCOSIS WITH BOWEL PERFORATION IN AN ADOLESCENT FEMALE WITH PRE-B ALL

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Background: Mucormycosis is a highly invasive fungal infection that is fatal without early detection and aggressive management. Involvement of the gastrointestinal tract is a rare presentation, most frequently diagnosed post-mortem due to nonspecific symptoms of fever and abdominal pain. Prompt recognition and initiation of treatment is critical for survival

Objectives: We describe a case of Gastrointestinal Mucormycosis presenting with bowel perforation in an adolescent female with high risk pre-B Cell Acute Lymphoblastic Leukemia (ALL).

Design/Method: A 19-year-old female with High Risk Pre-B ALL presented to the Pediatric Intensive Care Unit (PICU) for gram negative bacterial sepsis and typhlitis in the setting of prolonged profound neutropenia and recent steroid administration. She developed severe shock and multi-organ failure, requiring mechanical ventilation, pressor support, and continuous renal replacement therapy (CRRT). She clinically improved, treated with IV meropenem and IV caspofungin for her infection, when she suddenly developed new fever and acute abdominal pain. Abdominal XR demonstrated free air indicating bowel perforation. She was taken for emergent exploratory laparotomy requiring resection of necrotic sigmoid, terminal ileum, and appendix

Results: Gastrointestinal Mucormycosis was diagnosed histologically. The species was confirmed as Rhizopus arrhizus. Given her medical fragility from her ongoing recovery and the complexity of the surgical intervention required, she was not a surgical candidate for further exploration and debridement. Medical management was optimized via the use of IV Liposomal Amphotericin B (LAMB) and IV Isovuconazole. The patient has since recovered and remains on IV antifungals at home, now 10 weeks (about 2 and a half months) post diagnosis.

Conclusion: Mucormycosis with intestinal involvement has been described rarely in literature, though some reports state that it is associated with a lower overall survival rate in comparison to other locations. Risk factors for our patient include steroid administration and prolonged immunocompromised state. In this case, her recent episode of bacterial sepsis and prolonged courses of antibiotics may also have played a role in fungal overgrowth, and her bowel perforation likely led to disseminated disease throughout her abdomen. Gastrointestinal mucormycosis poses additional treatment challenges in immunocompromised patients due to its clinical similarity to typhlitis for which surgery and LAMB are not included in typical treatment. When diagnosed, this location is high risk for performing multiple debridements required to ensure complete removal of all fungal disease, relying on medication optimization as the mainstay of treatment. We hope that this case highlights an unusual presentation of invasive mucormycosis in a pediatric oncology patient.

Poster # 755

A CASE OF GATA1-POSITIVE ACUTE MEGAKARYOBLASTIC LEUKEMIA IN THE ABSENCE OF CLINICAL DOWN SYNDROME

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Background: Acute megakaryoblastic leukemia (AMKL) is a subtype of acute myeloid leukemia characterized by proliferation of megakaryoblasts. Pediatric AMKL is divided into two subgroups associated with unique subsets of disease-causing genetic alterations with distinctly different outcomes: children with Down syndrome (DS) and children without DS. DS-AMKL cells are characterized by the uniform presence of trisomy 21 (T21) and GATA1-mutations, shortening the GATA1 protein (GATA1s), which leads to transient myeloproliferative disorders and acquisition of additional mutations in GATA1 signaling that progress to DS-AMKL. Despite heightened chemotherapy sensitivity, DS-AMKL patients exhibit improved outcomes compared to non-DS AMKL patients. Non-DS AMKL is driven by different genetic pathways and feature oncogenic fusion proteins like RBM15 (OTT), MKL1 (MAL), CBFA2T3, GLIS2, and NUP98. Interestingly, a small fraction of non-DS AMKL cases without oncogenic fusions may be caused by similar genetic pathways as DS-AMKL, including acquisition of T21, increased copy number of Down syndrome critical region (DSCR) genes, or GATA1 mutations.

Objectives: Describe a case of a 2-year-old male diagnosed with non-DS, GATA1 positive AMKL without clinical symptoms of Down syndrome.

Design/Method: Case report.

Results: The patient is a previously healthy 2-year-old, African American male with non-DS AMKL, initially presenting with unilateral facial swelling. Examination demonstrated phenotypically normal appearance without evidence of Down syndrome, and he met developmental milestones for age, with advanced speech and fine motor development. Complete blood count noted a white blood count of 21,270/µl with 31% blasts, hemoglobin 8.8 g/dL, and platelets 9,000/µl. Flow cytometry was done on a peripheral blood sample, with 58% blasts positive for CD45 (moderate), CD7, CD4 (dim), CD34, CD13 (small subset), CD99, CD58, CD38, CD33, CD16+56 (small subset), CD117, CD71, and megakaryocytic markers (CD42+61), consistent with AMKL. FISH demonstrated trisomy of 8 and 21, as well as three

copies of the MYST3 gene in 108 out of 200 (54%) and three copies of the RUNX1T1 and RUNX1 genes in 108 out of 200 (54%) interphase cells examined, but no fusion protein was detected. Our institutional Heme DNA/RNA mutation panel demonstrated GATA1 mutation as a frameshift variant, as well as mutation of EPOR gene, which is known to cause activations in JAK/STAT signaling. This patient received standard chemotherapy with 5-cycles of treatment, no demonstration of increases sensitivity to therapy and had no residual disease after induction 1 (Cycle 1), demonstrating early response.

Conclusion: This case highlights the genetic complexities of AMKL that are associated with non-DS patients without evidence of a fusion protein.

Poster # 756

DISSEMINATED HISTOPLASMOSIS AS THE PRESENTATION OF MYELODYSPLASTIC SYNDROME

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Background: Myelodysplastic syndromes (MDS) are a group of disorders characterized by one or more cytopenias secondary to ineffective hematopoiesis. Anemia, bleeding, and infections are the most common presentations of MDS, but there are few documented cases of MDS presenting with a disseminated fungal infection.

Objectives: To describe a unique case of MDS presenting with disseminated histoplasmosis.

Design/Method: Case Report

Results: A previously healthy 2 year old female presented with 1 month of intermittent temperatures 99-100°F, left sided jaw swelling, easy bruising, and leg pain with refusal to bear weight. Complete blood count demonstrated anemia and thrombocytopenia with 3% blasts. X-rays demonstrated abnormal periosteal reaction of the femur and tibia with a hypodense, ill-defined lesion of the right distal femoral metaphysis, and MRI demonstrated diffusely infiltrated bone marrow of the pelvis and lower extremities with focal areas of abnormal signal in the bilateral distal femurs and tibias. Ultrasound of the left jaw identified an indeterminate 1.4 cm mixed solid/cystic nodule. Peripheral blood flow cytometry was negative for malignancy; bone marrow biopsy revealed scattered atypical megakaryocytes and rare blasts, and abnormal FISH (+7, +8, low percentage). Meanwhile, infectious workup resulted with positive urine *Histoplasma* antigen (0.42 ng/mL), positive *Histoplasma* antibody (H and M bands) by immunodiffusion, and positive anti-*Histoplasma* IgG (37.9 EU) and IgM (13.6 EU) by enzyme immunoassay. She was started on amphotericin B. Bone biopsy was taken from the lesions noted on MRI and reflected bone fragments and fibrovascular connective tissue with no evidence of malignancy. Although her clinical symptoms improved, her cytopenias did not, so repeat bilateral bone marrow biopsy was performed 3 weeks later and resulted with dysplastic megakaryocytes and rare blasts (less than 5%), abnormal cytogenetics and FISH (hyperdiploidy including +7, +8) and next-generation sequencing for MDS panel positive for EZH2 and JAK2 somatic mutations, consistent with a diagnosis of MDS. Excisional biopsy of the left jaw nodule was also performed and showed many atypical megakaryocytes in the background of histiocytic proliferate, consistent with myeloid sarcoma with megakaryocytic differentiation.

Conclusion: Primary MDS in pediatric patients is rare, and initial presenting symptoms are typically nonspecific, making diagnosis difficult. Disseminated histoplasmosis can have similar presentations to many other non-infectious systemic diseases including hematologic malignancy, with overlapping symptoms including prolonged fevers, bone lesions, and pancytopenia. Ultimately, repeat evaluations led to a diagnosis of MDS with myeloid sarcoma, which was treated with chemotherapy and hematopoietic stem cell transplant.

Poster # 757

HOW EXTREME CAN IT GET?: A CASE OF HYPERLEUKOCYTOSIS IN T-CELL ALL

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Background: Hyperleukocytosis (WBC >100 x 10^3/uL) and extreme hyperleukocytosis (WBC >200 x 10^3/uL) are oncologic emergencies associated with unfavorable outcomes in acute leukemias due to the complications related to hyperviscosity, tumor lysis syndrome, and disseminated intravascular coagulation (DIC). The current literature estimates a prevalence of hyperleukocytosis in 10-20% of patients, and extreme hyperleukocytosis in <10%, among patients with acute leukemia.

Objectives: Report a case of T-cell ALL complicated by extreme hyperleukocytosis, DIC, and multifocal intracranial hemorrhage.

Design/Method: Case Report

Results: A 6-year-old male presented to the emergency room with prolonged fever, fatigue and leftward eye deviation. Laboratory studies revealed extreme hyperleukocytosis (WBC: 811 x 10^3/uL), anemia (hemoglobin: 5.8 g/dL), thrombocytopenia (platelets: 34 x 10^3/uL), and an elevated lactate dehydrogenase (>4500 U/L). Due to extreme hyperleukocytosis, he urgently underwent two rounds of leukapheresis, which subsequently decreased his WBC to 400 x 10^3/uL. Despite this intervention, he required intubated and mechanical ventilation as a result of worsening tachypnea and increased oxygen requirements. Coagulation studies revealed an elevated PT/INR (24 s/2.11), prolonged PTT (43 s), decreased fibrinogen (69 mg/dL), and an elevated D-dimer (19,000 ng/mL). His peripheral flow cytometry revealed T-cell lymphoblastic leukemia (67% blasts) and treatment was started as per Children's Oncology Group study AALL1231 with stringent tumor lysis prevention and monitoring. CT head revealed prominent hemorrhages in the corpus callosum and in the left posterior parietal lobe, with multiple other small hemorrhages throughout the parenchyma, further confirmed on brain MRI. EEG revealed slowing in the left parietal-occipital region, consistent with a prominent hemorrhage. Up to two weeks following the start of induction chemotherapy, he continued to display evidence of coagulopathy. Although he remains neurologically impaired evidenced by persistent leftward gaze, left-sided hemiparesis, minimal vocalization and dysphagia, he displays promising purposeful movements and ability to follow commands.

Conclusion: This case report identifies a rare presentation of T-cell ALL with extreme hyperleukocytosis and multi-system complications associated with leukostasis and DIC. It also highlights the importance of prompt identification and treatment of this oncologic emergency to halt progression of complications

leading to better overall prognosis. In our patient, timely treatment with leukapheresis allowed for minimizing further complications from hyperleukocytosis.

Poster # 758

PROGRESSIVE LYMPHADENOPATHY IN RELAPSED/REFRACTORY ALL WITH T (1;19)

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Background: Data on the prognostic impact of t(1;19) in pre B acute lymphoblastic leukemia (ALL) have been inconsistent. In current COG protocols, this translocation is considered a neutral cytogenetic marker. Extramedullary relapse, particularly in the CNS has been described, but progressive lymphadenopathy in either isolated extramedullary or combined relapse has not been reported.

Objectives: To describe 3 patients with t(1;19) who had early relapses on therapy with progressive, refractory lymphadenopathy as a prominent component of their relapses. This highlights the need to consider relapse in patients with t(1;19) ALL who develop lymphadenopathy.

Design/Method: Case series

Results: All patients had pre B ALL with t(1;19) at initial diagnosis and relapse, with no known extramedullary disease at diagnosis.
Patient 1: 12-year-old male who was MRD negative at end of Induction (EOI). On consolidation day 1, he presented with inguinal lymphadenopathy, initially treated as lymphadenitis which waxed and waned during consolidation. Biopsy at end of consolidation (EOC) confirmed relapse and imaging showed extensive pelvic adenopathy. The lymphadenopathy progressed rapidly through high-dose methotrexate/cytarabine and etoposide/cyclophosphamide regimens. Bone marrow and CSF remained negative for leukemia until peripheral blasts noted on smear near end of life.
Patient 2: 7-year-old male with EOI MRD 0.01% but negative at EOC, who had an isolated bone marrow relapse 16 months from diagnosis. While receiving blinatumomab/nivolumab for reinduction, he developed inguinal lymphadenopathy, biopsy confirmed to be disease. PET scan demonstrated extensive metabolically active nodal and skeletal lesions. He then progressed through UKALL R3 reinduction, inotuzumab, and cyclophosphamide/etoposide/bortezomib prior to his death. Bone marrow remained positive, and he developed cord compression from epidural adenopathy, requiring emergent radiation.
Patient 3: 3-year-old female with EOI MRD 0.029% but negative at EOC. Twelve months from diagnosis, she developed a large cervical lymph node, with biopsy demonstrating relapse and bone marrow flow of 1.3% blasts. She received VXLD reinduction with persistent lymphadenopathy followed by blinatumomab, during which she presented with upper extremity weakness. MRI showed infiltration of the cervical foramina and epidural infiltration causing mass effect on the spinal cord and cervical vasculature. Blinatumomab was discontinued, and radiation to the affected area led to significant improvement. Bone marrow then demonstrated 85% B ALL involvement. This patient is now receiving high dose cytarabine

Conclusion: Extramedullary relapse or refractory disease should be highly considered in patients with

t(1;19) ALL who develop lymphadenopathy, prompting early imaging and biopsy. This lymphadenopathy may compromise function and be extremely refractory to therapy.

Poster # 759

CLONAL TRANSFORMATION OF T-LYMPHOBLASTIC LYMPHOMA TO TESTICULAR TCL IN A PEDIATRIC PATIENT

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Background: Testicular relapse of acute lymphoblastic leukemia is a rare event that may be clonally distinct from that of the ancestral bone marrow. In some instances, such clonally transformed neoplasm has a unique biological phenotype.

Objectives: To describe a case of sequential, clonally related T cell lymphoblastic lymphoma and primary testicular T cell lymphoma (PTTCL) with subsequent central nervous system (CNS) relapse.

Design/Method: Prospective chart review; literature review of PubMed and Cochrane databases.

Results: A previously healthy 15-year-old male was diagnosed with bone marrow- and CNS-negative T-lymphoblastic lymphoma of CD2pos;CD3pos;CD5pos;CD7pos;CD8pos;CD16/56neg;TdTpos immunophenotype. He achieved complete remission on COG AALL0434 protocol. Sixty months later, he presented with complaints of left-sided painless scrotal swelling secondary to an epididymal mass. The resected (hemiscrotectomy with en bloc orchidectomy) mass was found to be a PTTCL of CD2pos;CD3neg;CD5neg;CD7pos;CD8pos;CD16/56pos;CD52pos;TdTneg phenotype. Additional workup was negative for CNS, bone marrow and the contralateral testis involvement. The patient received six cycles of chemotherapy as per COG ANHL12P1 followed by the right hemiscrotum radiation therapy at 36cGy. The end-of-treatment scans revealed complete remission. Twenty-three months later, the patient presented with recurrent headaches evaluated with brain MRI, which revealed leptomeningeal infiltration. Cerebral spinal fluid (CSF) analysis revealed presence of atypical cells of mature lymphoid morphology and sCD3negs;CD8pos;CD34neg;TdTneg immunophenotype, resembling the ones of PTTCL. The patient underwent 10 rounds of intrathecal triple-chemotherapy, as well as one cycle of systemic chemotherapy with bendamustime and alemtuzumab resulting in CSF clearance of atypical cells. Unfortunately, the patient died of fulminant sepsis due to Escherichia Coli. Additional molecular analysis revealed that all three neoplasms shared the same clonal re-arrangement of TCRG A (V-J) chain loci at 179bp and 190bp.

Conclusion: Several factors, such as the relatively low body temperature in the scrotum and the reduced penetration of certain chemotherapy agents through the physiologic blood-testis barrier, are known to contribute to development of testicular relapse in patients with acute lymphoblastic leukemia. Within this immunologically privileged compartment, the atypical cells may continue to undergo further clonal evolution and maturation, the mechanism of which is to be elucidated. This case illustrates the clonal evolution of T-lymphoblasts into aggressive peripheral testicular T cell lymphoma with unique predilection for spreading into CNS.

Poster # 760

EXTRAMEDULLARY RELAPSE AFTER CAR-T CELL THERAPY IN A RELAPSED ACUTE LYMPHOBLASTIC LEUKEMIA CASE

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Background: Acute lymphoblastic leukemia (ALL) is the most common pediatric malignancy. Primary refractory or relapsed disease (R/R) during or after frontline therapy is approximately 20% and cure with chemotherapy alone is rare.

Objectives: Chimeric antigen receptor-T (CAR-T) cell therapy, which is CD19-directed, genetically modified, autologous T-cell through which a patient's own T cells are reprogrammed with a transgene to detect and eliminate leukemic blasts.

Design/Method: Herein, we present a patient treated with tisagenlecleucel, a CD-19 directed CAR-T product, for multiply relapsed B-ALL and presented with an isolated extramedullary relapse soon after, a phenomenon not previously reported in the literature.

Results: 4-year-old male with standard risk pre B-ALL at the age of 2 started therapy as per Children's Oncology Group (COG) AALL1731 chemotherapy and was Minimal Residual Disease (MRD) negative at the end of induction. Two years after his initial diagnosis and while receiving maintenance chemotherapy, he was found to have a bone marrow relapse. He then received reinduction therapy following COG AALL1331 and was MRD negative at the end of induction. Next he received 3 cycles of Blinatumomab with the plan being to proceed to haploidentical allogenic bone marrow transplantation (BMT). However, 4 days prior to scheduled BMT bone marrow biopsy revealed a second occult relapse. He was then offered and enrolled on COG trial AALL 1621 with inotuzomab ozogamicin, a CD-22 antibody-drug conjugate. He became MRD negative and then received tisagenlecleucel following cytoxan and fludarabine conditioning. Three months after tisagenlecleucel, he experienced facial swelling and left eye proptosis. Despite his bone marrow biopsy showing no residual leukemia, a PET CT and MRI revealed a new left posterior sinus/skull base mass. Biopsy of the mass revealed an identical clone to his prior multiply relapsed clone, confirming an extramedullary relapse of the pre-B cell ALL. He is clinically doing well 30 days post BMT after receiving 2 cycles of ICE chemotherapy and radiation.

Conclusion: Extramedullary relapse is rare after CAR-T cell therapy, and this is the first known case of extramedullary relapse with negative BM following CD-19 directed CAR-T cell therapy. There remains an ongoing unmet need to further understand clinical settings in which CAR-T cell therapy provide the greatest benefit which will hopefully be resolved by future clinical trials and real world experiences.

Poster # 761

FUNGAL INFECTIONS IN ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS TREATED WITH TYROSINE KINASE INHIBITORS

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Background: Pediatric patients with Philadelphia-positive (Ph+) and Philadelphia-like (Ph-like) B cell acute lymphoblastic leukemia (B-ALL) have historically had poor outcomes with less than 50% event free survival despite intensive chemotherapy. Disease outcomes have improved with use of intensive chemotherapy and tyrosine kinase inhibitors (TKI). AALL1122 studied addition of dasatinib to chemotherapy but reported significant toxicity including remission deaths related to fungal infections. Current efforts by the Children's Oncology Group (COG) are studying de-escalation of the cytotoxic chemotherapy backbone for patients with Ph+ B-ALL to minimize toxicity while trying to preserve improved outcomes (NCT03007147).

Objectives: Describe incidence and outcomes of invasive fungal infections in a cohort of patients with Ph+ or Ph-like B-ALL undergoing treatment with chemotherapy and TKI and suggest strategies to prevent fungal infection.

Design/Method: Single center retrospective review (1/2020-11/2023) of infectious complications in Ph+/Ph-like leukemia and review of the literature.

Results: In the past 3 years, we identified 6 patients diagnosed with Ph+ or Ph-like B-ALL at our institution. All patients were treated with chemotherapy and TKI; 3 patients developed invasive fungal infections. Patient 1, a 4-year-old female with Ph+ B-ALL treated on AALL1631, developed invasive fungal sinusitis and disseminated candidiasis during induction. Given severity of infection, she was taken off study and treated with AALL1631 investigational arm and TKI to try to minimize toxicity. The patient's treatment was later complicated by fatal septic shock in maintenance. Patient 2, a 12-year-old female with Ph-like B-ALL (PDGFRβ/ABL fusion) treated per AALL1732 with addition of imatinib, developed septic shock and disseminated candidiasis during delayed intensification leading to DIC, multiorgan failure, and death. Patient 3, a 7-year-old female with Ph+ B-ALL treated with EsPhALL backbone and imatinib, developed disseminated candidiasis during consolidation. She had a complicated course including multiple relapses managed with CAR-T cell therapy and bone marrow transplant. She ultimately died from complications of severe graft versus host disease. All patients were on antifungal prophylaxis during induction but none of the patients were on fungal prophylaxis when they developed fungal infections.

Conclusion: We observed significant incidence of fungal infections during periods of neutropenia in patients with Ph+ or Ph-like B-ALL treated with TKI and chemotherapy. As a result, our institution modified antimicrobial prophylaxis recommendations to include antifungal prophylaxis for patients treated with intensive chemotherapy and TKI during periods of neutropenia. Surveillance of this population is ongoing but no invasive fungal infections have been observed in 6 months since new prophylaxis recommendations.

Poster # 762

SKELETAL MUSCLE INDEX AND EARLY RESPONSE IN PEDIATRIC HODGKIN LYMPHOMA: A COG REPORT

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Background: Low skeletal muscle mass (measured using computed tomography [CT] scans as skeletal muscle index [SMI]) is associated with worse survival among adults with cancer, hypothesized either due to altered chemotherapy biodistribution or through inflammatory effects of cancer cachexia. Similar association between SMI and outcomes in childhood Hodgkin lymphoma (HL) remains understudied.

Objectives: We examined the association between pre-treatment SMI and centrally-reviewed slow early response (SER) in children with intermediate-risk (AHOD0031) or high-risk (AHOD0831) HL, given that early response is predictive of event-free survival (Friedman, *JCO* 2014; Kelly, *BJH* 2020).

Design/Method: Patients enrolled on AHOD0031 or AHOD0831 with pre-treatment digital abdominal CT images and response assessment after two cycles of chemotherapy were included. Two consecutive slices at L3 per patient were used to calculate skeletal muscle area (SMA, in cm^2) and total adipose tissue area (TAT= sum of visceral, subcutaneous, intramuscular adipose tissue, in cm^2) using sliceOmatic. Height and weight at diagnosis were used to calculate body mass index (BMI). BMI was converted into age- and sex-specific BMI percentiles to create BMI categories (underweight, normal weight, overweight/obese). SMA and TAT were normalized for patient height to calculate SMI and TATI (TAT index); these were divided into quintiles (Q1 [lowest] to Q5 [highest]). The association between SMI and SER was examined using logistic regression after adjusting for age at HL diagnosis, sex, race/ethnicity, stage, histology, bulk disease, 'B' symptoms, TATI and study. Association between BMI and SER was also examined. Logistic regression was also used to determine the predictors of low SMI.

Results: Among 1,321 eligible patients (AHOD0031=1,165 [88.2%]; AHOD0831=156 [11.8%]), 301 (22.8%) had SER (AHOD0031=223 [19.1%]; AHOD0831= 78 [50%]). Low SMI (Q1) was associated with greater odds of SER (SMI Q1 *vs* Q5: Adjusted Odds Ratio [aOR]=1.87, 95% confidence interval [CI]=1.12-3.13; *P*=0.02; SMI Q1 *vs* Q2-Q4: aOR=1.42, 95%CI=1.00-2.02, *P*=0.05). In contrast, BMI was not associated with SER (underweight: aOR=1.58, 95%CI=0.92-2.71, *P*=0.09; overweight/obese: aOR=1.06, 95%CI=0.78-1.43, *P*=0.7; ref=normal weight).
Predictors of low SMI (Q1) included age <12y (aOR=2.90, 95%CI=1.94-4.34, *P*<0.0001; ref=age≥12y), female sex (aOR=4.81, 95%CI=3.40-6.81, *P*<0.0001; ref=males), race/ethnicity other than African-American (aOR=3.18, 95%CI=1.70-5.92, *P*<0.0001), stage III-IV disease (aOR=1.77, 95%CI=1.27-2.47, *P*=0.0007; ref=stage I-II), bulk disease (aOR=2.02, 95%CI=1.34-2.23, *P*=0.007; ref=no bulk), 'B' symptoms (aOR=1.59, 95%CI=1.13-2.23, *P*=0.007; ref=no 'B' symptoms) and being underweight (aOR=10.26, 95%CI=5.75-18.31, *P*<0.0001; ref=normal weight).

Conclusion: SMI is a novel imaging-derived marker that is independently associated with slow early response in children with HL. Mechanisms underlying this association are currently being explored.

Poster # 763

IS DOSE REDUCTION JUSTIFIED IN PEDIATRIC BURKITTS LYMPHOMA TREATED WITH CHEMOTHERAPY AND RITUXIMAB

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Background: The addition of Rituximab to the established chemotherapy protocol significantly improved the survival rate in children with high-grade NHL. In limited-resource countries like ours, the outcome of intensive chemotherapy is adversely affected by the high rate of infectious complications. There are very few studies in support of reducing the dose of chemotherapy when used with Rituximab without compromising the outcome.

Objectives: The objectives of the study are: 1. To study the outcomes of pediatric patients diagnosed with Burkitt's Lymphoma (BL) and treated with intensive chemotherapy along with Rituximab. 2. What happens to outcomes when the dose of chemotherapy is reduced.

Design/Method: This is a retrospective study of pediatric patients, diagnosed with Burkitts Lymphoma (BL) who have been treated from 1st July 2019 to 30th June 2022. All patients were treated as BFM-98 Lymphoma protocol along with Rituximab (375mg/m2).

Results: The total number of patients was nine. Out of nine, six were males and three were females. The median age was 6 years (range: 3-13 years). Eight out of nine (88.8%) were of high risk (R2-1, R3-6, R4-2). Median doses of Rituximab were 5 (range: 3-6). Five out of nine (55%) required dose reduction due to severe neutropenia and infectious complications. All patients had developed febrile neutropenia while on therapy. Two out of nine (22.2%) required admission in pediatric intensive care unit. There were 27 episodes of febrile neutropenia. Out of 27 episodes of febrile neutropenia, two were having multidrug resistance, bacterial growth in blood, two had culture proven urinary tract infection. Two episodes were of radiology proven pneumonia. There was one episode of pancreatitis, parotitis, neutropenic colitis, and a perianal abscess. At the median follow-up of 28 months (range: 15-50 months) the event free survival (EFS) and overall survival were (OS) 100% in two groups (group-1, of 5 patients, who required dose reduction, group-2 of 4 patients received unmodified chemotherapy). Six months after completion of therapy, lymphocytes subset and serum immunoglobulin levels of four patients were available for analysis. All four patients had delayed in b lymphocyte recovery, two patients also had low level of NK-T cell. The serum IgG level was low in all 4 patients, three had low levels of serum IgM and 1 out of 4 had low serum level of IgA.

Conclusion: EFS and OS did not experience any impact from reducing chemotherapy dose. There was delay in immune reconstitution in patients treated with chemotherapy and Rituximab.

Poster # 764

FEASIBILITY OF MEASURING METABOLIC TUMOUR VOLUME IN CHILDREN WITH HODGKIN LYMPHOMA ON FDG-PET-CT

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Background: Assessment of metabolic tumour volume (MTV) in F18 FDG PET CT along with Deauville score and Standardised Uptake Value (SUV) has been reported to contribute in prognostication of adults with Hodgkin Lymphoma (HL). Such information is scarce in children with HL, hence this study was done to look at feasibility of assesing MTV in our patient cohort

Objectives: To assess feasilibity of measuring MTV in our patients and to comapare MTV with SUV max in children HL to assess its prognostic significance.

Design/Method: 61 Children with classic HL treated as per Euronet PHL C2 protocol at our centre from 2017-2020, who had diagnostic and interim PET (iPET) scan were included. SUV max and DL score were measured as per standard guidelines. MTV was measured in areas of tumour with a SUV of 2.5 or more. Patients were followed up for EFS and OS**.** MTV and SUV were compared at diagnosis and after two courses of chemotherapy. Appropriate statistical tests were done to analyze the data.

Results: 61 children, M: F 1.5:1, mean age 10.10 years. 16, 11 and 34 were treated in TG 1, 2 and 3 respectively. Based on iPET 47 were early responders and 14 were slow responders.
Median SUV and MTV at diagnosis for Stage 1: 8.04(6.06-10.7)/ 36.8(7.9-46.1) Stage 2: 9.95(7.4-16.7)/ 39.9(14.8105.3), stage 3: 10.3(9.12-15.01)/ 140(83.6-309.2), stage 4: 14(11.4-16.3)/ 362.4(180- 478.8). The same according to TG were TG1: 8.2(6.5-12.7)/ 36.8(8.8-51.1), TG2: 9.6(8.54-11.57)/ 39.9(14.8-105.3) and TG3: 13.7(9.5-16.3)/ 304(123.7- 452.7).
Overall, the median SUV max and MTV at diagnosis were 10.8 (8.51-15.01) and 107.19 (37.93-323.4) and at interim assessment were 0.01 (0.01-15.6) and 0.01 (0.01-509). Comparison of SUV max and MTV in diagnostic PET between rapid responders and slow responders: 10.73(8.47-14.61) vs 12.25(8.54-18.66) and 98.35(37.93-298.2) vs 145(84.43-463.5). On a median follow up of 2 years, the EFS was 88.5% and OS was 98.3%. Seven children had relapse/refractory disease, comparison of diagnostic parameters those who had or didn't have an event were SUV max 11.5(10.7-13.89) vs 10.5(8.4-15.7) with p value of 0.69 and MTV 304(30.45-452.7) vs 105.35(37.9-30.9.2) with p value of 0.82.

Conclusion: MTV was higher in children with advanced stage disease and slow responders, similar to that of SUV in F18 FDG PET CT Scan. It is possible to use this parameter in LMIC setting. Further studies are required to assess if MTV can predict outcome in children with HL.

Poster # 765

A 16-YEAR-OLD WITH PROGRESSIVE SKIN LESION IDENTIFIED AS A RARE TYPE OF NON-HODKIN LYMPHOMA

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Background: Primary cutaneous marginal zone lymphoma (PCMZL) is a type of Non-Hodgkin lymphoma (NHL) rarely seen in infants and adolescents. It consists of
<1% of all childhood NHL cases.

Objectives: To describe the clinical and immunophenotypic findings of pediatric patient with solitary skin lesion diagnosed with PCZML

Design/Method: Case Report

Results: A 16–year old male originally presented to a dermatologist with an 8-month history of a scaly, pruritic rash on the central posterior aspect of his right upper extremity. Patient was initially diagnosed with eczema and treated with topical steroid therapy. The patient's rash progressed over 8 weeks into a

localized erythematous papule. A needle biopsy was performed; histology (reviewed at Columbia University) revealed an atypical lymphocytic infiltrate of B-cell predominance. Six weeks later, due to the concern about neoplastic process, primary dermatologist performed an excisional biopsy with wide margins and had specimen sent to dermatopathology (reviewed at Tulane University) department where the diagnosis of primary cutaneous marginal zone B-cell lymphoma was confirmed.

Immunohistochemical staining revealed the presence of follicles appearing to contain reactive germinal centers highlighted by positivity for CD20, PAX5, CD10, BCL6, and Ki67. Notably, BCL-2 was negative. Additionally, a rich background of T-cells positive for CD3, CD4, CD8, and BCL2 were identified.

This adolescent patient was uniquely having complaints of intermittent hematochezia for nearly a year. This is relevant as PCMZL can be associated with mucosa-associated lymphoid tissue. His symptoms became worrisome enough to warrant a colonoscopy prior to his excisional biopsy, revealing no evidence of lymphoma involving his GI tract. Staging for primary cutaneous lymphoma was performed with CT chest/abdomen that showed no additional lymphadenopathy. An incidental sclerotic lesion involving his left lower extremity was followed up with a PET/CT that again revealed normal findings. Staging was confirmed as T1aN0M0 per European Organization of Research and Treatment Center (EORTC). He was determined to have completely resected primary cutaneous B-cell lymphoma. After discussion at an AYA tumor board, we made the decision to observe with serial physical exams and repeat imaging in 6 months. Patient has been doing well since initial diagnosis.

Conclusion: The rare incidence of cutaneous lymphomas in childhood makes it challenging to diagnose and manage patients in a consistent manner. Treatment for PCMZL is based on NCCN guidelines and based on immunophenotypic features. More information about the biology and pathology of PCMZL in children and adolescents is needed in order to develop age appropriate therapies.

Poster # 766

SILENT STAPH. AUREUS DISSEMINATION RESULTS IN MULTIFOCAL MYOSITIS IN A HODGKIN LYMPHOMA PATIENT

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Background: Infections are a major cause of morbidity and mortality in cancer patients. These infections may be attributed to the cancer cell-mediated immune alterations as well as use of chemotherapeutic agents.

Objectives: We report a case of multifocal myositis caused by Staphylococcus Aureus detected on 18FDG-PETCT performed for the treatment response assessment.

Design/Method: Prospective chart review; literature review of PubMed and Cochrane databases.

Results: A 16-year-old male with a past medical history significant for pustular acne, was diagnosed with stage IIIB classical Hodgkin lymphoma and treated on AVEPC+Bv (doxorubicin; vincristine; etoposide; cyclophosphamide; brentuximab vedotin) protocol. Antibacterial prophylaxis with fluconazole and TMP/SMX was used from the treatment onset. To facilitate neutrophil recovery, pegylated GCSF was

also used as per protocol recommendations. On D10 of cycle 1, the patient developed febrile neutropenia, for which he received an empiric course of cefepime, until neutrophil counts improved >500 cells/uL. Notably, blood cultures obtained prior to antibiotics remained negative for growth of any pathogens. At the end of cycle 1, the patient demonstrated worsening of his facial acne which was attributed to robust neutrophil recovery, as well as pain in distal legs and the lower back, which were thought to be secondary to the preceding therapies. During cycle 2, the patient demonstrated worsening of the right ankle and lower back pain. The pain was not associated with trauma or fever and it responded poorly to oxycodone. At the end of this cycle, on 18FGD-PETCT performed for the treatment response assessment, the patient was found to have a great metabolic response in the previously known-to be-involved lymphoma sites, but also new intramuscular hypermetabolic lesions in the lower right calf, paraspinal muscles on the right, and in the right axillary area. Biopsy of the paraspinal lesion was performed, which demonstrated presence of inflammatory infiltrates as well as gram-positive cocci in clusters, in the intra- and intercellular spaces, later identified as methicillin-resistant Staphylococcus Aureus. Blood samples obtained during this episode revealed no bacterial growth. The patient received a course of therapy with vancomycin and cefepime, which resulted in improvement of symptoms as well as normalization of laboratory parameters.

Conclusion: This case highlights the complex nature of immune dysregulation in patients with classic Hodgkin lymphoma, and their reduced ability to effectively control colonizing pathogens, as well as compromised ability to mound strong response to effectively eradicate infection. This case also appears to be the first one to report acute myositis caused by MRSA.

Poster # 767

MANAGEMENT OF CNS DIFFUSE LARGE B CELL LYMPHOMA IN A PATIENT WITH ATAXIA TELANGIECTASIA

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Background: Ataxia telangiectasia (AT) is an autosomal recessive disorder affecting DNA repair mechanisms, with increased susceptibility to malignancies. The risk of developing leukemia or lymphoma in AT is 10%- 30%. Managing this condition poses challenges due to associated comorbidities and sensitivity to chemotherapy and radiotherapy; consequently, a tailored approach becomes imperative.

Objectives: Describe the complex management of central nervous system (CNS) diffuse large B cell lymphoma (DLBCL) in a patient with AT.

Design/Method: Case report.

Results: This is a 12-year-old male with AT diagnosed at the age of 6. At age 9 he developed pseudotumor cerebri with progressive vison loss. He required ventriculoperitoneal shunt placement and computed tomography scan of brain and spine. Radiation exposure predisposes malignancy development in AT.

He presented with ventriculitis requiring shunt removal and subsequent persistent fever, vomiting, and

headaches. Cerebrospinal fluid (CSF) analysis revealed lymphocytic pleocytosis with atypical cells. Bone marrow aspiration was normal. Brain and spine MRI showed leptomeningeal enhancement and thickening of the lower conus. A tissue biopsy and CSF analysis confirmed DLBCL.

Considering therapy limitations with concurrent AT, he was treated with rituximab, cyclophosphamide, doxorubicin, vinblastine, prednisone (R-CHVP), and intraventricular rituximab alternating with intraventricular methotrexate, cytarabine, and hydrocortisone via Ommaya reservoir.

Adjustments to the chemotherapy regimen included reduced cyclophosphamide dosing and substitution of vincristine for vinblastine to minimize neurotoxicity risks associated with AT. He completed one cycle of R-CHVP, but course was complicated by meningitis and neutropenic colitis. He continued with rituximab via Ommaya reservoir for nine doses.

Post cycle 1, MRI showed near-resolution of intracranial leptomeningeal disease and stable disease in lower spine and cauda equina. Based on his poor tolerance of R-CHVP, treatment was changed to Capizzi methotrexate and ibrutinib combined with 4 intrathecal rituximab doses per cycle. Use of ibrutinib in a patient with AT has not been reported yet.

Follow-up imaging noted stable spine disease and continued near-complete resolution of leptomeningeal disease on brain MRI. Patient has remained clinically stable with no headaches and only occasional emesis as well as return of some vision.

Conclusion: This case highlights the complexity of CNS DLBCL management and the safety of ibrutinib use in a patient with AT. The individualized approach reflects the intricate balance required when managing complex medical conditions in conjunction with malignancies. Adaptation of the treatment plan and innovative therapeutic strategies remain crucial for the patient's successful management.

Poster # 768

BURKITT POST-TRANSPLANT LYMPHOPROLIFERATIVE DISORDER IN A POST-RENAL TRANSPLANT ADOLESCENT

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Background: Burkitt post-transplat lymphoproliferative disorder (Burkitt-PTLD) is an aggressive B-cell PTLD variant with no established standard treatment. While Burkitt lymphoma typically involves intense chemotherapy, such regimens pose significant risks in post-transplant patients necessitating alternative approaches. Limited data suggests the benefit of low to moderate dose chemotherapy in these cases may avoid toxicity and offer effective therapy.

Objectives: To detail the diagnostic and therapeutic approach in managing a case of EBV-negative monomorphic Burkitt PTLD in a 18-year-old male post-renal transplant patient.

Design/Method: Case presentation and review of literature.

Results: An 18-year-old male, post-renal transplant for obstructive nephropathy with chronic rejection

and stage III chronic kidney disease(CKD), presented with fever, night sweats, weight loss, and lymphadenopathy. Immunosuppressive regimen included tacrolimus, azathioprine, andprednisone at the time of diagnosis. Lab values showed elevated LDH (733 units/L), uric acid (15.6 mg/dL), and ESR (55 mm/hr). Serum EBV PCR was undetectable. Imaging revealed diffuse liver nodules, prompting biopsy. Liver biopsy confirmed EBV-negative, MYC-negative, monomorphic Burkitt-PTLD. Diagnostic workup including PET/CT and bone marrow biopsy, revealing widespread abdominal and bony disease.
A reduced-intensity R-COMP (Prednisone, Cyclophosphamide, Vincristine, Methotrexate, Rituximab) regimen was initiated to limit exposure to nephrotoxic medications. Vincristine, rituximab and cyclophosphamide were given on day 1. Prednisone was given on day 1-5 and vincristine and methotrexate were given on day 15. Methotrexate was dosed at 300 mg/m2 to minimize renal injury. Patient received 6 cycles each lasting 21 days. Immunosuppressive therapy was held aside from prednisone initially and tacrolimus was restarted mid-therapy. After 1 week of therapy, imaging showed over 50% tumor burden reduction. Treatment was complicated by tumor lysis syndrome resulting in worsening renal function, severe bone pain, and anaphylactic reaction to rituximab. Renal function returned to baseline with hydration and rasburicase. The patient did not require dialysis during therapy nor have longterm worsening of CKD. Patient achieved complete metabolic response following cycle 3. The patient had no evidence of disease after sixth cycle on PET-CT and remains in remission 3-months off-therapy..

Conclusion: This case underscores the intricate balance needed when managing Burkitt-PTLD in transplant recipients. The successful outcome highlights the importance of tailored, reduced intensity chemotherapy treatment and supportive care. Recognizing the potential for unexpected complications and adjusting therapy accordingly is paramount in achieving favorable outcomes in BL-PTLD patients and preserving function of transplanted organ.

Poster # 769

VERY LATE RELAPSE OF BURKITT LYMPHOMA IN A 17-YEAR-OLD MALE

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Background: Burkitt Lymphoma (BL) is an aggressive mature B-cell Lymphoma constituting about 40% of childhood Non-Hodgkin's Lymphoma. Adding Rituximab to previous standard Lymphome Maline B (LMB) chemotherapy has markedly improved event-free survival among high-risk children and adolescents, however, it does not fully prevent relapse. Relapses typically occur within 6 months due to the highly proliferative nature of BL.

Objectives: To review the case of a 17-year-old male with previously treated Burkitt Leukemia who did not receive concomitant CD20 immunotherapy and subsequently presented with very late relapse of Burkitt Lymphoma with distinct cytogenetics.

Design/Method: Case Report.

Results: A 17-year-old male with a history of CNS positive Burkitt leukemia, in complete remission (CR) since age 7 years, presented with a 12.6 cm abdominal mass. His previous Burkitt leukemia, notable for the classic t(8;14) MYC/IGH translocation, was treated with standard LMB chemotherapy per ANHL1131

group C3 but without Rituxumab secondary to an anaphylactic reaction. In the interim, he remained well but with notable allergic rhinitis that required allergen immunotherapy. A biopsy of the LLQ abdominal mass confirmed recurrent BL, with a t(2;8) MYC/IGK translocation. PET/CT demonstrated Stage III disease with scattered hypermetabolic lymph nodes (LN's) within the mediastinum, extensive peritoneal involvement, and the known LLQ mass. He was treated with Obinutuzumab, Ifosfamide, Carboplatin and Etoposide (O-ICE). He experienced anaphylaxis to Obinutuzumab but underwent successful rapid desensitization with subsequent doses. After two cycles of chemoimmunotherapy his PET/CT showed marked improvement in the abdominal disease with mild residual hypermetabolism (Deauville 4) but worsening hypermetabolism of a left prevascular mediastinal LN, concerning for pulmonary disease progression. Results of a comprehensive germline genetic immunodeficiency panel were unremarkble.

Conclusion: We present a case of an unusually late relapse of BL with a distinct MYC translocation ten years after CR from Burkitt leukemia. This case highlights the ability to perform rapid desensitization with an anti-CD20 monoclonal antibody despite the patient experiencing anaphylaxis to both Rituximab and Obinutuzumab. While it is possible that this case represents a second de novo BL, the literature suggests that dependent subclones present at primary diagnosis may undergo clonal evolution into a more aggressive dominant clone in the setting of relapsed disease. Additionally, a second de novo BL would be expected to be exquisitely sensitive to a regimen like O-ICE. It is also possible that this patient has an undefined immune dysregulation, contributing to a B-cell stimulatory host environment that increased his risk of BL relapse.

Poster # 770

SKIN LESIONS AS AN ATYPICAL PRESENTATION OF NON-HODGKIN LYMPHOMA

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Background: Non-Hodkin Lymphoma (NHL) is heterogenous in its clinical presentation, ranging from a single painless enlarged lymph node to a life-threatening oncologic emergency. Rarely, patients can present with skin lesions that precede more systemic symptoms of disease.

Objectives: We describe two patients who presented with skin lesions and were later diagnosed with NHL following biopsy.

Design/Method: Case series to describe cutaneous lesions as an atypical presentation of NHL.

Results: Patient 1 is a 17 year-old male who presented with a three-month history of progressively enlarging tender facial nodules associated with intermittent fevers that did not respond to treatment with antibiotics. He subsequently developed similar nodules on his chest, abdomen, and bilateral upper and lower extremities accompanied by weight loss and decreased appetite. There was no hepatosplenomegaly or lymphadenopathy appreciated on exam. Labs were remarkable for neutropenia (ANC 1180 TH/µL) and elevated inflammatory markers (ESR 16 mm, LDH 658 U/L). Whole body MRI demonstrated an extensive inflammatory process limited to the skin and subcutaneous fat. Biopsy of an abdominal lesion was diagnostic of subcutaneous panniculitis-like T-cell lymphoma (SPTCL) with alpha/beta T-cell phenotype. Genetic testing for HAVCR2 mutation was negative. PET/CT scan identified widespread metabolic lesions in the dermis and subcutaneous tissue. He was initially treated with

steroids with improvement in skin nodules, however, on steroid taper, he had recurrence of cutaneous lesions associated with high-grade fevers and elevated laboratory markers concerning for secondary hemophagocytic lymphohistiocytosis (soluble IL-2R 2145 U/mL, CXCL-9 118,436 pg/mL). He was treated with 1 cycle of ICE (Ifosfamide, Carboplatin and Etoposide) due to concerns for progression with follow up PET/CT scan demonstrating only moderate response. He was subsequently transitioned to cyclosporine monotherapy after which he achieved complete response.
Patient 2 is a 13 year-old female who presented with a three-month history of a progressively enlarging painless lump on her left hip. She was initially treated with antibiotics without improvement. She was referred to a dermatologist who additionally noted enlarged left inguinal lymph nodes on exam raising concern for malignancy. Punch biopsy of the lesion confirmed the diagnosis of B-lymphoblastic lymphoma (BLLy). Staging PET/CT demonstrated multiple sites of enhanced FDG uptake in the bone, soft tissue, and lymph nodes consistent with widespread lymphomatous involvement and Stage III disease. She was subsequently treated on the Children's Oncology Group Study AALL1732 study with complete response noted after induction chemotherapy.

Conclusion: This case series highlights the importance of considering NHL in the differential for atypical skin lesions.

Poster # 771

FAMILIAL NEONATAL HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS: SCOPING REVIEW AND ANALYSIS OF 95 CASES

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Background: Hemophagocytic lymphohistiocytosis (HLH) is a syndrome of pathologic immune activation and uncontrolled inflammation. Neonatal HLH (nHLH), defined as HLH that presents in the first month of life, is clinically devastating. nHLH is estimated to comprise 10% of familial HLH (fHLH) diagnoses. There have been few, large descriptive studies of familial nHLH.

Objectives: The primary objective of this study was to perform a scoping review and descriptive analysis of published cases of familial nHLH.

Design/Method: A comprehensive literature database search was performed. Cases of HLH were eligible for inclusion if clinical analysis was performed at age $\leq$ 30 days.

Results: 544 studies were assessed for eligibility. Studies were excluded if they did not discuss nHLH (n=280), aggregated nHLH patient data with all ages (n=83), provided insufficient detail and/or data describing nHLH (n=28), and for other reasons (n=8). 95 cases of nHLH were included.
Genetic causes of fHLH included mutations in *PRF1*, *STX11*, *STXBP2*, *UNC13D*, *NOCAR-H*, and *XIAP*.

Presenting features included fever (32%; n=30/95), hydrops fetalis (12.6%; n=12/95), respiratory distress (11%; n=10/95); and organomegaly (11%; n=10/95). The median age of symptom onset was day of life (DOL) 2 (IQR: 0-14) (n=65). Median age at diagnosis was DOL 14.5 (IQR: 5-32) (n=36). The median time from initial evaluation to initiation of HLH therapy was 8 days (IQR: 3-14) (n=22).

The median number of diagnostic criteria met by patients were 5/8 (IQR: 4, 6) (n=95). Diagnostic criteria were present in patients in the following frequencies: fever 83% (n=57/69); splenomegaly 97% (n=85/88); pancytopenia 63% (n=60/95); hypofibrinogenemia 83.6% (n=56/67); hypertriglyceridemia 48% (n=30/62); hemophagocytosis 81% (n=59/73); low/absent NK cell activity 94% (n=31/33); hyperferritinemia 99% (n=66/67); elevated soluble IL2R 91% (n=20/22).

Dermatologic manifestations were reported in 81% of cases (n=25/31). Liver injury (59%, n=38/65) and/or liver failure (31%, n=20/95) were common. CNS manifestations were frequently reported. Infections were reported in 20% of patients (n=12/59).

Discernable values for HLH diagnostic variables were reported between 23% (sIL2R) and 93% (organomegaly) of the time. Clinically relevant variables (e.g., CNS manifestations) often went unreported.

Conclusion: Fever and bicytopenia are not as common in neonatal familial HLH as in other age groups. Neurologic, dermatologic, and hepatic manifestations occur in the neonatal population. Current reports of nHLH suggest a grim prognosis. Future publications containing data on nHLH should report all clinically relevant variables. Studies looking at multiple patients in aggregate should provide supplemental information with detailed nHLH case description.

Poster # 772

REFRACTORY JUVENILE XANTHOGRANULOMA OF THE MASTOID BONE IN A CHILD WHICH RESPONDED TO TRAMETINIB

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Background: Juvenile xanthogranuloma (JXG) is a clonal non-Langerhans cell histiocytic disorder characterized by a variety of cutaneous and non-cutaneous manifestations, predominantly in children. The mitogen-activated protein kinase pathway (MAPK) is a key driver in many histiocytic disorders, including JXG.

Objectives: We report the case of a boy with refractory JXG which responded to trametinib.

Design/Method: A 6-year-old boy presented with a three-month history of a painless, left mastoid mass. He had two previous curettage procedures and antibiotic courses under the care of an otolaryngologist for presumed mastoiditis with no improvement. A biopsy was obtained during the 2nd procedure, and he was diagnosed with JXG. His physical exam at presentation was notable for a firm nontender left mastoid mass and several small papular lesions over his trunk previously diagnosed as molluscum contagiosum. At presentation, he had developed unilateral hearing loss from local tumor invasion and required a hearing aid. After the second surgery, the lesion grew back within several weeks, and demonstrated invasion into the skull base, so he was initiated on Langerhans cell histiocytosis (LCH)- based therapy using intravenous vinblastine and oral prednisone. The lesion remained stable initially but began to grow on therapy by the end of the first year, so he was changed to

clofarabine monotherapy. The lesion grew through 2 cycles of clofarabine, so he was switched to the oral MEK-inhibitor trametinib at 1mg per day. Molecular testing of the tumor showed low level mosaic chromosome loss but did not reveal any aberrant mutations in the MAPK pathway, including negative BRAF V600 alteration testing by PCR, and no other alterations in the MAPK pathway detected on next-generation screening. The dose was escalated to 2mg/day for optimal benefit which he tolerated with minimal cutaneous side effects.

Results: Subsequent CT scans showed no growth in the lesion and remodeling of the bone. He continued on trametinib for a total of 18 months when it was stopped because of stable appearance of the mass on CT. He is now 20 months off therapy and his imaging and physical exam remain unchanged, as does his hearing loss.

Conclusion: Trametinib was well tolerated by our patient and was effective in stabilizing the JXG lesion, despite it having no identifiable MAPK pathway mutation. Trametinib should be considered in treating patients with JXG if other systemic LCH therapy fails, even if they do not have a targetable mutation.

Poster # 773

SOMATIC MAP2K1 VARIANT DRIVER IN A CHILD WITH ROSAI-DORFMAN-DESTOMBES DISEASE AND VASCULAR ANOMALY

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Background: Somatic activating mutations in oncogenes, particularly of the mitogen-activated protein kinase (MAPK/MEK) pathway, are the most common cause of isolated, sporadic arteriovenous malformations (AVMs). The MAPK/Extracellular Signal-regulated Kinases (ERK) signaling node can function as a pro-oncogenic signal when normal tight regulation is disrupted. MAPK alterations have also been implicated in Rosai-Dorfman-Destombes disease (RDD), a rare non-Langerhans cell histiocytosis characterized most commonly by massive cervical lymphadenopathy with potential for extranodal organ system involvement. Histologically, RDD presents with large, pale histiocytes positive for S100, CD68, and negative for CD1a on immunohistochemistry. Here we report the first case, to our knowledge, of an individual with a vascular malformation and a histiocytic neoplasm both caused by the same somatic mutation.

Objectives: Report a case of RDD and vascular anomaly in a child with a common MAP2K1 variant driver

Design/Method: Case report and review of the literature

Results: The patient is a 5-year-old male who initially presented at age 1 year with cervical lymphadenopathy and normocytic anemia. Physical exam was also significant for hypertrophy and vascular lesions of the left upper and lower extremities, confirmed by magnetic resonance imaging (MRI) to be AVMs. Excisional biopsy of the lymph node revealed RDD. At age 4 he had recurrence of cervical lymphadenopathy and underwent a second excisional biopsy showing RDD. Somatic molecular analysis revealed a recurrent pathogenic MAP2K1 variant (NM_002755:c.169A>G, p.Lys57Glu). Biopsy with molecular analysis of the cutaneous vascular lesion identified the same MAP2K1 gene variant,

present at an allele fraction of 5%. Germline whole exome sequencing was negative for the MAP2K1 variant. At age 5 he had a second recurrence of cervical lymphadenopathy. MRI showed left lower extremity intramedullary foci, concerning for skeletal involvement. He was treated with sirolimus but developed toxicity and showed no response. He enrolled on a clinical trial of cobimetinib, an oral MEK inhibitor (NCT04079179).

Conclusion: This is the first case report of a patient with multiple neoplastic conditions with a common MAP2K1 genomic driver. The MAPK pathway is known to play a role in maintaining normal cellular activity and alteration of genes along the pathway may result in over-activation and/or loss of tumor suppression. In this case a mutation of MAP2K1 caused both a lymphoproliferative disorder, RDD, and AVM in a child. A targeted therapeutic approach with MEK inhibition is being pursued on a clinical trial.

Poster # 774

CONGENITAL MULTI-SYSTEM LANGERHANS CELL HISTIOCYTOSIS RESPONDING TO TARGETED THERAPY WITH TRAMETINIB

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Background: Langerhans cell histiocytosis(LCH) results from the clonal proliferation of dendritic cells, harboring recurrent genomic alterations in the mitogen-activated protein kinase(MAPK) pathway. This disease is rare and seldom presents at birth, usually as a cutaneous self-limiting disease. Thymic involvement is also rare, reported in only 2.6% of LCH cases.(1) Traditionally, LCH has been treated with cytotoxic chemotherapy regimens, which along with its multitude of adverse effects, have proven to have limited efficacy in multi-system disease with >50% of patients requiring more than one cycle of treatment.(2) Since the discovery of driving genetic alternations in the MAPK pathway, efforts have been undertaken to treat LCH patients with targeted therapy such as MEK inhibitor, trametinib. Targeted therapy offers the opportunity of improving patient outcomes without the toxicities of chemotherapy.

Objectives: We report a male infant with congenital multisystem LCH(MS-LCH) due to an activating mutation (p.Q56P) in *MAP2K1*, who responded dramatically to first line use of trametinib.

Design/Method: Medical records of the patient were reviewed and discussed at Cook Children's Medical Center's Precision Medicine Clinic meeting to study the molecular profile of this case and identify different treatment options.

Results: At the time of delivery, this male neonate presented with a widespread rash. LCH was diagnosed at 4 days of life, following a skin punch biopsy. At 1 month of life, cutaneous lesions worsened, prompting trametinib to be started immediately and PET-CT revealed thymic involvement as well as intense radiotracer uptake in the tongue. The patient experienced significant regression of widespread rash within 1 week of treatment. Repeat PET-CT at 4 months of life re-demonstrated thymic findings as well as an astounding decrease in uptake in the tongue. Additionally, at the time of the second scan, the skin manifestations had resolved, leaving only a miliary rash on the forehead. The last follow up marked 6 months of treatment with trametinib, and no skin manifestations or symptoms indicating disease progression along with no signs of medication intolerance were found.

Conclusion: This case serves as an addition to the limited literature on the seldom seen congenital and thymic LCH. With the administration of trametinib, this infant was able to completely avoid the numerous toxicities of chemotherapy, and achieve complete and sustained remission. The dramatic efficacy of MEK1/2 inhibition in MS-LCH further supports the change in treatment from cytotoxic chemotherapy regimens to front-line use of targeted therapy with trametinib.

1.Ducassou,*Ped Blood & Cancer*,2013
2.Allen,*N Engl J Med*,2018

Poster # 775

MULTI-SYSTEM LANGERHANS CELL HISTIOCYTOSIS PRESENTING WITH CO-MORBID PRENICIOUS ANEMIA

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Background: Langerhans Cell Histiocytosis (LCH) is a neoplastic clonal expansion of myeloid precursors that differentiate to CD1a+/CD207+ mononuclear cells with a highly variable clinical phenotype. In multisystem-LCH (MS-LCH), liver, spleen and/or bone marrow are considered “risk organs”, with risk organ involvement (RO+) necessitating more intensified systemic treatment due to higher rates of reactivation. In adults, higher rates of autoimmune conditions are correlated with LCH, suggesting LCH-associated autoimmunity possibly arising from broader immune dysregulation. The association of LCH and autoimmunity has not been described in pediatrics, but case reports of distinct autoimmune entities are described. Here, we present a pediatric case of MS-LCH presenting with antibody-positive pernicious anemia.

Objectives: To report a case of MS-LCH presenting with co-morbid pernicious anemia.

Design/Method: Case Report.

Results: A previously healthy 16-month-old girl presented with weight loss, rash, fevers, night sweats, diarrhea and emesis. On admission she had macrocytic anemia (hemoglobin 4.5 g/dL, MCV 87 fL), thrombocytopenia, hypoalbuminemia, and hyperbilirubinemia without leukopenia/neutropenia. A bone marrow aspirate and biopsy demonstrated normocellular marrow with trilineage hematopoiesis without abnormal blasts. Additionally, prominent hemophagocytosis was present with negative CD1a staining. Imaging demonstrated hepatosplenomegaly, a mandibular and multiple calvarial lytic lesions. A fine needle aspiration of the mandibular lesion demonstrated CD1a and S100 positive histiocytes with tumor genetic testing isolating a solitary BRAFV600E mutation. Concurrently, a skin biopsy was positive for CD1a, langerin and BRAFV600E. All results were consistent with MS-LCH. Evaluation of the macrocytic anemia demonstrated undetectable vitamin B12, normal methylmalonoic acid and low homocysteine. Intrinsic-factor (IF) blocking antibody was positive, solidifying the diagnosis of anti-body positive pernicious anemia. She began chemotherapy and intramuscular vitamin B12, which normalized her hemoglobin and MCV. Presently, she is receiving third-line salvage chemotherapy due to refractory disease but is now in clinical remission. She cleared her IF-blocking antibodies 12 months after diagnosis, but continues on parenteral vitamin B12 supplementation.

Conclusion: MS-LCH is an elusive diagnosis which can mimic neoplastic, inflammatory, metabolic and infectious diseases. Pediatric MS-LCH has been documented with co-morbid autoimmune conditions including autoimmune hepatitis, Evan's syndrome and lupus. Some theories for the pathogenesis of LCH-associated autoimmunity include unbalanced inflammasome and dysregulated T-cell function secondary to neoplasia of the antigen presenting cell. Although the pathogenesis is unknown, this represents a unique case of co-morbid LCH and antibody-positive pernicious anemia. While uncommon, co-morbid autoimmune disorders should be considered in children presenting with MS-LCH.

Ahmed, Cureus, 2020
Tsuji, International Journal of Hematology, 2007
Robak, Leukemia and Lymphoma, 2002

Poster # 776

A RARE PRESENTATION OF FAMILIAL HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH)

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Background: Hemophagocytic Lymphohistiocytosis (HLH) is a rare life-threatening disease caused by dysregulation with excessive immune activation resulting in hyper-inflammation and multi-organ failure. Familial HLH, an autosomal recessive disorder, commonly presents in infancy (80% by two years of age). Despite various symptoms, many manifest fevers, splenomegaly and cytopenias. We present a patient with a unique constellation of symptoms and complicated diagnosis of Familial HLH.

Objectives: Review a rare presentation of Familial HLH.

Design/Method: Case report obtained by comprehensive chart review.

Results: The patient is a 12-year-old female, with Usher Syndrome in the setting of MYO7A mutation, right sided conductive hearing loss, cerebellar atrophy, retinal vasculitis, growth hormone deficiency resulting in short stature with poor weight gain, hyperlipidemia, and splenomegaly referred to Connecticut Children's Hematology for evaluation of mild pancytopenia. Due to fluctuating then worsening pancytopenia, bone marrow biopsy was performed which revealed marked fibrosis, abnormal T cell population with cytotoxic T cells expressing CD57 consistent with large granular T cells, and mild elevation of double negative T cells at 2.1% in the setting of lymphopenia suggestive of Autoimmune Lymphoproliferative Syndrome (ALPS). Next Generation Sequencing was positive for 2 variant mutations in the FAS gene associated with Somatic ALPS. ALPS testing showed normal B12 level, elevated IL18 3473 pg/mL, IL10 110 pg/mL and soluble FAS ligand 1102 pg/mL. Although the patient did not meet all ALPS criteria, she initiated ALPS-like therapy with Mycophenolate and prednisone due to clinical decline with worsening pancytopenia, severe splenomegaly impacting nutrition, and progressive pericardial effusion. The patient demonstrated a good response to MMF and prednisone with normalization of CBC and resolution of pericardial effusion.
Given her complex medical history, whole genome sequencing was performed that revealed compound heterozygous variants in UNC13D gene (maternal c.1241G>T p.R414L, paternal c.751C>T p.Q251), associated with Familial HLH. HLH testing revealed absent NK function, elevated Soluble IL2R 27,627

U/mL, Soluble IL2Ra 42,700 pg/mL, CXCL9 94,443 pg/mL, Triglycerides 248 mg/dL, normal Ferritin 319 ug/L, and Fibrinogen 159 mg/dL. Given her underlying UNC13D mutations, a plan was made to transition the patient to HLH therapy that included Ruxolitinib followed by an allogenic stem cell transplant.

Conclusion: Patient exhibited a unique constellation of symptoms and complex presentation with mixed Familial HLH and ALPS based on genetic evaluation. Her UNC13D mutation associated with Familial HLH may have predisposed her to develop somatic ALPS secondary to the vulnerability of her immune system.

Poster # 777

A RARE CASE OF HLH AND CONCURRENT TTP IN A PEDIATRIC PATIENT WITH AN ACQUIRED STAT5B MUTATION.

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Background: Hemophagocytic lymphohistiocytosis (HLH) and thrombotic thrombocytopenic purpura (TTP) are rare, life-threatening diseases with unrelated pathophysiology. STAT 5b is a universal transcription factor implicated in immunodeficiencies, autoimmune diseases, cancers, and hematological diseases. STAT5b mutations have never been implicated in the pathogenesis of either TTP or HLH. There are rare case reports of TTP co-occurring with HLH, even less in the pediatric population; no reports of either HLH or TTP have yet involved a patient with STAT5b mutation.

Objectives: We report a 14-year-old male with episodic immune dysregulation meeting criteria for HLH, with concurrent TTP, found to have an acquired STAT5b mutation.

Design/Method: A retrospective chart review was completed.

Results: A previously healthy 14-year-old Haitian male presented with fever, headache, and MRI findings of multi-organ inflammation and lymphadenopathy. He was diagnosed with MIS-C (COVID PCR negative, IgG positive), and treated with IVIG, high-dose steroids, low-dose aspirin, and enoxaparin, with symptom resolution before discharge.

He presented two months later with fever, headache, and generalized abdominal pain. Notable findings included CRP 134 mg/dL, ESR 59 mm/hr, Uric acid 7.1 mg/dL, LDH 751 U/L, with splenomegaly measuring 12.8cm, and worsening lymphadenopathy, including enlarged supraclavicular lymph nodes bilaterally. Lymph node biopsy revealed hyperplasia and reactive lymphocytes. Flow cytometry and PET MRI were negative for malignancy. He improved with supportive care before discharge.

Three months later, he developed four days of fever with acute shock. Notable findings included marked hepatosplenomegaly (21cm and 15cm, respectively), WBC 23 K/UL, Hgb 6.7 g/dL, platelets 7 K/UL, ferritin 6,200 ng/mL, and stable lymphadenopathy. He developed hematochezia followed by cardiac arrest due to hypoxemia and bradycardia. Two rounds of CPR resulted in ROSC. He was intubated, sedated, and given vasopressors and blood products. He met the diagnostic criteria for HLH and was treated with dexamethasone, ruxolitininb, and anakinra. He was treated for suspected TTP with

therapeutic plasma exchange. Subsequent ADAMTS13 activity level was <0.03 IU/mL, confirming the diagnosis of TTP; caplacizumab was added. Biopsies of the liver, abdominal lymph nodes, and bone marrow showed no malignancy or other abnormalities. Genetic testing was remarkable for an acquired STAT5b mutation (N642H). He improved with ruxolitinib and aggressive supportive care, and was discharged home.

Conclusion: To our knowledge, this is the only report on a pediatric patient with concurrent HLH and TTP who survived. In addition, his acquired STAT5B mutation has yet to be associated with either HLH or TTP.

Poster # 778

NON-IMMUNE HEMOLYTIC ANEMIA AT PRESENTATION IN A PEDIATRIC PATIENT WITH HISTIOCYTIC SARCOMA

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Background: We report a 12-month-old female with non-immune hemolytic anemia, thrombocytopenia, and hepatosplenomegaly of unclear etiology, who was later diagnosed with histiocytic sarcoma.

Objectives: We report a unique presentation of a pediatric patient with histiocytic sarcoma.

Design/Method: We did a retrospective review of the medical record.

Results: We report a 12-month-old female, who on initial admission to the hospital presented with anemia (5.1 gm/dL), thrombocytopenia (75k/uL) and hepatosplenomegaly. Her white blood cell count was normal (12.1k/uL), but she had an elevated reticulocyte count (23%) and elevated indirect bilirubin (3.9 mg/dL). She had a negative direct Coombs test. Bone marrow biopsy and flow cytometry were negative for acute leukemia, showed 80% cellularity, and showed no dyserythropoiesis. There was concern for a non-immune hemolytic anemia, and a hereditary hemolytic anemia panel detected two variants of unknown significance in PIEZO1 and in SEC23B genes but had a negative osmotic fragility test. Bone marrow failure panel and primary immunodeficiency panel were significant for a pathogenic variant in the SLX4 gene which is associated with autosomal recessive Fanconi anemia. She required transfusions as an outpatient to maintain hemoglobin levels. The patient was admitted to the hospital at 16 months of age with anemia, worsening hepatosplenomegaly, diarrhea, and cervical lymphadenopathy. She underwent repeat bone marrow biopsy/aspirate along with lymph node biopsy and colonoscopy with biopsy. Flow cytometry showed a predominant myeloid phenotype but negative for acute leukemia. Next Generation Sequencing identified BRAF missense mutation from the bone marrow, gut and lymph node biopsies. Biopsies from colonoscopy and lymph node were diffusely positive for CD1a and S100. Langerin and BRAF staining showed patchy involvement. Patient also noted to be BRAFV600E positive by PCR in the serum. Gut biopsies confirmed malignant histiocytic neoplasm with closest subtype within the Langerhans' cell sarcoma phenotype. Skeletal survey was negative for bone lesions, but PET/CT showed disease in bilateral orbits, left occipital bone, cervical lymph nodes, bilateral maxillary sinuses, liver, and spleen. She started therapy with Clofarabine and Dabrafenib. Repeat MRI after 2 cycles of chemotherapy showed improvement in metastatic disease, hepatosplenomegaly, and resolution of her hemolytic anemia.

Conclusion: This case report highlights an extremely rare case of Langerhans cell sarcoma presenting as Coombs negative hemolytic anemia in an infant. Genetic mutations in PIEZO1 and SEC23B genes have been associated with hereditary stomatocytosis and congenital dyserythropoietic anemia respectively. Tumor sequencing confirmed BRAFV600E mutation. The non-immune hemolytic anemia resolved after initiation of chemotherapy.

Poster # 779

A CASE OF INFANT HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS PRESENTING WITH HEMOPHAGOCYTIC PANNICULITIS

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Background: Hemophagocytic lymphohistiocytosis (HLH) is a systemic immune hyperactivation syndrome characterized by multi-organ involvement that can rapidly progress and be life-threatening. Skin manifestations are variable, occurring in 6-65% of reported cases, with skin biopsies occasionally showing lymphocyte infiltration and hemophagocytosis.

Objectives: We report a case of secondary HLH in an infant who presented with minor flank trauma, later developing panniculitis and ulcerating skin changes, found to have lymphohistiocytic panniculitis with hemophagocytosis on skin biopsy, with subsequent biopsy findings consistent with subcutaneous panniculitis-like T cell lymphoma.

Design/Method: Case Report

Results: An 8-month-old female presented with mild trauma to left flank, with subsequent development of pain, skin changes, and persistent fevers. She was admitted locally in American Samoa, and found to have trilineage cytopenias, transaminitis, hepatosplenomegaly, and elevated ferritin. Infectious workup revealed RSV pneumonia, cellulitis, and presumed pyomyositis of the left latissimus dorsi treated with empiric antibiotics. Cytopenias resolved, but in outpatient follow-up she had ongoing hepatosplenomegaly, fevers, new ulcerating skin lesions and periorbital edema prompting referral to Seattle Children's Hospital (SCH) for further care.

On admission to SCH, she met 4 of 8 HLH-2004 diagnostic criteria with fever, elevated triglycerides, hyperferritinemia (20,026 ng/mL) and splenomegaly. She later met HLH-2004 criteria after developing anemia, thrombocytopenia, and elevated sIL-2R (47,061pg/mL). CXCL9 was later found to be markedly elevated (105,893pg/mL) while perforin, granzyme, and CD107a expression were normal, consistent with normal NK cell function. Bone marrow biopsy demonstrated hemophagocytosis without evidence of malignancy. Skin biopsy showed a lymphohistiocytic lobular panniculitis with focal hemophagocytosis; however, the features did not support a diagnosis of subcutaneous panniculitis-like T-cell lymphoma. Whole genome, mitochondrial and IKBKG long range sequencing studies were performed with no identifiable pathologic variants.

Therapy was initiated with anakinra, dexamethasone, IV immunoglobulin, and later emapalumab, with dramatic improvement in clinical stability, cytopenias, edema, and skin ulcerations. Inflammatory

markers normalized over the next 2 months. She was discharged on oral prednisone and ruxolitinib with weekly outpatient follow-up. One month into prednisone wean, she developed multiple new skin nodules, with repeat skin biopsy consistent with subcutaneous panniculitis-like T-cell lymphoma.

Conclusion: We present a case of an infant presenting with HLH and inflammatory skin changes, with subsequent biopsy demonstrating subcutaneous panniculitis-like T-cell lymphoma. Her course was managed with HLH targeted therapy, with improvement in clinical stability. This case report illustrates the benefit of upfront HLH-directed therapy, and the importance of close surveillance in patients without an identified genetic or clear secondary cause of HLH.

Poster # 780

10-YEAR-OLD WITH BLASTIC PLASMACCYTOID DENDRITIC CELL NEOPLASM

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Background: Blastic Plasmaccytoid Dendritic Cell Neoplasm (BPDCN) is an extraordinarily rare and aggressive neoplasm, especially within pediatrics. BPDCN often involves the skin, bone marrow, lymph nodes, and CNS. Given its rarity, there is no standard of care and there are no current clinical trials available for pediatric patients. We present a treatment approach of a 10-year-old with BPDCN.

Objectives: Review an approach to treatment of a 10-year-old with BPDCN.

Design/Method: Case report obtained by comprehensive chart review.

Results: A 10yo was referred to our clinic for a “hematoma” of the left thigh, which had grown, following minor trauma, over 1.5 years. The physical exam showed a large, round, raised, erythematous, warm, non-tender lesion on the lateral aspect of the left thigh (4.5x5cm), with left inguinal adenopathy. Left thigh MRI showed a heterogeneous mass of the anterolateral left thigh with left femoral/inguinal and external iliac adenopathy concerning for malignancy. Mass biopsy pathology showed a pattern of antigen expression, using flow cytometry, characteristic of BPDCN. Bone marrow biopsy and peripheral flow cytometry were negative for malignancy. PET showed lymphatic spread of disease, to bilateral inguinal and external iliac lymph nodes and paratracheal lymph nodes.

In collaboration with BPDCN experts, the patient initiated dual therapy with Bcell ALL High-risk induction therapy (per AALL1732), with Venetoclax, a BCL2-antagonist, that targets BPDCN’s BCL-2 antiapoptotic function. Following induction therapy, restaging imaging showed complete metabolic resolution of the primary tumor, with a partial response of the patient’s left and right inguinal lymph nodes. To direct the next stage of therapy, an excisional biopsy of the left inguinal lymph node was performed and was negative. Assuming remission at the end of induction, Bcell ALL High-Risk therapy was continued instead of transitioning to Tagraxofusp (targets CD123, expressed in all BPDCNs) with or without Venetoclax, followed by an allogenic stem cell transplant. Post-consolidation MRI showed complete resolution of the previously seen lymph nodes, and therapy was continued per Bcell ALL High-Risk protocol. The patient is currently undergoing delayed intensification and is tolerating treatment well with no evidence of disease recurrence.

Conclusion: A 10-year-old diagnosed with BPDCN was treated with high-risk Bcell ALL therapy (per AALL1732) and Venetoclax with a positive metabolic response. This treatment approach serves as an example for future cases of pediatric BPDCN, in which there is currently no standard of care.

Poster # 781

EPSTEIN-BARR VIRUS-ASSOCIATED HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS MIMICKING FOLLICULAR LYMPHOMA

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Background: Epstein-Barr virus (EBV)-associated lymphoproliferative diseases are a group of disorders involving one or more types of lymphoid cell types. EBV-lymphoproliferative disease include EBV-associated reactive lymphoid proliferations and EBV-associated B cell or natural killer/T cell lymphoproliferative diseases. Hemophagocytic lymphohistiocytosis (HLH) is a syndrome involving uncontrolled immune activity with macrophage activation. EBV commonly causes HLH. Furthermore, EBV-associated HLH and lymphoma are difficult to distinguish owing multiple overlaps between these two entities.

Objectives:

Design/Method: We report a case of EBV-associated HLH, mimicking disease recurrence, in a patient with follicular lymphoma (FL).

Results: A 13-year-old boy with FL was admitted for fever and neutropenia. The patient complained of shortness of breath. On physical examination, the patient had multiple enlarged cervical lymph nodes and hepatosplenomegaly. Two months before his visit, the patient was diagnosed with FL and underwent two cycles of chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisolone. Hematologic studies revealed a leukocyte count of 200 cells/μL, hemoglobin concentration of 9.9 g/dL, and platelet count of 55,000 platelets/μL. Blood chemistry revealed a triglyceride level of 374 mg/dL (reference value, 30–86mg/dL) and ferritin level of 3,290 ng/mL. Positron-emission tomography and computed tomography scan revealed an increase in the number of enlarged neck, chest, and abdominal lymph nodes with fluorine-18 fluoro-deoxy-glucose uptakes (SUVmax = 10.9). Diagnosed with recurrent FL on imaging, the patient underwent chemotherapy with cyclophosphamide, vincristine, prednisone, doxorubicin, high-dose methotrexate and rituximab.
A biopsy specimen was taken from the neck lymph node, and bone marrow examination was conducted to confirm the diagnosis. The biopsy revealed hemophagocytosis and scattered cells with a positive EB encoding region in situ hybridization. On immunohistochemistry, the sample was positive for CD3 and CD8, but negative for CD20 and CD56. The patient was diagnosed with EBV-associated HLH without recurrent FL. Following chemotherapy, the patient's symptoms resolved, and he was discharged.

Conclusion: We reported a case of EBV-associated HLH in a patient with FL. Distinguishing lymphoma progression from EBV-associated HLH is difficult. Therefore, a biopsy is required to confirm the diagnosis.

Poster # 782

A UNIQUE CASE OF CNS DIFFUSE, NON-SYSTEMIC ALK+ HISTIOCYTOSIS

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Background: Histiocytic disorders are a group of rare diseases with accumulation of macrophages, monocytes, or dendritic cells in various parts of the body. ALK-positive histiocytosis is a rare subtype of histiocytic neoplasm first described in 2008 that is very rarely described in pediatrics.

Objectives: To describe a unique clinical case that can contirubute to the literature and inform management in the future.

Design/Method: A 20 month old male presented to an adult hospital after a prolonged period of headaches, vomiting, and loss of developmental milestones. Imaging demonstrated severe hydrocephalus and extensive thickened leptomeningeal enhacement with mass effect and he subsequenrly underwent ventriculoperitoneal shunt placement and was transferred to Children's Hospital Colorado. He had a shunt replacement due to malfunctioning, T7-T10 laminectomy, and tumor debulking performed by neurosurgery. Extensive molecular testing, including DNA and RNA analysis by next generation sequencing (NGS) was performed and a *CLTC::ALK* fusion was identified, along with Tier III DNA variants, yielding a diagnosis consistent with ALK-Positive Histiocytosis, with diffusivity in the central nervous (CNS) system. Full evaluation demonstrated no involvement of the peripheral nervous system or other systemic involvement. He initially demonstrated signs of neuro-irritation and lower extremity clonus, consistent with upper motor neuron symptoms, but clinical stability and ability to start directed treatment.

Results: After review of very little literature publish on similar patients, although none with a clinical picture matching his, he was started on a treatment course of high dose dexamethasone, vinblastine, and lorlatinib, with the lorlatinib being directed an the ALK+ mutational status of his disease. On disease evaluation scans two months into treatment, he showed no change in his disease burden. He was subsequently transitioned to clofarabine cycles with daily lorlatinib for continued targetted therapy. After six total cycles, he demonstrates a high partial to complete remission (allowing for evidence of scarred tissue) and tremendous neurologic and developmental milestone gains.

Conclusion: This case demonstrates a unique presentation in which there is little described in the literature in way of clinical features or treatment standards, and further none exactly similar to this patient. After undergoing extensive evaluation and therapy modication, he responded remarkably well and continues to have optimal quality of life.

Solid Tumors (801-863)

Poster # 801

SYNERGISTIC TARGETING OF BCL-2 AND MCL-1 IN RHABDOMYOSARCOMA

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Background: Rhabdomyosarcoma, the most common sarcoma in childhood, presents substantial challenges, particularly for high-risk metastatic patients with limited therapeutic advancements. Recent genetic testing has revealed increased expression levels of pro-survival proteins, BCL-2 and MCL-1, in rhabdomyosarcoma cells. This elevation contributes to enhanced evasion of apoptosis, fostering cell growth and survival[1]. BH3 mimetics, a novel class of small-molecule anticancer drugs, offer specific targeting of these proteins. Venetoclax/ABT-199, a BCL-2 inhibitor, represents a pioneering approved agent for cancer treatment. Notably, concurrent inhibition of both BCL-2 and MCL-1 is often imperative to achieve optimal efficacy and circumvent resistance[2].

Objectives: This study aims to assess the responsiveness of rhabdomyosarcoma cells to BCL-2 and MCL-1 inhibitors, individually and in combination. Additionally, we seek to identify gene signatures associated with and predictive of sensitivity to these inhibitors, exploring potential synergistic effects.

Design/Method: Approximately 15 rhabdomyosarcoma cell lines, exhibiting varying expressions of BCL-2 family members determined through RNA-seq and immunoblotting, were screened for sensitivity to BCL-2 and MCL-1 inhibitors. The cells were treated with ABT-199, a known BCL-2 inhibitor, and MIK-665, a known MCL-1 inhibitor, both as single agents and in combination. Synergy was determined through grid serial dilution for combination therapy, evaluating cell viability with the CellTiter-Glo Luminescent Cell Viability Assay. Incucyte Live Cell Imaging System monitored cell death through YOYO-3 staining in real time.

Results: RNA-seq analysis revealed differential expression of Bcl-2 family genes in rhabdomyosarcoma tumors, identifying a subset expressing both anti-apoptotic BCL-2 and MCL-1, as well as apoptosis effectors BAX and BAK. Single-agent treatments (ABT-199 and MIK-665) demonstrated varied responses among cell lines, with some showing increased cell death. Notably, combining ABT-199 and MIK-665 exhibited synergy, resulting in enhanced cell death at lower concentrations.

Conclusion: Our findings indicate promising outcomes, particularly in specific subtypes of rhabdomyosarcoma cells, where simultaneous inhibition of BCL-2 and MCL-1 demonstrates synergy and increased cell death. These results could lead to further work with the possibility of new targeted treatment regimens for patients expressing these genetic changes with the hopes of improving patient outcomes.

Resources:

1. Kehr S, et.al., Cancer Letters, 2020
2. Oliveira RC, et. al., Explor Target Antitumor Ther, 2023

Poster # 802

DROSHA DEPENDENT PD-L1 UPREGULATION IN WILMS TUMOR AND INDUCIBLE PD-L1 EXPRESSION AFTER CHEMOTHERAPY

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Background: Wilms tumor remains the most common pediatric renal cancer, and accounts for approximately 6% of all childhood cancers. Of those patients, 20% have driver mutations in microRNA processing enzymes such as DROSHA. Most patients will be cured with standard therapies, but patients with high-risk features face significantly worse outcomes. Immune checkpoint inhibitors have been increasingly used in the treatment of many adult cancers, but this has not translated into the realm of pediatric cancer to the same extent. There is significant need for research to elucidate potential subpopulations within pediatric oncology that could benefit from immune checkpoint inhibition.

Objectives: Prior analysis of 102 DROSHA-mutant Wilms tumors from UT Southwestern and Sydney Children's Hospital showed higher levels of PD-L1. Interestingly, tumor samples from patients who had received chemotherapy prior to surgical resection showed higher PD-L1 expression compared to their chemotherapy-naive counterparts. We hypothesized that DROSHA loss will correlate with PD-L1 expression in Wilms tumor and that chemotherapy can itself induce PD-L1 upregulation. Our secondary aim was to identify the mechanisms by which PD-L1 expression is induced.

Design/Method: Analysis of DROSHA-mutant tumors was completed using reverse-phase protein arrays and RNA-seq. After DROSHA was knocked down in WIT49 Wilms tumor cells using CRISPR interference, PD-L1 expression was measured using qRT-PCR, Western blot, and flow cytometry. Flow cytometry was also used to measure PD-L1 expression after treatment with chemotherapeutic agents in WiT49 cells. This was repeated in 17.94 cells as well as neuroblastoma and rhabdomyosarcoma cell lines.

Results: In addition to finding higher PD-L1 expression in DROSHA-mutant tumor specimens, gene set enrichment analysis showed that eight of the top ten most enriched gene sets were inflammatory or immune-related. DROSHA-silenced cells showed increased levels of PD-L1 via qRT-PCR, Western blot and flow cytometry. Additionally, phosphorylation of IKK-a/b, AKT1, and STAT3 was found to be increased, indicating involvement of the JAK/STAT and NF-kB signaling pathways. Increased PD-L1 expression was also seen after treatment with either doxorubicin or vincristine, but not in cells treated with cyclophosphamide, irinotecan, temozolomide, or dactinomycin. Similar results were seen in the other tested cell lines.

Conclusion: Our data demonstrates PD-L1 upregulation in Wilms tumors driven by DROSHA mutations or treated with certain chemotherapy agents. These results suggest that combining conventional chemotherapy with checkpoint blockade could prove successful, even in childhood cancers that are initially immunologically quiet.

Poster # 803

CHARACTERIZING THE EXPANSION OF TUMOR-ASSOCIATED ANTIGEN T-CELLS TARGETING PEDIATRIC SOLID TUMORS

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Background: The treatment of pediatric solid tumors includes chemotherapy, surgery and radiotherapy. However, few options remain for children with relapsed/refractory malignancies. Chimeric Antigen Receptor (CAR) T cells have shown success for B cell malignancies, but has had limited success in pediatric solid tumors. Investigators in the Program for Cell Enhancement and Technologies for Immunotherapy have shown that multi tumor-associated antigen-specific T cells (TAATs) can target antigens expressed in pediatric solid tumors, including PRAME, a broadly and preferentially expressed tumor antigen of pediatric solid tumors, and enhance tumor-specific T cell responses in vivo and improve clinical outcomes in relapsed/refractory patients. These products and the process of generation have yet to be fully optimized. Therefore, we sought to characterize this novel therapy with the intent to enhance the potency of T cell therapy options for pediatric solid malignancies.

Objectives: Characterization of TAAT products, and the antigen presenting cells (APCs) used to stimulate them, is an important step in gathering foundational knowledge. In this study, we explored the phenotypes of these products to be used for relapsed/refractory solid tumors. We hypothesize that our novel manufacturing approach will produce polyclonal, multifunctional TAAT products with an activation phenotype for ultimate use as an "off-the-shelf" treatment for patients with solid tumors.

Design/Method: Peripheral blood mononuclear cells derived from healthy donors were cultured with a novel method for specificity to the tumor antigen PRAME. The APC and final T-cell products were grown under various cytokine conditions and collected for multi-channel flow cytometry. Panels were designed for appropriate detection and characterization of the populations' phenotypes. Patterns of expression were established through a T-lymphocytic gating strategy utilizing FlowJo software analysis.

Results: Preliminary results suggest that with this method, the APC population and TAAT product population express distinct markers. The APCs universally expressed both MHC classes and costimulatory moieties (i.e CD80, CD86) required for optimal antigen presentation, as well as ligands distinct to this protocol (41BB-L). Stimulation with these APCs resulted in PRAME specific TAATs with helper (CD4) and cytotoxic (CD8) phenotypes as well as novel markers for activation (T-bet, 88.1%) and exhaustion (TIGIT, 67.6%).

Conclusion: Characterization of TAATs and the APCs required for priming and expanding such products is crucial for the development of potent T cell therapeutics in the setting of pediatric solid tumors. Future plans will investigate correlation to clinical outcomes. Developing novel and potent TAATs will provide a useful foundation for future combination immune based therapies including CAR engineered TAATs.

Poster # 804

A MULTI-ASSAY LIQUID BIOPSY APPROACH TO IMPROVE DETECTION OF BONE AND SOFT TISSUE SARCOMAS

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Background: Bone and soft tissue sarcomas are among the most common extra-cranial solid tumors of childhood, yet advances in liquid biopsies lag behind what has been achieved across adult cancers. Solid

tumors that lack recurrent genetic mutations or translocations, such as bone and soft tissue sarcomas, are more difficult to detect in circulation using established assays, such as ddPCR.

Objectives: We have developed a pipeline to analyze cell-free DNA (cfDNA) using two molecular profiling techniques that we hypothesized would improve detection of circulating tumor DNA at diagnosis for patients with bone and soft tissue sarcomas.

Design/Method: cfDNA was isolated from plasma of patients with osteosarcoma (OS) (n= 36) and fusion-negative rhabdomyosarcoma (FN-RMS) (n= 7) at multiple timepoints. Methods for detecting tumor DNA in cfDNA included ultra-low coverage whole genome sequencing (ULC-WGS, 0.5x) and ultra-deep targeted sequencing (UDP, ~1000x) using a panel of 11 and 22 tumor-associated genes for OS and FN-RMS, respectively. ULC-WGS data underwent ichorCNA analysis to define percent tumor content of each sample. UDP analysis identified somatic variants through variant callers, Mutect2, Lancet, strelka, and DELLY2, with ClinVar to annotate and define tumor-specific variants in each sample. Combining ULC-WGS and UDP data, an integrated tumor score was developed and assessed in diagnostic samples.

Results: 136 OS and 30 FN-RMS cfDNA samples were collected during the patients' disease courses. Circulating tumor material was detected in 18/23 (78%) OS and 7/7 (100%) FN-RMS samples at diagnosis. The most frequent copy number aberrations were seen in the region of chromosome 8q containing the cMYC gene. cMYC amplification was found in 11/23 (48%) of diagnostic OS samples and 2/7 (29%) of diagnostic FN-RMS samples. UDP analysis identified variants in 17/23 (73%) and 7/7 (100%) of diagnostic OS and FN-RMS samples respectively. The most commonly detected variants included TP53, BRCA2, MET, and BRAF. Of the 23 diagnostic OS samples, four had TP53 translocations. The integrated tumor score detected the presence of tumor associated material within diagnostic samples with a sensitivity of 25/30 (83%), compared to the sensitivity of ULC-WGS or UDP alone, which was 15/30 (50%) and 24/30 (80%) respectively.

Conclusion: A multi-assay liquid biopsy has promise to improve disease detection and monitoring for patients with solid tumors that lack recurrent driver mutations. We plan to integrate additional molecular profiling technologies to improve sensitivity and specificity of our cfDNA assays and aim to adapt our pipeline across additional cancers.

Poster # 805

CHARACTERIZATION OF T-CELL POPULATIONS IN PEDIATRIC PATIENTS WITH OSTEOSARCOMA AND EWING SARCOMA

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Background: Advances in immune-checkpoint blockade and cellular therapies are rapidly altering our approach to treating several tumors. However, to date, these approaches have had minimal efficacy in pediatric solid tumors, in particular, osteosarcoma and Ewing sarcoma (ES).

Objectives: To characterize the immunophenotype of the peripheral blood in patients with osteosarcoma and ES to enable rational trial design moving forward.

Design/Method: In this IRB-approved study, peripheral blood was collected from pediatric and young adult patients with osteosarcoma, ES, and neurofibromatosis type 1 (NF1). NF1 patients with a Riccardi severity of 3 or less and no malignant tumors were utilized as a comparison group. Peripheral blood mononuclear cells (PBMCs) were isolated using a Ficoll density gradient and frozen for storage. At the time of analysis, PBMCs were rapidly thawed, washed, and stained for several immune markers. Samples were then run through a spectral flow cytometer and a minimum of 10,000 cellular events were obtained. Populations are reported as a percent of live cells unless otherwise noted. Two-sided Student's t-test was performed to determine significant differences between groups.

Results: Eight osteosarcoma, 15 ES, and 14 NF1 patient samples were analyzed. The patients in this study were 48.6% female and the median age was 14 (range 5-36). Patients with NF1 had more non-lymphoid cells (NF1 24%, ES 14.4% $p<0.05$, osteosarcoma 16% $p<0.01$) while patients with osteosarcoma and ES had more CD3+ cells (69% and 67%) compared to NF1 (57%, $p = .005$ and $p=.03$). This increase was driven by CD8+ T-cells (NF1 13%, osteosarcoma 27%, ES 20%, $p <.001$). There were significantly more T-regulatory cells (CD4, FoxP3+ and CD25+) in the patients with osteosarcoma (7.2% of CD4+ cells) and ES (6.4%) compared to NF1 patients (1.1%, $p <.001$ for both). CD8+ T-cells in osteosarcoma and ES expressed higher levels of the activation marker CD69 (NF1 1.0%, osteosarcoma 25% $p<0.01$, ES 20% $p<0.001$). CD8+ T-cells also expressed higher levels of T-cell exhaustion markers PD1 (NF1 3.9%, osteosarcoma 25% $p<0.001$, ES 10% $p<0.001$) and Tim-3 (NF1 0.1%, osteosarcoma 0.46% $p<0.05$, ES 2.0% $p<0.01$).

Conclusion: This data suggests an adaptive immune response is initiated in osteosarcoma and ES, however, these CD8+ T-cells become exhausted. Future cellular therapy and immunotherapy trials in should include approaches to combat this exhaustion. The limitations of this study include a relatively small sample size, a high number of patients with recurrent disease, an arbitrary comparison group, PBMCs collected a various time points, and no tumor tissue.

Poster # 806

INTEGRATED WHOLE GENOME, TRANSCRIPTOME AND GERMLINE ANALYSIS IN PEDIATRIC POOR PROGNOSIS CANCERS

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Background: Although increasingly accessible, the role for routine integration of whole genome and transcriptome analysis (WGTA) for poor prognosis pediatric cancers remains undetermined.

Objectives: We aimed to determine feasibility, clinical actionability and utility of WGTA in a pediatric poor prognosis pan-cancer cohort.

Design/Method: Children and adolescents with relapsed, refractory, or poor prognosis (predicted overall survival <30%) malignancies underwent somatic WGTA and matched germline sequencing. We

characterized somatic mutations, structural rearrangements, copy number variants, gene expression, immuno-profiles and germline cancer predisposition variants. Clinically actionable variants were annotated by levels of evidence, and outcomes of molecularly informed therapies were described.

Results: Seventy-nine participants with a median age at enrollment of 8.8y (range 6 months to 21.2y) were included. Participants were enrolled within one month of diagnosis in 33% of cases and 70% of samples were obtained at the time of a clinically indicated procedure. The 2-year event-free and overall survival from the time of enrollment was 28.6 ± 10.0% and 48.5 ± 11.2%, respectively, with a median time to progression of 6.1 months. Germline pathogenic/likely pathogenic variants were identified in 12% of participants, of which 60% were newly identified. High immune presence (>80th percentile in the cohort) as inferred by CIBERSORT deconvolution of RNA data to derive immune scores was observed across a range of tumor types including tumors with SMARCB1/A4 loss (chordoma, rhabdoid tumors), neuroblastoma, rhabdomyosarcoma and osteosarcoma, and high grade CNS tumors. Therapeutically actionable variants were identified by targeted gene report and whole genome in 32% and 62% of participants, respectively, and increased to 96% after integrating transcriptome analyses. Thirty-two molecularly informed therapies were pursued in 28 participants with 54% achieving a clinical benefit rate, objective response, or prolonged stable disease (≥ 6 months). Among 32 therapies pursued, 11 were based on RNA evidence only while 14 were supported by combined DNA and RNA alterations. Four of nine patients assessed for response to therapies based on RNA evidence alone achieved benefit while 6 of 12 patients benefited from therapies based on combined DNA/RNA evidence.

Conclusion: Integrated WGTA for children with poor prognosis cancer identifies previously unknown germline cancer predisposition variants facilitating access to cancer surveillance and cascade testing for family members at risk. Beyond next-generation panel sequencing approaches, the integration of whole genome and transcriptome data can identify therapeutically actionable variants in almost all cancers and these can directly inform and benefit clinical care.

Poster # 807

TARGETING GLYCOGEN METABOLISM AS A POTENTIAL THERAPY FOR EWING SARCOMA

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Background: Approximately half of patients with Ewing sarcoma will develop recurrent or metastatic disease, of these patients <20% long-term survival. Standard of care treatment includes multi-modal approach of chemotherapy with surgery and/or irradiation. A feature of EWS is accumulation of large glycogen-like granules, Periodic Acid-Schiff (PAS) aggregates. Glycogen is a macro-metabolite with multiple roles within cells ranging from metabolism, signaling, to epigenetic regulation. Aberrant glycogen metabolism is known to drive pathogenesis in multiple neurodegenerative diseases and some cancers. Glycogen is synthesized by glycogen synthase1 (GYS1) and glycogen branching enzyme, and broken down by glycogen debranching enzyme, laforin, and glycogen phosphorylase. Despite its vast physiologic and emerging clinical significance, the lack of sensitive tools to assess glycogen has prohibited the understanding of glycogen's impact on disease progression. To overcome this limitation, the Sun and Gentry laboratories developed a robust workflow utilizing matrix-assisted laser desorption/ionization mass spectrometry imaging (MALDI-MSI) of complex carbohydrates, a spatial

technique to visualize and quantify glycogen *in situ* using formalin-fixed paraffin-embedded tissue samples. Glycogen metabolism is regulated by AMP-activated protein kinase (AMPK), which is a well-known tumor suppressor. AMPK is up regulated by metformin and thus there are currently in phase 1 and 2 clinical trials using metformin as an additive treatment

Objectives: Evaluate the therapeutic potential of targeting glycogen in EWS by reducing glycogen levels in EWS cells (A673, TC71, TC32) using both genetic (CRISPR-Cas9) and pharmacological (guaiacol) interventions of multiple glycogen metabolism enzymes.

Design/Method: A cohort of EWS patient tumors samples were analyzed using MALDI-MSI. Analysis demonstrated spatial glycogen accumulation dramatically higher in intra-tumoral regions for all EWS samples compared with surrounding tissues and most other cancers. In cancer patients, high-glycogen accumulation with high GYS1 expression have a significantly longer overall survival than those with low GYS1 expression *($p < 0.05$)*; whereas no significant impact of GYS1 was observed in low-glycogen accumulation patients' overall survival.

Results: Our preliminary data demonstrates the high glycogen levels in EWS inhibit AMPK which overrides the action of metformin. Excitingly, we found by reducing EWS glycogen levels via targeting glycogen synthase (*GYS1*) in A673 cells synergizes metformin action in activating AMPK therefore limiting proliferative and clonogenic ability of these cells.

Conclusion: Moving forward, we plan to systematically test GYS1 inhibitors as a single agent, and in combination with metformin in patient-derived xenograft or cell line-derived xenograft EWS models to carefully evaluate efficacy and toxicity for the future planning of translation studies/clinical trials in patients with EWS.

Poster # 808

BENZYL GUANIDINE AND NOREPINEPHRINE TRANSPORTERS: CLOSING THE DATA GAP

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Background: Over 90% of neuroblastomas overexpress norepinephrine transporter (NET), which is a target for meta-iodobenzylguanidine (mIBG), a norepinephrine analog that can be radiolabeled for imaging and therapeutic applications. Limited sensitivity and quantification of SPECT imaging with [^{123}I]mIBG and the long half-life of [^{124}I]mIBG on PET imaging have prompted the development of the alternative PET imaging agent, [^{18}F]meta-fluorobenzylguanidine ([^{18}F]mFBG). The relationship between [^{18}F]mFBG uptake and NET tissue expression is currently unknown, and we hypothesize that there will be a correlation between histological NET expression and [^{18}F]mFBG uptake in vivo, as measured through imaging.

Objectives: This study aims to investigate the relationship between [^{18}F]mFBG uptake in vivo, as seen on PET imaging in rats, and tissue expression of NET and VMAT2, another catecholamine transporter that also displays affinity for norepinephrine and its analogs. We also aim to define how a NET enhancer or inhibitor co-administered with [^{18}F]mFBG affects its avidity on PET scan.

Design/Method: We used 150-250g Sprague Dawley rats. Control animals (n=9) received [^{18}F]mFBG immediately prior to a 20 minute dynamic PET scan followed by a 10 minute attenuation CT. Similar imaging experiments were performed with a NET expression enhancer (n=6), 10 mg/kg IV vorinostat, and a NET expression blocker (n=6), 1 mg/kg IV desipramine, with both drugs administered 20 minutes prior to [^{18}F]mFBG. After imaging, animals were euthanized and the heart, lungs, liver, adrenal glands, salivary glands, and thyroid were extracted for immunohistochemical (IHC) staining of NET and VMAT2. Samples will be analyzed by a veterinary pathologist for intensity of staining and % of cells stained.

Results: Preliminary qualitative results indicate high [^{18}F]mFBG uptake in the tissues that we are using for histological analysis, with generally higher uptake in the animals that were administered vorinostat, and generally lower uptake in the animals that were administered desipramine. NET and VMAT2 tissue expression was present in adrenal glands of three control animals, with additional analyses ongoing.

Conclusion: Initial in vivo imaging analysis demonstrates NET-dependent [^{18}F]mFBG uptake, including in the adrenal glands, which also have high NET and VMAT2 expression on histological analysis. Next steps in preparation for clinical application of [^{18}F]mFBG include defining the effects of NET enhancers and inhibitors on [^{18}F]mFBG uptake, as well as the relationship between [^{18}F]mFBG uptake and NET expression in tumor tissue in patients with neuroblastoma. This study aids in determining if [^{18}F]mFBG PET imaging has potential to improve diagnostic imaging and outcomes in neuroblastoma.

Supported by a grant from Innervate Radiopharmaceuticals.

Poster # 810

NEOADJUVANT TO SURGERY INTERVAL EFFECTS ON TUMOR NECROSIS AND OUTCOMES IN PATIENTS WITH OSTEOSARCOMA

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Background: Optimal osteosarcoma treatment includes chemotherapy and surgery. In ideal cases, resection of the primary tumor occurs within two weeks of completion of neoadjuvant chemotherapy. However, scheduling challenges and medical complications can result in delay. Tumor necrosis is determined by pathological analysis of the surgically removed tumor specimen and has been well defined as a prognostic variable.

Objectives: The goal of this study is to determine if delay between completion of neoadjuvant therapy and primary surgical resection correlates with decreased tumor necrosis and worse outcomes in children and young adults with osteosarcoma.

Design/Method: We conducted a retrospective chart review of 121 patients age less than 40 years diagnosed with osteosarcoma who were treated at Vanderbilt University Medical Center between 2000-2022. Inclusion criteria included the receipt of two cycles of neoadjuvant MAP (defined as 2 courses of cisplatin and doxorubicin and at least 2 but no more than 6 doses of methotrexate) and surgery performed at Vanderbilt. 92 patients met inclusion criteria and adequate records were available for 83 patients.

Results: There was no correlation between interval length between completion of induction chemotherapy and surgery with tumor necrosis. However, patients with a surgery interval greater than 16 days had worse outcomes as defined by 5-year event free survival (EFS), which was more pronounced in patients with initially localized disease ($p = 0.02$ for all patients, $p = 0.003$ for patients with localized disease). Multivariate analysis of patients with initially localized disease revealed that interval >16 days, tumor necrosis <90%, and positive surgical resection margins correlated with decreased 5-year EFS (HR = 3.86, $p = 0.0035$; HR = 4.01, $p = 0.010$; HR = 4.45, $p = 0.011$). Sex, age, tumor site, histologic subtype, and treatment year did not correlate with outcome. An interval >16 days was not significantly correlated with lower 5-year EFS when patients with metastatic disease at the time of diagnosis were included in the multivariate analysis.

Conclusion: Delays in local control were not associated with lower tumor necrosis. This is consistent with the hypothesis that tumor necrosis is a biologic marker of a tumor's sensitivity to chemotherapy and may not be significantly affected by minor regimen aberrations. However, surgical delay greater than 16 days from completion of induction chemotherapy conferred worse outcomes.

Poster # 811

INCIDENCE OF CHEMOTHERAPY-INDUCED THROMBOCYTOPENIA AND OUTCOMES IN PEDIATRIC SARCOMA PATIENTS

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Background: Thrombocytopenia is a well-established hematologic consequence of chemotherapy treatment. Chemotherapy-induced thrombocytopenia (CIT) is a significant contributor to treatment delays in the pediatric sarcoma population. Such deviations from scheduled chemotherapy regimens may have implications for adverse clinical outcomes.

Objectives: Evaluate the incidence, duration, and timing of chemotherapy cycle delay due to CIT. Determine if delays due to chemotherapy induced thrombocytopenia adversely affects outcomes.

Design/Method: We conducted a retrospective chart review of pediatric sarcoma patients treated at the University of Iowa from 2010 to the 2023. Patients were included if they had at least two years of follow-up from the end of treatment. Patients were stratified by initial staging (localized, malignant), chemotherapy regimen, and by outcome after treatment (remission, relapse/recurrence, and progression).

Results: A total of 82 patients were included in the analysis with a mean age of 11.2 years [0.2-18.5]. Diagnoses included Rhabdomyosarcoma (n=30), Ewing Sarcoma, (n=26), Osteosarcoma (n=19), and other sarcomas (n=7). The total incidence of cycle delays due to CIT was 14.0% and accounted for 42.4% of total cycle delays. Patients with localized (n=61) vs metastatic (n=21) sarcomas had an average of 1.4 and 2.8 (p = 0.11) cycle delays per regimen due to CIT for an average total duration of 10.7 and 22.1 (p = 0.04) days per regimen respectively. Patients who remained in remission (n=45), relapsed (n=23), and progressed (n=14) had an average of 2.3, 1.7, and 1.6 (p = 0.59) cycle delays per regimen due to CIT for an average total duration of 14.2, 15.8, and 13.6 (p = 0.93) days per regimen respectively. The incidence

of cycle delays due to CIT was 3.2%, in cycles 1-4, 16.0% in cycles 5-8, 26.9% in cycles 9-12, and 33.3% in cycles 13-16.

Conclusion: The overall incidence of cycle delays due to CIT was 14.0%. The incidence of cycle delays due to CIT differed by chemotherapy regimen and increased throughout the duration of chemotherapy treatment. Patients who presented with metastatic disease had longer duration of delays due to CIT compared to patients with localized sarcomas. The number of cycle delays or duration of delays due to CIT were not associated with any adverse outcomes.

Poster # 812

CYCLOPHOSPHAMIDE AND TOPOTECAN CHEMOIMMUNOTHERAPY IN MULTIPLY RELAPSED/REFRACTORY NEUROBLASTOMA

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Background: High-risk neuroblastoma has been historically challenging to treat with high relapse rates and poor survival outcomes. Recent advances in treatment and incorporation of GD2-directed immunotherapy have improved outcomes. However, a significant percentage of patients remain who experience relapse or refractory disease. The use of chemoimmunotherapy in the relapsed/refractory neuroblastoma setting was evaluated in the randomized Children's Oncology Group clinical trial ANBL1221, showing significant antitumor activity with the combination of a chemotherapy backbone including irinotecan and temozolomide with sargramostim and dinutuximab. At second or greater relapse following ANBL1221-like therapy, combination of dinutuximab with other chemotherapy backbones is often utilized, but little information is published regarding safety and efficacy of these regimens. Evaluation of optimal chemotherapy dosing and toxicity is critical to guide treatment selection in a heavily pre-treated population.

Objectives: To characterize the safety and efficacy of non-irinotecan/temozolomide based chemotherapy regimens in combination with dinutuximab for relapsed/refractory neuroblastoma

Design/Method: A retrospective cohort study was conducted for patients aged 0–24 years who received dinutuximab and chemotherapy for relapsed high-risk neuroblastoma treatment from 2018–2022. Cycles containing ANBL1221-like therapy with irinotecan and temozolomide or treatment received at an outside hospital were excluded. An exemption designation from the Institutional Review Board (IRB) was obtained. Data were extracted from the electronic medical record. Baseline demographics, tumor specific information such as MYCN and ALK status, chemotherapy dosing, and adverse effects were collected. 1-year overall (OS) is reported from the start of the first cycle of non-irinotecan/temozolomide chemoimmunotherapy.

Results: Thirty-three patients were identified, and 10 met inclusion criteria. Median age at time of relapse was 6.5 years (range: 2.4-23.6 years), and 50% were female. All included patients (100%) had previous exposure to GD2 therapy and were treated with a relapsed chemoimmunotherapy backbone containing cyclophosphamide 250–400 mg/m^2 and topotecan 0.75–1.2 mg/m^2 for 3–5 days with dinutuximab 17.5 mg/m^2 for 4 days. Dose modifications occurred in 30% of patients. Treatment resulted in 10% complete response, 40% stable disease, and 40% progressive disease with median time to

progression of 5.0 months (range: 0.9–8.4 months). Median number of cycles received was 3.5 (range: 1–16). 1-year OS was 60%. Most common adverse effects were hematologic, with 90% of patients experiencing ≥ grade 3 neutropenia and thrombocytopenia.

Conclusion: Dinutuximab with cyclophosphamide/topotecan maintains treatment responses in multiply relapsed neuroblastoma despite previous GD2-directed treatment exposure and may be considered as a treatment option following ANBL1221-like therapy with chemotherapy dosing selection balancing quality of life and treatment toxicity.

Poster # 813

END OF INDUCTION RESPONSE CORRELATES WITH CLINICAL OUTCOME IN HIGH-RISK NEUROBLASTOMA PATIENTS

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Background: High-risk neuroblastoma (HRNB) has an approximately 50% 5-year overall survival rate and presents a significant clinical challenge due to its heterogeneous nature and variable prognosis. The treatment paradigm for HRNB is complex and involves intensive multimodality therapy consisting of induction, consolidation, and post-consolidation phases. Clinical practice often uses disease status at end of induction (EOI) to guide subsequent treatment such as administering a bridge therapy prior to consolidation for patients with a poor EOI response.

Objectives: This study aims to assess the association between EOI response and long-term clinical outcomes in patients with HRNB, focusing on comparing Complete Response (CR) at EOI against all other response categories. This comparative analysis aims to elucidate the prognostic significance of achieving CR at EOI and its influence on the subsequent clinical trajectory of patients with HRNB.

Design/Method: We conducted a retrospective analysis of data from patients diagnosed with HRNB between January 1, 2013, and January 1, 2019, at Beat Childhood Cancer Research Consortium (BCC) participating institutions. All patients received 5-6 cycles of standard induction therapy per COG backbone. Disease status at EOI was classified according to the 1993 International Neuroblastoma Response Criteria and correlated with progression free and overall survival. Hazard ratios and associated p-values were calculated using a Cox model.

Results: Analysis of 460 patients with HRNB (145 CR and 315 non-CR at EOI) showed a significant survival advantage for patients with CR at EOI. Specifically, CR was associated with a 33.5% reduction in the risk of mortality (OS, HR = 0.665, p = 0.027) and a 30.7% reduction in the risk of relapse or death (PFS, HR = 0.693, p = 0.04) compared to non-CR.

Conclusion: The findings demonstrate the prognostic value of achieving CR at EOI in patients with HRNB. The notable improvement in both OS and PFS associated with CR at EOI underscores its potential as a surrogate endpoint in clinical trials. Establishing CR at EOI as a surrogate marker could expedite trial processes, accelerate regulatory approvals, and facilitate earlier access to effective therapies.

Poster # 814

COMPARISON OF NEUROBLASTOMA OUTCOMES BY STAGING METHOD – A GRAPHICAL REPRESENTATION USING A TIMELINE

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Background: Neuroblastoma, a solid malignancy originating from neural crest cells, is the most common pediatric extracranial solid tumor. Presentation and disease course vary greatly, with some cases regressing spontaneously, while others have disease with aggressive metastases resistant to intensive treatment. This wide range of presentations led to the creation of staging and risk stratification guidelines in an attempt to streamline diagnoses to guide research and therapy. Prior to 2009, neuroblastoma was staged with the International Neuroblastoma Staging System (INSS), a postsurgical staging system. In 2009, a pretreatment risk classification system was developed, the International Neuroblastoma Risk Group Staging System (INRGSS), eliminating the necessity of surgery for staging. In 2021, the Children's Oncology Group (COG) released a revised neuroblastoma risk classifier (version 2) that uses INRGSS and segmental chromosome aberrations to define pretreatment risk.

Objectives: We have developed a graphical timeline that tracks the treatment course of 83 neuroblastoma patients diagnosed starting in 2007, through 2023. The timeline allows easy comparison of risk classification using the various staging methods in use during this period.

Design/Method: Patient data was gathered from patients diagnosed with neuroblastoma at Penn State Hershey Medical Center between 1/1/07 and 12/20/23. The information collected included date of birth, date of diagnosis, INSS or INRGSS stage, risk classification, treatment given, and where applicable, date of resection, stem cell transplant, and death. The data is displayed in a 2-dimensional timeline. Using the timeline, we then compared outcomes based on the various staging systems.

Results: The timeline allows us to see our institutional experience with neuroblastoma at a glance, in order to propose and address intriguing research questions. For example, we have used the timeline to determine the concordance of risk groups using different staging systems, and to compare outcomes based on stage.

Conclusion: For 80 of our patients, there was sufficient clinical information to determine stage based on both the INSS and INRGSS systems. For 73 of these the risk was concordant (20 low, 15 intermediate, 38 high) and for 7 the risk group changed (4 low to intermediate, 2 intermediate to low, and 1 high to intermediate). Outcomes after 2009 are significantly improved compared to prior to 2009, especially in higher risk patients. Although the INRGSS facilitates staging, this improvement in outcome is more likely related to improvements in therapy rather than due to improvements in staging but discordant staging may have an impact.

Poster # 815

FEASIBILITY OF TREATING ADULTS WITH RHABDOMYOSARCOMA WITH PEDIATRIC CHEMOTHERAPY REGIMENS

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Background: Rhabdomyosarcoma is the most common pediatric soft tissue sarcoma. It is a malignant tumor arising from striated muscle. This cancer is much rarer in adults and characterized by a poorer prognosis compared to children. There is currently insufficient literature assessing outcomes using the standard pediatric regimen in the adult population, partly due to concerns regarding the ability of older patients to tolerate side effects related to chemotherapy. However, use of this pediatric regimen may confer a survival benefit in adult patients and was investigated in this study.

Objectives: The goal of this study was to perform a detailed descriptive analysis of pediatric and adult patients with rhabdomyosarcoma including tumor characteristics and treatment. We additionally evaluated overall survival and event-free survival, compared proportions of patients with dose reductions, and compared proportions of patients with toxicities by age group.

Design/Method: We performed a retrospective chart review of all patients at OHSU with embryonal or alveolar rhabdomyosarcoma. SlicerDicer was used to identify all patients with a diagnosis of rhabdomyosarcoma and a patient encounter from 1/1/2009 through 12/31/2021. 39 patients were included. We included six adults who received chemotherapy outside OHSU, for a total of 26 pediatric patients and 13 adult patients. Patients with a non-aRMS/eRMS diagnosis were excluded.

Results: The percentage of aRMS diagnoses was slightly higher in the adult group compared to the pediatric group (53.8% vs 46.2%). Adults were more likely to have tumors that were parameningeal or pelvic/GU in origin. Adult patients were more likely to present with metastases at diagnosis (30.8% vs 23.1%). Adults were more frequently in the high-risk group (30.8% vs 19.2%). In the adult treatment group, 84.6% completed their scheduled chemotherapy. 38.5% required a dose reduction and 69.2% had one or more doses held. Among the six adults with data on toxicities, the incidence of neutropenic fever was 33.3%. The proportion surviving at 5 years was 50.0% for the adult group and 65.7% for the pediatric group. The proportion event-free was 42.0% for the adult group and 63.8% for the pediatric group.

Conclusion: Adult patients were more likely to present with high-risk tumors in unfavorable sites or with metastases at time of diagnosis compared to children. Fusion status was similar between the two groups. Treatment modalities did not vary considerably between the adult and pediatric populations. Overall, the adults tolerated the pediatric chemotherapy regimens with few side effects resulting in dose reductions and holds.

Poster # 816

HIGH RISK HEPATOBLASTOMA TREATED WITH SIOPEL 3 HR : EXPERIENCE OF TERTIARY CARE CENTER FROM INDIA

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Background: Hepatoblastoma (HB) is a rare neoplasm of the liver, accounting for about 1% of all pediatric cancers. The outcome of hepatoblastoma (HB) include preoperative chemotherapy followed by complete anatomical resection of tumor, followed by chemotherapy.

Objectives: The objective of the present study is to report our experience with HBs over a period of four years from a tertiary centre in Central India

Design/Method: This is a retrospective observational study. The data of all patients who were diagnosed with HB between November 2019 and December 2022 was reviewed.

Results: Eleven patients who were diagnosed and treated for HB at our center were included in the study. Ten (90.9%) of them were male. The median age of presentation was 24 months(range 5-72). An abdominal distention (n=11, 100%) and abdominal pain (n=3, 25%) were the most common presenting symptoms. The median level of serum alpha-fetoprotein at the time of initial evaluation was 418973 (63-9,00,000) ng/dL. The fetal variant (n=54.5%) was the most common histological subtype. Zero (0%), 2 (16.6%), 6 (50%), and 4(33.33%) patient were found to have pre-treatment extent of tumor (PRETEXT) stages 1, 2, 3, and 4, respectively. One (9.09%) children were classified as standard risk and Ten (90.9%) children as high risk.
All the patients received neoadjuvant chemotherapy (NACT) followed by surgery. None of them had perioperative mortality. As local management two patients were advised liver transplantation but refused and later on developed disease progression .Two (16.6%) patients developed chemotherapy-related complications. One had relapsed and salvaged .The median duration of follow-up was 18 (range 5-35) months .With median follow up18 months EFS was 72% and OS 80%.

Conclusion: This study shows that the overall outcomes of HB are good with the adoption of multi-modality treatment. In LMIC delay in diagnosis and referral leads to widespread disease. Early referral and strengthening supportive care with availability of surgical facilities including liver transplant will greatly impact survival.

Poster # 817

NO BONES ABOUT IT: A PILOT STUDY OF BONE HEALTH IN CHILDREN WITH SOLID TUMORS

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Background: Pediatric solid tumor malignancies require aggressive multimodal therapy that may lead to acute and late bone health complications. It is unknown if bone health is impacted from time of diagnosis and throughout active treatment/early surveillance.

Objectives: Our aims are 1) to determine feasibility of completing bone health assessments with 2 predetermined criteria for success: ≥50% of eligible patients recruited and ≥75% of recruited patients completing all assessments; 2) to evaluate the usefulness of early bone health surveillance.

Design/Method: A prospective single institution pilot study including patients aged 1-21 years with high-risk neuroblastoma, osteosarcoma, Ewing sarcoma, or medulloblastoma within 3 years of diagnosis at Nationwide Children's Hospital from November 1st, 2022 through November 30th, 2023. Informed consent/assent was obtained via institutional protocol. Each patient had two study visits six months apart. Each study visit included a bone mineral density (BMD) by dual energy X-ray absorptiometry, serum vitamin D (25-OHD) level, physical therapy assessment, and patient/caregiver survey. Bone health screening data were assessed for vitamin D deficiency (25-OHD <20 ng/dL) or insufficiency (25-OHD 20-30 ng/dL), low BMD (Z-score < 2), fractures, and bone health interventions.

Results: Forty-two patients were eligible for enrollment. Twenty-nine (69%) patients enrolled and 88.8% of study tasks were completed, meeting both of our feasibility goals. Of the first study visits, 7 (25%) patients were found to have vitamin D deficiency, while an additional 6 (21.4%) had vitamin D insufficiency. Vitamin D supplementation was initiated for six patients. At the second visit, only one (4.3%) patient was vitamin D deficient, with 6 (26.1%) insufficient. Three (16.7%) patients had low height-adjusted total body BMD Z-scores, and an additional 8 (44.4%) patients had a "low normal" either height-adjusted total body or height-adjusted lumbar spine BMD Z-scores at study visit 1, with similar results for visit 2. Notably, patients with neuroblastoma or medulloblastoma consistently demonstrated low-normal height-adjusted BMD Z-scores at both visits, while sarcoma patients did not. Functional mobility scores increased by 7.28%. One patient experienced a tibial fracture during the study. Caregivers appreciated the bone health surveillance and expressed interest in having this routinely included.

Conclusion: Bone health assessments were feasible within pediatric patients with solid tumor malignancies with high acceptance rate among caregivers. High prevalence of vitamin D deficiency and bone mass deficits were found during early bone surveillance that warrants incorporation into routine clinical practice. Multisite prospective studies are needed to better understand the impact of current therapies on bone health in this patient population.

Poster # 818

GUT MICROBIOME AND PERIPHERAL IMMUNOSUPPRESSIVE CELL CHANGES IN CHILDREN WITH SOLID TUMORS

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Background: Changes in gut microbiome in adults have been linked to cancer outcomes and complications including immunosuppression. Chemotherapy may induce immunosuppression through the preferential differentiation of mobilized progenitor cells into myeloid-derived suppressor cells (MDSCs), M2-tumor-associated macrophages (M2-TAMs), and regulatory T cells (Tregs). Nothing is known about changes in gut microbiome and frequency of peripheral immunosuppressive cells in children with newly-diagnosed solid tumors.

Objectives: We aimed to 1) define changes in gut microbiome diversity and frequency of peripheral blood immunosuppressive cells during induction chemotherapy and 2) correlate these changes to

infection- and disease-related outcomes in pediatric solid tumor patients.

Design/Method: This feasibility study enrolled 22 patients ages 0-19 years old at diagnosis with solid tumor malignancies diagnosed between 1/1/2018 and 12/31/2019. After exclusion criteria, 16 patients with peripheral blood and stool samples collected at specific treatment timepoints were analyzed. MDSCs, M2-TAMs, and Tregs in blood samples were measured (% of peripheral blood mononuclear cells) through flow cytometry. Alpha diversity (measured in operational taxonomic units [OTUs] and inverse Simpson index [Inv Simp]) was compiled for stool samples using 16Sv4 rRNA gene sequencing.

Results: Thirteen patients (81%) submitted both pre-chemotherapy blood and stool samples. Eight patients (50%) submitted both samples at one-month on-therapy, and four patients (25%) submitted both samples at three-months on-therapy. All patients received PJP prophylaxis per protocol. Eleven patients (69%) had documented infections over the first three months of therapy and received therapeutic antibiotics. In patients with documented infections, gut microbiome diversity was lower than those without infections in pre-therapy (Inv Simp 5.416 [95% CI 2.939-7.894] vs. 9.644 [95% CI 5.814-13.48], p=0.0348) and in one month on-therapy samples (Inv Simp 6.144 [95% CI 2.771-9.516] vs. 8.244 [95% CI 0.1088-16.38], p=0.4522). In patients with documented infections, MDSCs increased between pre-therapy and one-month on-therapy blood samples (0.7267% [95% CI 0.2474-1.206%] to 2.612% [95% CI 0.8071-4.417%], p=0.0347) versus those without infections (2.411% [95% CI -1.174-5.997%] to 2.642% [95% CI -1.476-7.761%], p=0.9117).

Conclusion: The study was feasible, although a significant drop-off in sample acquisition was related to stool submission by patients. Gut microbiome and peripheral immunosuppressive cell frequency changes during chemotherapy were associated with development of infection, a sign of immunosuppression, in children with newly-diagnosed solid tumors. Concomitant antibiotic administration further modifies this association. Future studies should include a larger and homogenous study population, follow-up for adequate sample acquisition, and use of age- and household-matched controls.

Funding: Dan L. Duncan Comprehensive Cancer Center Pilot Project Grant.

Poster # 819

ANALYZING GUT MICROBIOTA IN ADOLESCENT AND YOUNG ADULTS RECEIVING CHECKPOINT BLOCKADE FOR MELANOMA

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Background: Melanoma is the third most common cancer in adolescent and young adults (AYA), a unique cohort defined as patients between 15-39 years of age per the National Cancer Institute. Immune checkpoint inhibitors (ICI) have changed the landscape for advanced melanoma treatment, and the gut microbiota has been shown to remodel the tumor microenvironment to improve ICI efficacy. There is a paucity of research in this cohort, however studies show that AYA patients have historically not seen the same survival gains as other age groups.

Objectives: To compare the gut microbiota of AYA melanoma patients who received ICI with older non-

AYA patients.

Design/Method: The AYA cohort in this retrospective review is from the 2021 Science publication entitled *Dietary fiber and probiotics influence the gut microbiome and melanoma immunotherapy response.* This cohort was matched on a 2:1 basis with older non-AYA patients 50-70 years of age.

Results: Our AYA cohort of 23 patients is comprised of 15 females, 22 caucasians, 20 with primary cutaneous melanoma, 12 with stage III at the start of treatment and 11 with stage IV. 17 were BRAF positive, 8 received combined immunotherapy, 20 were treatment naïve, and 11 were responders. We found a statistically significant ($p<0.0001$) worse progression free-survival (PFS) amongst AYA patients who were previously treated versus those who were treatment naive as well as a statistically significant ($p<0.022$) worse PFS between previously treated AYA and older non-AYA patients. We found no difference in alpha or beta diversity in AYA and older non-AYA patients, however alpha diversity increased with age. This is consistent with literature regarding aging gut microbiomes. Furthermore, we noted the most common microbes found between these groups varied considerably. Using differential analyses, we found, for example, a higher abundance of Ruminococcacaeae, at the family level, in older non-AYA patients and a higher abundance of Bacteroides stercoris in AYA patients. Literature shows Bacteroides stercoris correlates positively with intake of fiber, grain, and vegetables.

Conclusion: We found that the gut microbiota of AYA and older non-AYA melanoma patients differ . Establishing microbial features in the AYA population can help with microbiome modulation as a therapeutic strategy. Enriching modalities include fecal microbiota transplantation, probiotics, and improving diet and fiber intake. We will also look at dietary and fiber data to assess external causes for the different enrichment of microbiota in the two groups. We need to further explore why treatment naive AYA's have significantly worse PFS than older non-AYA's.

Poster # 820

UNSUSPECTED FRACTURES IN CHILDREN WITH NEW HEPATOBLASTOMA DIAGNOSES

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Background: Limited data support that children with hepatoblastoma may be at increased risk of fractures. Given the young age of children with hepatoblastoma, incidentally discovered fractures often necessitate ruling out non-accidental trauma in this vulnerable pediatric population. We expanded on the data pertaining to incidence of unsuspected fractures in children around the time of their hepatoblastoma diagnosis.

Objectives: To determine the incidence of fractures in patients with newly diagnosed hepatoblastoma who were treated at Rady Children's Hospital San Diego, one of the largest standalone children's hospitals in the U.S., between 2003 and 2023.

Design/Method: We performed a retrospective chart review of all patients diagnosed with or treated for hepatoblastoma at Rady Children's Hospital San Diego between 2003-2023. We gathered information on each patient including gestational age, age at diagnosis, AFP, vitamin D level, stage/risk stratification, and presence or absence of metastases. We then re-reviewed all available imaging studies

for patients within 30 days leading up to or 30 days after their initial diagnosis to identify radiographically significant fractures.

Results: Of the 18 children included in this study, only one had radiographically identifiable fractures (~5.6%). This patient had a rib fracture that was missed on initial abdominal CT read, but noted on re-review. Skeletal survey was then completed which also had evidence of an old radial fracture. This patient had no unique lab values, staging considerations, or demographic findings to differentiate them from other patients.

Conclusion: Finding fractures in children near the time of their initial hepatoblastoma diagnosis has been reported, but the incidence remains unclear. Previous study by Towbin et al (2018) cited an incidence of up to 17.8%, with a mean number of 4.9 fractures per patient. Expanding this work with a larger number of subjects is pivotal to better understand this connection.

Poster # 821

OUTCOMES OF BONE SARCOMAS IN A RURAL STATE

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Background: Osteosarcoma and Ewing sarcoma are the two most common primary malignant bone tumors in children. Long-term survival ranges from 60-75% in patients with localized disease while survival rates in those with metastatic disease is 20–25%. Tumor size, stage at presentation and treatment at a regional referral center are some of the variables that affect survivorship. Additionally, previous studies have shown that the overall rurality of a patient's county of residence is an independent risk factor for mortality. Prior research has suggested that rural patients are at increased risk of mortality when compared to those residing in urban counties however these studies have not focused on a population in a rural state.

Objectives: We hypothesized that patients who live in rural counties are likely to have worse overall survival and present to a regional treatment center at an advanced stage when compared to patients who reside in urban counties.

Design/Method: From 2006 through 2022, we retrospectively reviewed the medical records of all patients at a single institution for Osteosarcoma or Ewing sarcoma. All patients underwent treatment consistent with the current standard of care for their disease including a combination of chemotherapy, surgery, and radiation therapy. We utilized univariate and multivariate modeling in addition to survival analysis to analyze patient and tumor characteristics.

Results: There were 93 patients that met the inclusion criteria. The overall five year survival for the entire group was 62.2 %. When comparing patients who resided in rural vs urban counties, there was no significant difference in 5 year survival (65.4% vs 58.5%, p = 0.58) for either type of malignancy. There was also no difference between stage at presentation when stratified by rural or urban status. Furthermore, there was no difference in stage at presentation between patients who lived >150 miles from regional referral center compared to those who lived <150 miles away (Stage 2 65.2% vs 68.6%, p =

0.76; Stage 4 34.8% vs 29.6%, p = 0.64).

Conclusion: For patients with Osteosarcoma and Ewing sarcoma that reside in a rural state, there is no difference in 5 year survival or stage at presentation when stratified based on rural vs urban status.

Poster # 822

ASSESSMENT OF HOUSEHOLD POVERTY EXPOSURE IN PATIENTS WITH HRNB RECEIVING DFMO MAINTENANCE TREATMENT

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Background: Survival of patients with HRNB continues to be poor at around 50% from the time of diagnosis despite advances in upfront treatment. Bona et. al 2021 show children from families with a lower socioeconomic status have even poorer outcomes.

DFMO was recently approved for maintenance therapy in HRNB patients using a propensity-score matched (PSM) analysis comparing DFMO treated patients to a control group of non-treated patients (Oesterheld et al., 2023). The PSM covariates were based on potential prognostic importance and availability. However, insurance information was unavailable.

Bona et al., (2021) reported a 35% household poverty exposure rate, defined by sole public insurance coverage, within a similar group of HRNB patients. The cohort of poverty-exposed patients had nearly double the risk of an EFS event. Thus, a theoretical imbalance in poverty prevalence between DFMO and control groups could influence outcomes.

Objectives: Retrospective collection of insurance information on DFMO patients informed a range of sensitivity analyses to characterize impact of poverty on the reported treatment effect.

Design/Method: We retrospectively collected insurance type for patients in the DFMO group to apply poverty exposure definitions consistent with Bona. The primary PSM analysis of EFS favored DFMO with a HR of 0.48 (95% CI 0.29, 0.85) which assumed equal poverty exposure in the groups. Sensitivity analyses following Lin et al (1997) assessed the effects due to unmeasured poverty exposure. We assumed a 35% rate for the control arm and a hazard ratio for the unmeasured confounder of 1.9, both consistent with Bona's report. A range of assumptions were assessed for the potential impact of differences in poverty exposure between the groups.

Results: Patients in the DFMO group had 30% household poverty exposure based on retrospective review. Maintaining an assumed 35% poverty exposure in the control group, HRs from the sensitivity analysis adjusting for the unmeasured confounder ranged from 0.51 (95% CI 0.29, 0.85) to 0.66 (0.37, 1.17), assuming 30% to 0% household poverty in the DFMO treated group.

Conclusion: Household poverty exposure for DFMO treated patients was similar to the rate reported by Bona. Across the range of sensitivity analyses, the adjusted hazard ratios were of similar magnitude as the primary analysis even with the most conservative handling, assuming no poverty exposure in

the DFMO treated group.

Funding for the statistical analysis and medical writing assistance was provided by USWM, LLC.

Poster # 823

TREATMENT OF ADVANCED GERM CELL TUMOR WITH MODIFIED CHEMOTHERAPY IN A DIALYSIS-DEPENDENT ADOLESCENT

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Background: Germ cell tumors (GCTs) make up 14% of cancers in adolescents 15-19 years old. Malignant somatic transformation (MST) of GCTs is uncommon, accounting for 3-6.6% of GCTs [1]. Advanced GCTs are treated with platinum-based multiagent chemotherapy, however for patients on current hemodialysis (HD) the dosing and timing of agent administration are not well-established, particularly in the pediatric population. Further, a paucity of data exists to inform optimal timing of solid organ transplantation after completion of chemotherapy.

Objectives: To report the treatment and long-term management of an HD dependent adolescent with advanced testicular teratoma with MST, now post-kidney transplant.

Design/Method: Case report and review of literature.

Results: A 15-year-old previously healthy male presented with 1 year of left testicular swelling and discomfort. An ultrasound identified a large heterogenous testicular mass, and bloodwork showed an elevated b-HCG (1502) with normal AFP and LDH. Left radical orchiectomy was performed revealing teratoma with 25% MST (embryonal rhabdomyosarcoma). b-HCG normalized after orchiectomy. Staging imaging demonstrated large left retroperitoneal and inferior mediastinal adenopathy. Uncertain of the nature of the adenopathy, a retroperitoneal lymph node dissection was performed, which was complicated by a right total nephrectomy, left renal vein injury with thrombosis, and ultimately hemodialysis dependence. Pathology showed mixed germ cell tumor, predominately embryonal carcinoma. While recovering he developed 3 pulmonary nodules concerning for metastatic spread.

He was treated with a modified cisplatin, etoposide, ifosfamide (VIP) chemotherapy protocol. Every cycle consisted of 5 days of chemotherapy with hemodialysis performed 1 hour after completion of each cisplatin infusion. Cycle 1 consisted of etoposide (50 mg/m2) and cisplatin (10 mg/m2). Cycle 2, doses were increased to etoposide (75 mg/m2) and cisplatin (20 mg/m2). Cycle 3, cisplatin and etoposide doses were maintained and ifosfamide (600 mg/m2) was added with mesna and prophylactic thiamine. Cycle 4 the ifosfamide dose was increased (900 mg/m2). Therapy was well tolerated, though complicated by severe malnutrition and febrile neutropenia. He maintained a biochemical remission through treatment, and end of therapy scans showed no evidence of disease. After 2 years of remission, he successfully underwent an unrelated donor kidney transplant, and 6 months post-transplant he remains in remission.

Conclusion: We report the successful treatment of a metastatic testicular mixed germ cell tumor + teratoma with MST in a HD dependent adolescent using dose-modified VIP. This case supports the

curative use of modified chemotherapy protocols in HD dependent patients, and kidney transplant in selected patients <5 years from completion of therapy.

Poster # 824

A NOVEL CASE OF TARGETED IMMUNOTHERAPY RESPONSE IN METASTATIC AMELOBLASTOMA

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Background: Ameloblastoma is classified as an odontogenic tumor that is traditionally managed through surgical resection, even in the setting of locally invasive behavior and high recurrence rate. It rarely occurs in the pediatric population, and even rarer does it advance to metastasizing ameloblastoma. Because of this, there is a paucity of data and an absence of standardized treatment approaches outside of surgery, with limited roles of chemotherapy and radiotherapy reported in the literature. Of the limited populations that have undergone molecular profiling, BRAF, FGFR2, and SMO mutations are the most commonly reported with varying responses to their targeted therapy counterparts. We report a rare ALK alteration in ameloblastoma with molecular-guided therapy against this specific target.

Objectives: We describe a case of recurrent ameloblastoma with pulmonary metastasis that achieved complete remission following treatment with crizotinib, an ALK-inhibitor.

Design/Method: This is a case report of an 8-year-old girl with metastasizing ameloblastoma. The patient's chart was reviewed and data were collected, including imaging, surgical pathology, and molecular profile results.

Results: The patient presented with left cheek swelling at 3 years of age. Pathology was diagnostic for localized ameloblastoma following radical resection of a left maxillary cyst. Over the next 3 years, the patient underwent three additional resections, including left orbitotomy and additional partial maxillectomy, for recurrent disease. Due to persistence of disease, pediatric oncology was consulted prior to her fourth debulking and reconstructive procedure. Metastatic evaluations including a chest CT revealed bilateral, too numerous to count lesions in the lungs. A repeat CT chest at a 3 month interval without treatment was notable for progression showing a range of 21-38% increase in mean diameter of target lesions. Molecular profiling was performed and revealed a targetable KANK1-ALK fusion, which was predicted to be an activating alteration of Anaplastic Lymphoma Kinase (ALK), a receptor tyrosine kinase that serves as an upstream pathway signal for cell proliferation, survival, and angiogenesis. The patient was started on crizotinib, a well-tolerated ALK-inhibitor, and achieved complete response with no evidence of disease after 13 months of treatment. The patient has not experienced recurrence of disease to date (24 months post treatment initiation) and continues on crizotinib.

Conclusion: We use this case to report a novel molecular target of an extremely rare pediatric malignant ameloblastoma and discuss the role of precision oncology and multidisciplinary approach in a traditionally surgical case.

Poster # 825

SELUMETINIB IN PEDIATRIC HYPERTROPHIC NEUROPATHY ASSOCIATED WITH KRAS G12D MOSAIC MUTATION

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Background: RASopathies are a group of genetic syndromes caused by germline mutations in genes of the Ras/ mitogen-activated protein kinase (MAPK) pathway. RASopathies often display overlapping clinical features, presumably owing to common RAS-MAPK signaling pathway activation driving dysregulated cell proliferation. Currently, no curative treatments exist for RASopathies, only symptom-directed management. In this report, we detail a unique case of a child exhibiting diffuse spinal root hypertrophy and epidermal nevus syndrome, linked to a mosaic KRAS G12D mutation, treated with selumetinib, a MEK1/2 inhibitor. According to available evidence, this report represents the first documented use of selumetinib for hypertrophic neuropathy in a patient with a mosaic KRAS variant.

Objectives: To highlight the novel application of selumetinib in treating a pediatric case of epidermal nevus syndrome with hypertrophic neuropathy linked to a KRAS G12D mutation, assessing its therapeutic potential through clinical and radiological findings.

Design/Method: We present a case of a seven-year-old girl with epidermal nevus syndrome, who was referred to our Pediatric Oncology clinic for the management of progressive multilevel spinal root hypertrophy leading to cervical cord compression. Medical history was notable for epidermal nevi, congenital heart disease, polycystic kidneys, and pelvic ganglioneuroma. Whole-exome sequencing revealed a KRAS G12D mutation in samples obtained from epidermal nevus and Schwann cells but not in the blood, indicating a mosaic KRASopathy. Surgical intervention was deemed infeasible due to the disease extent. Inhibiting the RAS-MAPK pathway with a MEK inhibitor such as selumetinib is a proven, effective strategy in patients with NF1-associated inoperable plexiform neurofibroma. While the effectiveness of MEK inhibitors like selumetinib is established in NF1-associated inoperable plexiform neurofibromas, their use in conditions stemming from hyperactive KRAS remains unproven. Shared molecular dysregulation and overlapping clinical features between these conditions suggest potential for successful therapeutic application.

Results: The use of off label selumetinib halted the progression of the spinal nerve root enlargement and markedly improved the appearance of the epidermal nevi. Eighteen months post-treatment initiation, MRI of the spine continues to demonstrate stable disease. The patient continues to tolerate the medication well without significant adverse effects.

Conclusion: This case underscores the potential of selumetinib as a targeted therapy for pediatric patients with hypertrophic neuropathy due to KRAS mosaic mutations, expanding treatment options in this clinical area.

Poster # 826

AGGRESSIVE IMMATURE TERATOMA IN A PATIENT WITH CYSTIC FIBROSIS AND LYNCH SYNDROME

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Background: Immature teratoma is a type of germ cell tumor consisting of all three germ cell layers, with grade 3 consisting of primarily neuroepithelium tissue. Teratomas in children present with a rapidly enlarging mass and elevated AFP. The primary treatment is surgical resection, with most patients becoming tumor free after complete resection. Immature teratomas are associated with an increased risk of recurrence and may require additional chemotherapy after surgery. Standard regimen consists of cisplatin, etoposide, and bleomycin, however there are no recommendations for patients with comorbid conditions such as cystic fibrosis.

Objectives: To report a case of a patient with cystic fibrosis who developed grade 3 immature teratoma with genetic testing positive for Lynch Syndrome.

Design/Method: Review of the electronic medical record and consultation with the treating physicians.

Results: We present an 8-year-old female with history of cystic fibrosis who developed an enlarging abdominal mass. Imaging showed a large cystic mass in the abdomen extending to the left adnexa with peritoneal deposits. She also had elevated AFP (1545) and LDH. She underwent resection of the mass and pathology results showed grade 3 pure immature teratoma. Tumor markers declined after surgical resection, however started increasing again one month after surgery. Repeat CT at that time showed lymph node enlargement. Decision was made to start systemic chemotherapy with etoposide and cisplatin. Bleomycin was initially deferred to avoid any potential pulmonary complications due to her cystic fibrosis history. She had disease progression after cycle 1 of chemotherapy with EP, therefore bleomycin was added to chemotherapy regimen for cycles 2 and 3 with resulting decrease in tumor markers. Imaging after completion of cycle 3 showed increase in size of the pelvic mass and nodules along the liver. Biopsy of these enlarging lesions showed mature neural tissue, suggesting transformation of the previously immature teratoma to growing mature teratoma syndrome. She then had gross total resection of the disease. Genetic testing of tumor cells and germline resulted positive for heterozygous PMS2 gene mutation consistent with Lynch Syndrome. Her tumor burden has currently remained stable after two major surgical resections.

Conclusion: This is a unique case of a pediatric patient with cystic fibrosis who developed metastatic immature teratoma with underlying Lynch Syndrome. Teratomas are a common germ cell tumor in children however Lynch Syndrome rarely manifests in childhood. Further research is needed to determine underlying genetic connection of these disorders and to further guide management.

Poster # 827

ATYPICAL PRESENTATION OF PLEUROPULMONARY BLASTOMA; A CASE REPORT

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Background: Pleuropulmonary Blastoma (PPB) is a rare, highly aggressive and malignant tumor in children that originates from either the lungs or pleura. PPB is classified into subtypes, and historically type II and type III PPB are associated with poor prognosis. PPB has a strong genetic association with variants in DICER1.

Objectives: Our aim is to report a case of a 14-month-old who presented with neck stiffness. Imaging showed a mass in the superior aspect of the left lung with extension to the intradural space from C5-T4. Biopsy showed Type III PPB with two variants in DICER1 and one in SUFU.

Design/Method: Our patient is a previously healthy 14-month-old male who presented to his pediatrician with complaints of neck stiffness for 2 days, not associated with any other neurological deficit. He was referred to our emergency department where MRI showed a large hyperdense/enhancing intraspinal lesion measuring 1.6 x 1.3 x 6.0 cm from C5 to T4 with cord compression and with apparent extension to the posterior superior aspect of the left lung. CT chest/abd/pelvis showed a partially calcified mass in the posterior superior aspect of the left lung measuring 2.7 x 2.3 x 3.1 cm with apparent extension from the spinal cord. Patient underwent laminectomy and tissue biopsy/resection from the spinal lesion.

Results: Pathology showed Type III PPB with two variants of strong significance in the DICER 1 gene and one in the SUFU gene. He enrolled in the International PPB/DICER1 Registry and started chemotherapy with Ifosphamide, vincristine, actinomycin and doxorubicin (IVADo). The patient completed two cycles of chemotherapy and underwent pleural mass resection and pathology revealed treated PPB type III. He is receiving ongoing chemotherapy and is stable with continued neurological deficits.

Conclusion: PPB is a rare and aggressive tumor and patients with pleural, mediastinal, or extra pulmonary involvement at the time of diagnosis, have worse prognosis. These patients are treated with aggressive multimodal therapies including surgery and chemotherapy. The finding of the SUFU gene variant in PPB is not well described in the literature. Genetic analysis of rare tumors such as PPB is important for better understanding of cancer predisposition syndromes and development of targeted therapies to improve survival.

Poster # 828

INCURABLE METASTATIC OVARIAN IMMATURE TERATOMA CONTAINING CENTRAL PRIMITIVE NEUROECTODERMAL TUMOR

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Background: Neoplasms with central nervous system (CNS) components that are found in the pelvis or reproductive organs are exceedingly rare and are often found in association with a mature or immature teratoma. There are no established guidelines as to the treatment of these tumors and 5-year overall survival ranges from 15-40%. Here, we report a case of a 13-year-old female diagnosed with a FIGO Stage IVB ovarian tumor consisting of a grade 3 immature teratoma and a central primitive neuroectodermal tumor (cPNET).

Objectives: To present a case of a patient with a mixed ovarian tumor comprised of immature teratoma

and cPNET components who progressed through four regimens of chemotherapy before expiring.

Design/Method: Case Report

Results: A 13-year-old female presented with abdominal pain and constipation; MRI revealed a right ovarian malignant neoplasm, cardiophrenic mass above the diaphragm, and carcinomatosis. This led to exploratory ex-laparoscopy with abdominal washout, right salpingo-oophorectomy, and right ovarian tumor resection. Pathology confirmed cPNET associated with immature teratoma with elevated serum levels of AFP, BHCG, CA-19, and CA-125. It was felt that R0 surgical intervention would not render her complete remission. The patient was started on ACNS0332 (vincristine, cisplatin, and cyclophosphamide) that targeted her cPNET first, but stopped after 2 cycles due to tumor growth and elevated CA-19 levels. She was switched to AGCT1532 with bleomycin, etoposide, and cisplatin to target her teratoma and completed 2 cycles but stopped after labs showed that BHCG, CA-19, and CA-125 were up-trending with an increase in her anterior mediastinal mass. Her third line treatment, ACNS0821 (temozolomide and irinotecan, omitted bevacizumab), targeted her cPNET component again; however, she stopped after completing 1 cycle because of continued growth of the mediastinal mass and progression of carcinomatosis, despite down-trending tumor markers. Her last cycle of chemotherapy was vincristine, doxorubicin, and cyclophosphamide (2100mg/m^2/dose) to target her cPNET component further, which she continued for 2 cycles. Follow up surveillance imaging showed disease progression in her mediastinal mass, after which her family elected to stop chemotherapy and focus on quality of life.

Conclusion: CNS neoplasms associated with immature teratomas that arise from the gonads represent a rare group of malignancies with dismal outcomes. This case report describes multiple unsuccessful chemotherapy regimens used to treat a 13-year-old female with a cPNET arising from an ovarian immature teratoma. Novel treatment options are urgently needed.

Poster # 829

NEONATAL RHABDOID TUMOR PRESENTING AS FEEDING INTOLERANCE AND VOMITING

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Background: Rhabdoid tumor predisposition syndrome (RTPS) is most commonly caused by SMARCB1 mutations (85-95% of cases). A related syndrome, RTPS-2, occurs secondary to heterozygous germline mutations in SMARCA4 (5-15% of cases), which encodes BRG1. Greater than 50% of SMARCA4-mutated tumors are in the cerebellum; when found outside of the CNS, small-cell carcinoma of the ovary, hypercalcemic type (SCCOHT) is the most common tumor associated with this mutation. Hasselblatt et al demonstrated that 6/7 SMARCA4-mutated atypical teratoid/rhabdoid tumors (AT/RT) were secondary to germline mutations versus 9/33 SMARCB1-mediated AT/RT. Furthermore, SMARCA4 mutations carry a worse prognosis, with survival rates of 3 months compared to 24 months for SMARCB1.

Objectives: We present a case of bilious emesis in a neonate with intraperitoneal carcinomatosis secondary to rhabdoid tumor with a pathologic variant in SMARCA4.

Design/Method: The patient presented as a previously healthy three-week-old term female with feeding intolerance, non-bloody, non-bilious emesis, and tactile fevers. On hospital day 2, she had

bilious emesis with workup negative for malrotation with midgut volvulus. Abdominal ultrasound showed large volume, debris-laden ascites, concerning for enteric contents and paracentesis demonstrated turbid, bloody fluid with negative Gram stain. On hospital day 4, the patient was intubated due to respiratory compromise and clinical decline and underwent exploratory laparotomy, which revealed bloody ascites and innumerable, fleshy-appearing, friable masses involving over 90% of the peritoneal cavity and omentum. There was neither malrotation nor intestinal compromise, but a 4cm mass 20cm distal to the ligament of Treitz causing luminal obstruction was found. A segmental bowel resection, omentectomy, and metastasectomy were performed.

Results: Pathology demonstrated malignant rhabdoid tumor with heterozygous loss of SMARCA4 (pathologic variant c.490C>T (p.Gln164*)) with retention of SMARCB1. Despite improved respiratory status post-operatively, the patient's prognosis was poor due to high disease burden and poor clinical status, leading to discussions about futility of pursuing disease-directed treatment. Ultimately, the family decided to pursue comfort-focused care, and the patient died at five weeks of life. Post-mortem genetic testing revealed a germline mutation in *SMARCA4*.

Conclusion: This case represents a rare cause of bilious emesis in a newborn secondary to SMARCA4-mediated RTPS-2 leading to small bowel obstruction, abdominal compartment syndrome, rapid disease progression and ultimately neonatal demise. Alterations in SMARCA4 must be considered when INI1 is maintained; in this case BRG1 expression was lost, indicating loss of SMARCA4.

Poster # 830

IMATINIB THERAPY IN A CASE OF CHERUBISM WITH HYPOPLASTIC LEFT HEART SYNDROME

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Background: Cherubism is a rare autosomal dominant condition that affects craniofacial bones in an autoinflammatory manner. Mutation in SH3BP2 leads to over activation of SRC and related Tyrosine-kinases, especially in osteoclasts. Fibro-osseous cysts tend to grow in childhood and then typically regress and ossify after puberty. While surgery has been a mainstay of treatment, targeted agents inhibiting osteoclastic activation are an appealing adjunct, though given the rarity of the disease, data on efficacy is limited. Here we present the first known case of a 5-year-old female with Cherubism and surgically palliated hypoplastic left heart syndrome (HLHS), most recently s/p Fontan operation, who had developed a moderate burden of cystic jaw lesions and was treated with targeted inhibitor therapy.

Objectives: To select and administer an appropriately targeted therapy to slow or reverse our patient's jaw lesions, while avoiding undue hemodynamic or cardiac functional burden.

Design/Method: Case: Imatinib, at a dose of 300 mg/m2[1], was selected over other agents described for Cherubism[2], such as denosumab, to avoid the latter's effect on calcium and cardiac function. Dosing was initiated slowly, at half strength for two weeks to acclimate to potential side effects before advancing to full dosing. Hematologic and electrolyte levels were monitored before initiation and then monthly. Cardiac function was measured with serial echocardiograms and NTproBNP levels. Jaw x-rays were obtained at the 3-month mark for comparison.

Results: Over the three-month period of monitoring, side effects included mild nausea and vomiting, which improved with appropriate anti-emetic therapy. A mild macrocytic anemia developed. Her echocardiogram remained unchanged, but her NTproBNP did uptrend. Repeat jaw x-ray demonstrated partial remineralization of her large central mandibular cyst as well as improvement of lateral cystic changes.

Conclusion: In this case of a patient with Cherubism and HLHS we were able to safely achieve stabilization of her jaw with only 3 months of imatinib therapy and minimal manageable side effects despite cardiac palliation. The rise of her proBNP may be related to anemia or fluid retention, known imatinib side effects. Close follow up with cardiology will help determine either dose or diuretic adjustment. A cardiac genetics panel was negative, and no link has been previously shown between HLHS and Cherubism.

[1]Ricalde, J Oral Maxilofac Surgery, 2019
[2]Cailleaux, Front Endocrinol, 2023

Poster # 831

SIMULTANEOUS XERODERMA PIGMENTOSA, METASTATIC MELANOMA, AND A CNS ANGIOSARCOMA

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Background: Xeroderma Pigmentosum (XP) is an autosomal recessive disorder characterized by extreme sensitivity to ultraviolet radiation, predisposing patients to skin cancer. Angiosarcomas are blood vessel tumors occurring in different parts of the body but uncommonly the brain. The chances of having these concurrent neoplasms is extremely rare. Previous studies have shown that angiosarcomas could arise from exposure to certain environmental factors, such as prior radiation therapy, however, the exact cause is still unknown. Though new genetic sequencing has found that angiosarcomas can possess mutations induced by ultraviolet exposure, similar to melanomas.

Objectives: To describe the clinical course of an 18-year-old female, with Xeroderma Pigmentosum and unresectable metastatic melanoma which was successfully treated with immunotherapy, who later developed an angiosarcoma of the brain.

Design/Method: Chart and literature review.

Results: An 18-year-old female, who was diagnosed with XP at 4 years of age, initially presented with a three-year evolving right cheek metastatic melanoma that was surgically resected at time of onset. She then received three-month-long immunotherapy with Nivolumab and Ipilimumab, followed by Nivolumab for a total of 14 cycles, with complete response. Unfortunately, she was involved in a traumatic MVC a year later. A CT scan of the head revealed a massive right frontotemporal intracranial hemorrhage with intraventricular hemorrhage. Shortly afterwards, the patient underwent a decompressive hemicraniectomy, with subsequent pathology that revealed an angiosarcoma. A ventriculoperitoneal shunt was placed and during her admission, the frontotemporal hemorrhage worsened with increased surrounding edema and mass effect with leftward midline shift, with

impending herniation. As her neurologic status and clinical condition continued to deteriorate, a decision was made to pursue comfort care measures until her passing.

Conclusion: Central nervous system angiosarcomas have a poor prognosis and represent a challenge given there is no established consensus for adequate treatment. Some success has been previously seen in patients able to receive adjuvant chemotherapy followed by radiation therapy. The simultaneous presence of both XP and angiosarcoma made this an unusual and complex case. Literature reveals how immunotherapy is proving to play a crucial role in evolving treatments, and some checkpoint inhibitors such as anti-PD1 are currently in clinical trials, which could represent a new alternative for these patients.

Poster # 832

A NEAR MISS CASE OF ADVANCED PEDIATRIC MELANOMA WITH A RARE BRAF V600K ACTIVATING MUTATION

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Background: Pediatric melanoma is rare, and diagnosis is often challenging, especially for those tumors with Spitzoid morphology. Adult-type, or conventional melanoma, encompasses those tumors with non-Spitz features. Despite this, a subset of Spitzoid morphology tumors exist for which molecular genetics remain essential for accurate classification in the current 2018 World Health Organization (WHO) schema, in which melanocytic neoplasms that harbor BRAF mutations are excluded from the Spitz family. BRAF mutations are found in about 50% of conventional adult melanoma and 80% of pediatric conventional melanoma. Of these, V600E is the most common mutation (80-90%) with V600K mutations accounting for 10-20%. V600K mutant melanomas are typically seen in older Caucasian males, in chronic sun-exposed areas, with increased tumor thickness and higher mitotic activity, and display more aggressive clinical behavior with increased risk of relapse and distant metastasis, and overall poorer prognosis than their V600E counterparts' display.

Objectives: Describe a rare pediatric case of BRAF V600K mutant melanoma, associated challenges with diagnosis, and clinically aggressive course.

Design/Method: Single subject case report

Results: A 13-year-old previously healthy boy presented to Dermatology with a one-year history of a 1.5 cm brown-gray firm nodule on his central upper back. Shave biopsy was performed and showed an atypical compound melanocytic neoplasm with uncertain biological potential, partially sampled. Dermatopathology recommended repeat full thickness excisional biopsy for complete evaluation, subsequently revealing thick (9.5mm Breslow) tumor with high-grade cellular atypia, Spitzoid morphology, and increased mitotic activity consistent with melanoma. Immunohistochemistry (IHC) for BRAF mutation was negative, though next generation sequencing (NGS) showed an activating BRAF V600K mutation. Standard wide local excision, sentinel lymph node biopsy and CT scans were performed resulting in final diagnosis of stage IIIC [T4aN2aM0] nodular melanoma. The patient received one year of adjuvant nivolumab with no evidence of disease 13 months following diagnosis.

Conclusion: Biological data on BRAF V600K mutant melanoma supports a clinically aggressive behavior based on dysregulation of various antiapoptotic pathways. While IHC for BRAF mutation is a good screening test for V600E mutations, it is unable to identify V600K mutations, as was detected in this case, highlighting the need for routine NGS or PCR-based testing. This case highlights the need for both full thickness diagnostic biopsy for cutaneous lesions concerning for malignancy to allow for complete tumor histopathological assessment, and the importance of accurate molecular assessment of melanocytic tumors in children, to guide appropriate treatment for this potentially aggressive cancer.

Poster # 833

PANCREATOBLASTOMA IN A CHILD WITH SIMPSON-GOLABI-BEHMEL SYNDROME: THE IMPORTANCE OF AFP MONITORING

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Background: Simpson-Golabi-Behmel Syndrome (SGBS) is a rare X-linked genetic syndrome characterized by pre- and post-natal overgrowth. Predisposition to embryonal malignancies, specifically Wilms tumor and hepatoblastoma, is well documented, however cases of other malignancies have been reported. Screening for hepatoblastoma and Wilms tumor is recommended for patients with SGBS, including abdominal ultrasonography (US) with or without serum alpha fetoprotein (AFP) testing. European guidelines for hepatoblastoma screening advise against AFP screening due to concerns over test interpretation, invasiveness of blood draws, and unproven utility. In contrast, most North American guidelines argue that AFP elevation may precede detection of a mass on imaging, leading to a more timely diagnosis. In addition to hepatoblastoma, elevated serum AFP is a useful marker for pancreatoblastoma, which has not previously been reported in SGBS. We report a case of a child with SGBS presenting with pancreatoblastoma, the diagnosis of which was aided by serial AFP monitoring.

Objectives: To report a case of pancreatoblastoma in SGBS, and to highlight the role AFP screening plays in tumor surveillance in this population.

Design/Method: Case Report

Results: A female infant presented at birth with macrocephaly, macroglossia, hyperinsulinism, and markedly elevated serum AFP. Abdominal US revealed a diffusely enlarged pancreas and liver mass, confirmed on cross-sectional imaging. AFP rose to over 500,000 ng/mL, prompting hepatic mass excision with distal, subtotal pancreatectomy. While the hepatic mass was negative for malignancy, the pancreatectomy specimen revealed a small (<1 cm) pancreatoblastoma in a background of nesidioblastosis, with tumor in 11/15 regional lymph nodes. The patient received four cycles of adjuvant chemotherapy with cisplatin and doxorubicin with dexrazoxane. AFP levels down-trended during therapy, eventually normalizing. A multi-gene hereditary cancer panel detected a variant of unknown significance (c. 1398G>A (p.L466)) in GPC3. Without an alternative explanation for her syndromic features despite comprehensive testing, her geneticist felt this mutation was the likely explanation for her clinical features, diagnosing her with SGBS.

Conclusion: The presence of pancreatoblastoma in our patient suggests this tumor may fall into the

spectrum of disease in SGBS. Tumor surveillance in SGBS may or may not include AFP monitoring, depending on which guidelines are followed. Because ultrasound used for surveillance of the liver is often suboptimal for evaluation of the pancreas due to overlying bowel gas, AFP monitoring is beneficial in detection of pancreatoblastoma. A rising AFP with absence of a liver mass on US warrants further evaluation of both the liver and pancreas with additional imaging and/or surgical exploration.

Poster # 834

METASTATIC MYOEPITHELIAL CARCINOMA PRESENTING AS ENLARGING SKIN LESION IN A NEONATE

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Background: Myoepithelial carcinoma (MC) is an aggressive neoplasm that rarely affects children. In the largest case series of 29 pediatric patients with MC, only four were less than one year of age. Myoepithelial neoplasms were first described in salivary glands, but now recognized in breast, lung, skin, and soft tissues. They are associated with a high risk of recurrence and distant metastasis. Histologically, they are often composed of more than one myoepithelial cell type, including epithelioid, clear, spindle, and/or plasmacytoid cells. They display immunoreactivity for epithelial markers (keratin and EMA) and myoid markers (p63, calponin, SOX10, S100) without evidence of ductal components. Genetic rearrangements in soft tissue MCs have been reported in EWSR1 and PLAG1 genes, among others. In 2014, the Italian TREP (Tumori Rari in Eta Pediatrica) project, an initiative aimed at improving management of rare pediatric cancers, proposed guidelines for treatment of MC after evaluating outcomes in seven patients. Given the low incidence of this neoplasm in children, treatment remains challenging given no standardized protocol exists.

Objectives: Describe a case of an infant presenting with an enlarging congenital scalp lesion found to have metastatic myoepithelial carcinoma.

Design/Method: Case Report

Results: A three-month-old male presented with a scalp lesion that had been growing rapidly since birth. Physical exam was pertinent for a 0.5 cm x 1.0 cm pink plaque on the left occipital scalp with local adenopathy. Initial biopsy of the lesion was concerning for MC. He underwent complete wide excision of the lesion with negative margins. Pathology revealed a multinodular, highly cellular lesion composed of spindle cells with central necrosis. Immunohistochemical stains were positive for cytokeratin AE1/3 and SOX10. No specific gene fusion, including EWSR-1 rearrangement, was found through cytogenetic analysis. Further testing revealed MTAP and CDKN2A/B loss. Staging showed metastasis to a single regional lymph node and lung. Neoadjuvant chemotherapy was initiated per the protocol proposed in the TREP project: four cycles of ICE (ifosfamide, cisplatin, and etoposide) therapy and three cycles of IVE (ifosfamide, vincristine, and etoposide) therapy. The patient was evaluated for radiotherapy as recommended in TREP, but ultimately did not receive due to his age. He achieved complete remission after two cycles of ICE chemotherapy.

Conclusion: Myoepithelial carcinoma is a rare and aggressive neoplasm in the pediatric population. There is no established standardized treatment. In the described patient case, the boy remains in

complete remission one month off chemotherapy per TREP project recommendations, despite not receiving recommended radiotherapy.

Poster # 835

RESPONSE TO NEOADJUVANT SELPERCATINIB IN AN ADOLESCENT WITH ADVANCED PAPILLARY THYROID CARCINOMA

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Background: Papillary thyroid carcinoma (PTC) is the most common form of differentiated thyroid cancer in children and adolescents. Children often present with more advanced disease compared to adults. *RET* fusions have been reported in 25% to 30% of children with PTC. Selpercatinib is an oral small-molecule RET inhibitor approved by the U.S. Food and Drug Administration for radioactive iodine (RAI)-refractory advanced or metastatic *RET* fusion-positive thyroid cancer, including some children with RAI-refractory PTC. The use of selpercatinib as neoadjuvant therapy in children with PTC has not been described and may be considered in select patients to reduce treatment-related morbidity.

Objectives: To describe an adolescent patient with metastatic PTC harboring a *RET* fusion with extensive disease who achieved a radiographic and biochemical response with neoadjuvant selpercatinib.

Design/Method: Case report.

Results: A 17-year-old female presented with a 7-month history of anterior neck swelling and a 3.6-kg weight loss. Computed tomography (CT) scan of the neck showed diffuse enlargement of the thyroid gland with abnormally enlarged and hyperenhancing lymph nodes involving right levels 3-6 and left levels 2-6 nodal locations. Chest CT revealed innumerable bilateral pulmonary lesions. Fine-needle aspiration cytopathologic evaluation of the thyroid and bilateral cervical lymph nodes demonstrated PTC. *NCOA4::RET* fusion was identified through targeted next-generation sequencing of the tumor specimen. Due to invasive regional nodal and extensive pulmonary disease, patient was started on neoadjuvant oral selpercatinib 120 mg twice daily. Radiographic and biochemical response was noted following 16 weeks of selpercatinib. Thyroglobulin decreased from 562.2 ng/mL at diagnosis to 140.3 ng/mL and 71.4 ng/mL after initiation of selpercatinib (after 10 weeks and 16 weeks of treatment, respectively). Total thyroidectomy and central and lateral lymph node dissection was performed after four months of selpercatinib given radiographic and clinical improvement. Selpercatinib was resumed for an additional 23 weeks until receiving RAI treatment to potentially reduce metastatic disease burden, mitigate risk of radiation-induced pulmonary fibrosis, and increase iodine avidity. She tolerated selpercatinib without adverse events. The patient continues to remain in biochemical remission 18 months after RAI with no evidence of disease recurrence.

Conclusion: Selpercatinib is associated with tumor and biochemical response prior to surgery and RAI, and may be considered as neoadjuvant therapy in select children with advanced invasive PTC as an alternative approach to improve treatment-associated morbidity.

Poster # 836

REFRACTORY INFANTILE CHORIOCARCINOMA CONDITIONED WITH GEMCITABINE, DOCETAXEL, MELPHALAN & CISPLATIN

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Background: Infantile choriocarcinoma is an aggressive, rare tumor, with paucity of literature for management. In more recent years, adult studies have favored Ifosfamide, Carboplatin, and Etoposide (ICE) as a high dose chemotherapy (HDC) regimen with autologous stem cell transplant (aSCT) rescue. While Gemcitabine has been used in refractory solid tumors and lymphomas in the adult population, its use in pediatrics has been considered to carry significant toxicity. In adult literature, Gemcitabine with Docetaxel, Melphalan and Cisplatin (GemDMC) has been used with good response in the treatment of germ cell tumors with poor prognosis. Here, we report the use of GemDMC in a pediatric patient with refractory hepatic infantile choriocarcinoma with disease progression after the first autologous transplant. We demonstrate that the use of GemDMC prior to a second aSCT was associated with manageable toxicity and led to complete remission following a second aSCT.

Objectives: To describe the clinical course of a child with refractory infantile hepatic choriocarcinoma treated successfully with GemDMC followed by aSCT rescue.

Design/Method: Case report

Results: A 15m old female from China presented with refractory hepatic choriocarcinoma with lung metastases. She had increasing beta-HCG despite multiple chemotherapy regimens, and partial liver and lung resections. Due to refractory disease despite multiple chemotherapy regimens including bleomycin, etoposide and cisplatin, the patient completed HDC with Carboplatin, Thiotepa and Etoposide followed by aSCT. However, she experienced a rise in beta-HCG on day +21 following transplant concerning for refractory disease. As she was refractory to the prior HDC regimen, the patient underwent a second aSCT with a conditioning regimen of GemDMC due to its support in adult literature. The patient's course was complicated by grade IV mucositis requiring patient-controlled analgesia and Precedex. The patient was not noted to have any infections; she engrafted neutrophils on Day+12 and engrafted platelets on Day+35.

Conclusion: There is little published data for effective treatment regimens in refractory hepatic infantile choriocarcinoma. Here, we describe the first documented use of GemDMC followed by aSCT rescue in refractory infantile choriocarcinoma. We demonstrate its use is associated with manageable toxicities and can lead to resolution of disease refractory to multiple chemotherapy regimens. Moreover, the combination did not lead to significant delays in neutrophil engraftment or carry an increased risk of bleeding or infection. The use of GemDMC followed by aSCT in pediatric patients with metastasized, refractory choriocarcinoma may provide a further option for cure.

Poster # 837

USING SELPERCATINIB IN MULTIDISCIPLINARY APPROACH TO SPORADIC METASTATIC MEDULLARY THYROID CARCINOMA

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Background: Medullary Thyroid Carcinoma (MTC), an aggressive thyroid cancer driven by *RET* proto-oncogene activation, is rarely seen in the pediatric population and necessitates a multidisciplinary management approach. In the case of metastatic disease not amendable to upfront resection, targeted therapies including multikinase inhibitors demonstrate benefit but with potential for early breakthrough and systemic side effects. Selpercatinib, a highly selective *RET* kinase inhibitor, shows promise in adult cases with recent FDA approval for patients ≥12 years of age. This case highlights the efficacy and toxicity profile of selpercatinib as part of treatment in a 10-year-old patient.

Objectives: Describe a single patient experience using selpercatinib in treating pediatric *RET*-positive MTC, addressing knowledge gaps in its application and outcomes in this patient group.

Design/Method: Case report.

Results: A previously well 10-year-old male presented with progressive left neck swelling, pain, stridor, and decreased appetite. Imaging revealed a substantial neck mass (~10 cm) involving the left thyroid with tracheal narrowing and esophageal involvement. It surrounded both common carotid arteries with associated cervical lymphadenopathy and bilateral pulmonary micronodules. Laboratory findings showed elevated calcitonin (32264 pg/ml, normal <=6.0 pg/mL) and carcinoembryonic antigen (CEA 20.0 ng/ml, normal <3.0 ng/mL). Core needle biopsy confirmed MTC, and molecular analysis identified the *RET c.2753T>C,p.M918T* pathogenic variant. Germline testing for *RET* gene pathogenic variants was negative. PET dotatate demonstrated uptake in the neck and chest correlating to CT findings without evidence of other metastases. The patient was initiated on selpercatinib, and treatment outcomes were monitored through clinical, radiological, and laboratory assessments. The patient exhibited a partial response, marked by significant reduction in the size of the neck mass and resolution of symptoms.Selpercatinib led to near normalization of calcitonin and CEA levels and was well-tolerated with minimal side effects like fatigue and mild headaches. Following six months of treatment, he underwent tumor debulking with planned total thyroidectomy, central node dissection, and bilateral neck dissection. Attempts were impeded by carotid encasement and invasion of the neck floor, leading to a conservative approach to minimize morbidity.He resumed selpercatinib following postoperative recovery.

Conclusion: This case highlights successful application of selpercatinib in sporadic metastatic MTC in a pediatric patient, emphasizing early efficacy and tolerability as part of a multimodal treatment approach. The positive clinical response and favorable safety profile underscore selpercatinib as a promising therapy for *RET*-mutated metastatic MTC in children, addressing a gap in treatment and stressing the importance of molecular characterization. Continued follow-up is needed to evaluate treatment response long-term.

Poster # 838

ESOPHAGEAL SQUAMOUS CELL CARCINOMA PRESENTING IN AN ADOLESCENT FEMALE

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Background: Esophageal squamous cell carcinoma (ESCC) is traditionally seen in older adults due to its association with cumulative exposure to toxins including smoking, alcohol ingestion, and N-nitroso containing foods. ESCC has been previously described in pediatric and young adult patients but is rare. Given the paucity of data, evidence-based treatment recommendations are limited.

Objectives: To describe an uncommon etiology of an esophageal mass and the treatment approach for ESCC in an adolescent patient.

Design/Method: Case Report. We conducted a review of the patient chart and relevant literature.

Results: A 16-year-old female who recently immigrated from Afghanistan presented to the Emergency Department with sore throat, dysphagia, and fever. CT scan of the neck demonstrated circumferential esophageal wall thickening with a lobulated left eccentric mass with near complete esophageal occlusion and multiple periesophageal enlarged lymph nodes. Endoscopic biopsy was performed, but results were inconclusive due to limited tissue sample. After multidisciplinary discussion, otolaryngology performed an open biopsy of an involved cervical lymph node with pathology demonstrating metastatic squamous cell carcinoma with faint cytoplasmic p16 staining. PET scan obtained as part of disease staging was notable for extensive disease involvement of the cervical through thoracic esophagus 3.3 cm by 2.5 cm by 11 cm, extensive lymph node involvement including subcarinal lymph nodes, and a small focus of increased FDG uptake in the right iliac spine consistent with a single metastatic site. The patient started chemotherapy with weekly carboplatin and paclitaxel for 10 weeks concurrently with 6 weeks of proton-beam radiation. Treatment was well tolerated with hemoglobin ranging from 8.0-10.6 g/dL, platelet count from 118-366 K/mcL, and absolute neutrophil count from 1.06-14.41 K/mcL throughout chemotherapy and radiation. Interval decrease in the size of the neck mass from 5.1 by 2.7 cm at the level of the thyroid gland at start of treatment to 4.3 by 1.7 cm following 8 weeks of chemotherapy and 4 weeks of radiation, decreased PET avidity of the bone lesion, and improvement in dysphagia were observed. Maintenance treatment with nivolumab is planned at present.

Conclusion: ESCC is a rare etiology of an esophageal mass in an adolescent patient who presented with dysphagia, fever, and sore throat. As part of ongoing treatment, referral to Cancer Genetics team is in place to evaluate for underlying inherited predisposition to ESCC. We hope to guide future clinicians in the appropriate diagnosis and treatment of ESCC in pediatric patients.

Poster # 840

OSTEOBLASTOMA: A CASE SERIES

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Background: Osteoblastoma (OB) is a rare tumor constituting only 1% of all primary bone tumors. It typically occurs in males, in the second decade of life, and primarily affects the vertebral column and long bones. While it is generally considered benign due to its slow growing nature and inability to metastasize, OB can occasionally exhibit aggressive features of growth, causing significant bone destruction, infiltration of the soft tissues, and epidural extension. The current treatment of choice is complete surgical resection, reserving radiotherapy and chemotherapy for aggressive or surgically unresectable tumors. Next-generation sequencing (NGS) is not included in the typical evaluation and may offer novel insight into genetic alterations associated with OB.

Objectives: With the description of these three cases, we aim to highlight the extraordinarily diverse ways that OB can present and behave, from a highly aggressive course in the cervical spine that progressed even after 4 surgeries to dormant disease affecting the clavicle, requiring only local curettage for diagnosis and no further treatment. Additionally, we present genetic information acquired by NGS testing, not conventionally part of the work-up for OB.

Design/Method: This case series examined NGS results, surgical margin outcomes, treatment modalities, imaging, and relevant scientific literature for each case, as well as pertinent information from each patient's medical history.

Results: Of the three cases we reviewed, all were female, ages 8, 9 and 11. Tumor locations varied, affecting the thoracic vertebrae T8-9, cervical vertebra C7, and clavicle. The disease courses of these patients ranged from inoperable spinal tumor necessitating radiotherapy, to residual disease after 4 vertebrectomy surgeries to dormant disease of the clavicle with resolution after curettage. Furthermore the differential diagnoses considered among these cases consisted of primary aneurysmal bone cyst, chondroblastoma, osteosarcoma, Ewing sarcoma, lymphoma, rhabdomyosarcoma, giant cell tumor, and chronic recurrent multifocal osteomyelitis, demonstrating the potential difficulty in diagnosing OB. NGS testing was performed on tumor samples of 2 out 3 of the patients and revealed a WWTR1-FOSB translocation and a germline ATM mutation. The two patients with vertebral involvement, experienced progressive disease within 7 months postoperatively and the remaining patient presented with normally maturing bone 3 months postoperatively.

Conclusion: This case series emphasizes the capability of OB to present and progress in incredibly diverse ways. Moreover, there is currently a lack of knowledge regarding the genetic drivers of this disease process and we believe that NGS testing may assist in furthering the genetic characterization of this tumor.

Poster # 841

A CASE REPORT OF NOVEL CRTC1-NCOA2 FUSION IN EPITHELIOID SARCOMA

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Background: Soft-tissue sarcomas (STS) account for approximately 7% of pediatric cancers. They represent a heterogeneous group of neoplasms of presumed mesenchymal origin with a wide range of biologic activity. While precise histopathologic diagnosis is a critical step to appropriate management,

comprehensive molecular testing utilizing next-generation sequencing (NGS), methylation profiling, and other modalities continues to refine our understanding of STS tumorigenesis. Additionally, this testing has led to the discovery of novel genomic alterations that provide new biologic insight and inform therapeutic decision making.

Objectives: We present the case of a 12 year-old female diagnosed with spinal epithelioid sarcoma exhibiting a novel CRTC1-NCOA2 fusion and discuss the mechanistic implications and prognostic impact of this fusion.

Design/Method: Standard radiographic and histopathologic diagnostic procedures were implemented. Due to the non-specific nature of the initial diagnosis, further comprehensive molecular profiling utilizing a 500 gene NGS panel as well as DNA methylation analysis was performed.

Results: Magnetic resonance imaging of the spine revealed a heterogeneous mass in the L3/4 region of the lumbar spine. Immunohistochemistry showed positive staining for FLI1, SSTR2A and CD99 suggestive of a diagnosis of anaplastic meningioma. However, methylation profiling failed to match with any known tumor class. Additionally, NGS demonstrated a novel rearrangement involving CRTC1 on chromosome 19 and NCOA2 which has not been reported in meningioma or any other specific neoplasm. A consensus diagnosis of epithelioid sarcoma with a novel CRTC1-NCOA2 fusion was reached. Following gross total resection, the patient received focal proton radiation at 57 Gray in 32 fractions. She remains disease free two years post-radiation.

Conclusion: Epithelioid sarcoma (ES) is a rare, aggressive soft tissue tumor that accounts for 4-8% of pediatric non-rhabdoid sarcomas. Cytogenetic analysis of ES has demonstrated complex patterns of genetic alterations including the loss of SMARCB1/INI1 protein expression. Alterations in the CREB-regulated transcription coactivator 1 (CRTC1) gene on chromosome 19 have been implicated in the pathogenesis of myriad solid tumors including mucoepidermoid carcinoma, hidradenoma, and cutaneous melanocytic tumor. Likewise, changes in the nuclear receptor coactivator 2 (*NCOA2*) gene on chromosome 8q13.3 have been associated with mesenchymal chondrosarcoma, infantile spindle cell rhabdomyosarcoma, acute leukemia, and uterine tumors. To our knowledge, fusion of these two genes has not been previously documented. As such, analyzing the role of these fusion partners in ES tumorigenesis offers key mechanistic insight. Further research is needed to elucidate diagnostic and therapeutic implications of this novel fusion.

Poster # 842

DIAGNOSIS OF MOSAIC RASOPATHY IN A CHILD WITH RHABDOMYOSARCOMA

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Background: Phacomatosis pigmentokeratotica (PPK) is a subtype of epidermal nevus syndrome characterized by the co-existence of a sebaceous nevus and a speckled lentiginous nevus and described in approximately 30 cases in literature. PPK is now recognized as a mosaic RASopathy due a postzygotic mutation in the Ras-Raf-MEK-ERK pathway. RAS variants are also known to contribute to tumorigenesis, in some pediatric cancers, including rhabdomyosarcoma.

Objectives: Describe the presentation and evaluation of a child with pelvic rhabdomyosarcoma and evolving skin lesions found to have a rare mosaic-RASopathy.

Design/Method: Case Report

Results: The patient is a former 32-week premature female who presented to dermatology clinic at 2 months of age for birthmarks on her back and right shoulder. She was diagnosed with epidermal nevi and congenital melanocytic nevi with the possibility of having an epidermal nevus syndrome. At 4 months of age, she was hospitalized for obstructive renal failure secondary to a pelvic mass. Biopsy of the mass was diagnostic for embryonal rhabdomyosarcoma with gain of chromosomes 2, 3, 5, 8 and 11, and copy-neutral loss of heterozygosity of 11p15.5. Molecular testing revealed *HRAS* G13R mutation in the tumor, but not in a blood sample. Five months after her cancer diagnosis she underwent tumor resection and skin biopsy. Whole exome sequencing of the skin biopsy showed a variant of uncertain significance in *PORCN* gene. While receiving chemotherapy and post-treatment, her skin lesions continued to evolve with increased size and number of nevi. A single nucleotide polymorphism-based microarray was performed on blood to assess for any germline copy number variants but was negative. Due to ongoing concerns for PPK, she underwent her second and third skin biopsies. The two lesions biopsied and showed the same *HRAS* G13R mutation as her tumor, confirming a diagnosis of a mosaic RASopathy almost 2 years after her first dermatology visit.

Conclusion: Mosaic RASopathies remain a diagnostic challenge. Tissue involvement can be varied and subtle, DNA sequencing of the blood is often negative, and phenotypes can depart from germline RASopathies, even when caused by the same mutation. With only case reports and small case series describing an association between cutaneous mosaic RASopathies and rhabdomyosarcoma, there is a need for further awareness of this association as it may impact treatment decisions. Also, despite cancer screening guidelines for germline RASopathies being well established, they are not available for mosaic cases, leading providers to question future malignancy risks in this patient population.

Poster # 843

A RARE DIAGNOSIS OF FOLLICULAR DENDRITIC CELL SARCOMA IN AN ADOLESCENT PATIENT

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Background: Follicular dendritic cell sarcoma (FDCS) is a rare neoplasm that usually occurs in the adult population, with median age of onset at 44 years. Since its first description in 1986, fewer than 10 cases of FDCS in children or adolescents have been reported. FDCS arises from antigen presenting cells (APCs) in nodal and extranodal lymphoid follicles. Due to its rarity, there is currently no standardized treatment protocol for FDCS, particularly in the pediatric population.

Objectives: In this report, we present a rare case of FDCS in an adolescent showing treatment response to ifosfamide and doxorubicin.

Design/Method: Case Report

Results: A 14-year-old male presented with a 6-month history of enlarging bilateral cervical lymphadenopathy, worsening snoring, and 10-pound unintentional weight loss. CT revealed enlarged cervical lymph nodes with internal necrosis, enlarged pharyngeal and palatine tonsils, and a singular right apical lung nodule. Open biopsy of the right neck mass confirmed FDCS. The patient then underwent bilateral selective neck lymph node dissection.
Three months after initial resection, surveillance CT revealed enlarged adenoids and left maxillary sinus atelectasis. Subsequent resection revealed FDCS in the bilateral tonsillar tissue. Seven weeks after resection, the patient was treated with adjuvant radiation therapy. Scans performed 3 months after completion of radiation therapy revealed a new 7x5 mm pulmonary nodule in the left lower lobe, which was confirmed as FDCS on biopsy. PD-L1 expression by immunohistochemistry was identified with a tumor proportion score (TPS) greater than 1%, so the patient was treated with immune checkpoint inhibitor atezolizumab.
After his second dose of atezolizumab, he noticed a new lump on his neck, which was shown to be FDCS by biopsy. Repeat PET scan revealed development of several hypermetabolic lesions of left neck, left hilum, cardiophrenic lymph nodes, and multiple pulmonary nodules. The patient was started on ifosfamide and doxorubicin per Children's Oncology Group protocol ARST0332 with evidence of treatment response on imaging after four cycles.

Conclusion: For many patients with FDCS, surgical resection may be curative. Many other patients go on to develop local and distant recurrence without a currently accepted standard of care therapy. Systematic research is required to determine the best treatment options by focusing on specific tumor markers and genetic changes within FDCS. Progress must be made in treating this rare and aggressive tumor via international collaboration.

Poster # 844

TRANSPLACENTAL METASTASIS OF NEONATAL UNDIFFERENTIATED SARCOMA IN A TRIPLET PREGNANCY: A CASE REPORT

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Background: Transplacental fetal transmission of leukemia is well documented, prompting assessment of identical twin siblings. Similar risk is unclear in solid tumors. While metastases of fetal soft tissue sarcomas to the maternal compartment of the placenta and visceral organs in the mother are reported, this is the first report of a transplacental spread of genetically identical sarcoma to another fetus in a multi-gestation pregnancy.

Objectives: To describe a case of transplacental transmission of a high-grade undifferentiated sarcoma in a triplet pregnancy.

Design/Method: Case Report.

Results: We report three male triplets born at 32 6/7 weeks gestation to a 31-year-old mother with a dichorionic (Baby A and B monochorionic) tri-amniotic pregnancy. Baby B was prenatally diagnosed with a left cervical mass. Postnatal biopsy demonstrated an undifferentiated high-grade sarcoma. Given prematurity and associated low birth weight, chemotherapy was initiated with vincristine and

dactinomycin; however, baby B died at one month old due to rapidly progressive disseminated disease. Baby A, who shared the same placenta as baby B, underwent screening after his sibling's diagnosis and at one month old was found to have multiple masses (left arm, right and left liver) with pathology identical to his deceased sibling. Cancer cytogenomic microarray analysis and next-generation sequencing of both tumors revealed shared loss of 6q26, 12q24.31, 16p13.13, gain of 10q11.22, and HNF1A mutations. Examination of the placenta revealed rare microscopic foci of stromal hypercellularity within the chorionic villi of baby B, reflective of placental metastatic disease. No such foci were seen in the placenta of baby A. Placental immunohistochemical staining for baby B was comparable to that seen in the biopsies from baby A and B, indicating that the neoplastic lesions in Baby A were acquired via transplacental hematogenous spread. Chemotherapy with vincristine, doxorubicin and cyclophosphamide was initiated for baby A with dose reductions given his age and prematurity. After two cycles of chemotherapy, liver lesions resolved and R0 resection was performed. Once reaching full term, chemotherapy was changed to ifosfamide and doxorubicin. He is currently 4 months off therapy with no evidence of disease. Baby C, who did not share a placenta with A or B, is alive with no evidence of disease.

Conclusion: To our knowledge, this is the first description of a congenital sarcoma with transplacental metastatic spread from one monochorionic sibling to the other. Additionally, we highlight the utility of molecular testing to confirm the identity of these tumors.

Poster # 845

COMPLETE RESPONSE OF RECURRENT TENOSYNOVIAL GIANT CELL TUMOR TO PEXIDARTINIB IN A PEDIATRIC PATIENT

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Background: Tenosynovial giant cell tumors (TGCT), formerly known as pigmented villonodular synovitis, are rare locally aggressive neoplasms that overexpress colony-stimulating factor 1 (CSF1). This diagnosis should be considered in pediatric patients with chronic inflammation in a single large joint and is strongly suggested by MRI findings. Surgical excision is the standard of care. Recurrence rates are low with the localized subtype of TGCT but are common with the diffuse subtype. Both recurrences themselves and multiple surgeries can lead to extensive joint damage and functional impairment. The CSF1 inhibitor pexidartinib is now approved to treat TGCTs in adults presenting with significant morbidity and for whom surgery is not an ideal option. The impressive treatment response observed on the drug's licensing trial must be balanced against the risk of severe hepatotoxicity. Pediatric study of pexidartinib thus far is limited to a single Phase I clinical trial.

Objectives: This case report details successful treatment of progressive TGCT of the left knee in a 16-year-old male, with pexidartinib inducing a complete response.

Design/Method: Pexidartinib was initiated at the adult dose of 400 mg BID taken apart from fatty meals and later was changed to 250 mg BID with low-fat meals at manufacturer direction.

Results: Prior to therapy initiation, the patient was offered repeat arthroscopy and synovectomy for recurrent, diffuse TGCT of the left knee. Initial surgery was 16 months prior, and there was a high risk of

recurrence and worsening knee function. Prior to initiation of pexidartinib, the patient was unable to extend the knee fully, required daily over-the-counter analgesia, and had stopped wrestling and playing football due to pain and functional limitations. Full symptom resolution and a marked partial response were noted on MRI following three months of treatment despite intermittently poor patient adherence, and a full response was seen on MRI after nine months of treatment. No therapy interruptions or clinically significant laboratory abnormalities occurred. Pexidartinib was well tolerated with occasional extremity rash that self resolved and with iatrogenic achromotrichia. Pexidartinib was discontinued following 14 months of therapy at patient preference with no recurrence of disease five months off therapy.

Conclusion: Pexidartinib was effective and well tolerated in a pediatric patient with progressive TGCT and should be considered as a reasonable alternative to surgery in pediatric patients with diffuse disease.

Poster # 846

ALVEOLAR SOFT PART SARCOMA WITH NON-CANONICAL FUSION: A CASE REPORT

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Background: Alveolar soft part sarcoma (ASPS) is a rare malignancy, associated with high risk of metastasis and chemotherapeutic resistance. In children, the most common sites of origin are the tongue and orbit. In almost all cases, ASPS is characterized by an unbalanced translocation, der(17)t(X:17)(p11;p25), resulting in an *ASPSCR1-TFE3* fusion product. Here we present a case of ASPS associated an alternate fusion.

Objectives: Describe a pediatric case of ASPS with a *PRCC-TFE3* fusion.

Design/Method: Patient completed evaluation at a pediatric quaternay care center including imaging, clinical examination and pathology review. FISH analysis was performed at Mayo Clinic Laboratories. Molecular characterization was completed through the MiOncoSeq program at University of Michigan.

Results: A 13 year-old female with one-year history of recurrent epistaxis presented following 3-week history of right eye swelling and headaches. Physical exam was remarkable for right-sided proptosis, ecchymosis and edema of the right lower eyelid. CT imaging showed a large mass centered in the right ethmoid sinus with substantial intracranial extension through the olfactory groove, into the anterior cranial fossa. MR imaging revealed the mass to be T1 isointense, heterogeneously T2 hyperintense,and contrast enhancing. Metastatic workup was negative.

Biopsy revealed zellballen appearance with epithelioid cells showing nuclear pleomorphism, prominent nucleoli and abundant eosinophilic finely granular cytoplasm. Immunostaining was positive for NSE, ATRX, cathespin K, and progesterone receptor. *TFE3* rearrangement was not detected by FISH. However, tumor sequencing was notable for t(X;1)(p11.23;q23.1) leading to *PRCC-TFE3* fusion and PD-L1 expression. Germline sequencing demonstrated no pathogenic variants.

While debulking resection was possible, the anticipated result was an R1 resection, and tremendous

arterial bleeding was noted at initial biopsy. Treatment was thus initiated with axitinib and pembrolizumab with initial imaging stability. Following 10 months of treatment, she had clinical progression with vision changes. R1 resection was then completed., She is currently receiving proton radiation with concurrent sunitinib.

Conclusion: ASPS is characterized molecularly by an unbalanced translocation der(17)t(X:17)(p11;p25), resulting in an *ASPSCR1-TFE3* fusion product. However, Dickson et al. reported three cases of ASPS associated with novel fusion products. Here, we report a fourth case of non-canonical fusion protein in ASPS and the second case with *PRCC-TFE3* fusion product.
Like *ASPSCR1-TFE3* fusions, *PRCC-TFE3* fusions lead to increased activation of *TFE3*, albeit at a more potent level, which has been associated with the Akt/MAPK pathway and increased MET expression. This case highlights the under-recognized genetic heterozygosity of ASPS and importance of molecular testing in such enigmatic malignancies.

Poster # 847

INFANTILE FIBROSARCOMA TUMOR WITH KIAA 1549-BRAF REARRANGEMENT AND GERMLINE PALB2 MUTATION

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Background: Infantile Fibrosarcomas (IFS) are soft tissue tumors typically occurring in patients two years or younger. It is the most common non-rhabdomyosarcoma soft tissue tumor type for this age group, and common sites are the extremities or trunk. Histological IFS are characterized by poorly circumscribed masses of small to large spindled cells in fascicles with high cellularity, nuclear atypia, and pleomorphism. In 70% of cases, there is translocation of t(12;15)(p13;q25), resulting in an ETV6-NTRK3 transcript. However, there have been rare cases of IFS morphology with fusions of other receptor kinases.

Objectives: We describe a case of Infantile fibrosarcoma sarcoma with KIAA 1549-BRAF rearrangement and germline pathogenic PALB2 mutation

Design/Method: Retrospective chart review.

Results: A two-month-old male presented with an enlarging right soft tissue mass in the right upper arm. Upon examination, the patient had some limitation of motion of the right arm with noted bicep fullness with a firm mass. An MRI showed fusiform enlargement of bicep muscles measuring 1.6x1.7 cm. Core needle biopsy showed moderately cellular monotonous ovoid to spindle cells with no necrosis present; mitosis was inconspicuous. ETV6 FISH and TRK immunohistochemical staining were negative. Next-generation sequencing showed KIAA 1549-BRAF and PALB2 LOF variant. Germline PALB2 testing was positive for a pathogenic variant.

Due to diffuse muscle involvement, complete surgical resection would lead to significant morbidity. The patient was started on Trametinib at 0.032mg/Kg daily. Within the first 2 months of therapy, his bicep decreased in size with improved arm mobility. He had one dose reduction to 50% after developing

paronychia of the right great toe. Additionally, he had a morbilliform rash, which was controlled with topical steroid treatment. A repeat MRI performed after 3 months of therapy showed resolution of the forearm mass lesion with no abnormal enhancement or restricted diffusion of the bicep muscle. He continues with no evidence of disease almost one year after starting trametinib.

Conclusion: Diagnosis of IFS is made based on histologic findings and genetic characteristics, typically ETV6-NTRK3. There are limited cases of BRAF-altered spindle cells with IFS-like morphology. The primary treatment for IFS is surgery. Typically, systemic chemotherapy is used as second-line treatment. MEK inhibitors for BRAF-altered tumors have lessened the tumor burden. This case highlights the importance of looking at additional molecular drivers for a comprehensive treatment plan with targeted therapies. Further studies are needed to evaluate the efficacy and long-term toxicities.

Poster # 848

RARE CASE OF SPINDLE CELL RHABDOMYOSARCOMA IN A PEDIATRIC PATIENT WITH DE NOVO NFIX:TCF3 FUSION

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Background: Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma (STS) in children, accounting for 40% of all pediatric STS. There are four main subtypes of RMS and spindle cell/sclerosing RMS, is an uncommon variant. Those with *MYOD1* mutations affect a wide age range of patients and has a poor prognosis, while *VGLL2* or *NCOA2* fusions occur in infants with spindle cell RMS and have a favorable prognosis. A fusion involving *NFIX* in mesenchymal tumors has only been reported in solitary fibrous tumor *(NFIX:STAT6).*

Objectives: Discussion of a novel fusion in a pediatric patient with spindle cell RMS.

Design/Method: Case Report.

Results: A 14-year-old female with scoliosis presented with pain in the right hip, radiating to the lower extremity with associated numbness and right foot swelling. Magnetic Resonance Imaging revealed an 11.2 X 3.7 X 11.5 cm enhancing mass in the right obturator internus, with possible encasement of the right S1 nerve root. The mass was biopsied revealing a hypercellular malignant spindle cell tumor and by immunohistochemistry, the tumor cells were positive for ALK and focally positive for MYOD1, consistent with a spindle cell RMS. Next-generation sequencing revealed *NFIX:TCF3*(chr19:12995864:+/chr19:1621970:) fusion. Given the absence of metastatic disease on PET-CT, the patient was risk stratified as intermediate risk (stage III, group III) and is being treated per Children's Oncology Group protocol D9803 with VAC/VA (*NCT00003958*). On querying a large CLIA-certified laboratory (Caris Life sciences ®) database with more than 5000 sarcoma patient samples, including 32 patients with spindle cell RMS, *NFIX:TCF3* rearrangement has only been documented in one other tumor–glioblastoma that arose in an adult.

Conclusion: Spindle Cell RMS can be associated with different mutations and fusions, however *NFIX:TCF3* fusion has not been previously reported in any sarcoma. *TCF3* is a transcriptional

activator, implicated in lymphoid malignancies and *NFIX* fusions have been noted in breast, skin, and lung malignancies. The implications of this fusion are not yet known and warrant further study.

Poster # 849

INI-1 NEGATIVE PEDIATRIC CHORDOMA: EXCELLENT RESPONSE WITH EWING'S BASED THERAPY

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Background: Chordomas are rare tumors in the United States, with about 300 new cases annually and pediatric chordomas make up only 5% of the cases. Most pediatric chordomas are located at the base of the skull. Poorly differentiated chordomas, a rare histological subtype that is more common in pediatrics, are defined by loss of integrated interactor-1 (INI-1). Positive brachyury immunohistochemistry staining is diagnostic for chordomas. Due to the rarity of this malignancy, there is no standard of care treatment.

Objectives: Describe a rare case of INI-1-negative, poorly differentiated pediatric chordoma, emphasizing the significance of brachyury staining to facilitate early identification and report an excellent response with Ewing's based therapy.

Design/Method: A single-subject case report.

Results: A 14-year-old male presented with a palpable mass (6cm) in his left neck. The patient exhibited limited range of motion due to pain, without focal deficits and normal neurological exam. A magnetic resonance imaging soft tissue neck confirmed a mass in the cervical spine, originating from the C2 vertebra with an extradural component invading the spinal canal, causing spinal cord deviation. Treatment was initiated with high-dose dexamethasone; chest computed tomography and positron emission tomography scans showed no evidence of metastatic disease.
After biopsy, the initial pathology suggested a malignant INI-1-negative tumor, not otherwise specified with possible diagnosis of epithelioid sarcoma (ES), proximal variant type, exhibiting features of malignant rhabdoid tumor. Patient received urgent treatment with ifosfamide and doxorubicin for an unspecified sarcoma, suspected ES, and prognosis was thought to be extremely poor. Ultimately after literature review and consultation with experts, brachyury immunohistochemistry staining was performed and was positive, confirming the diagnosis of INI-1-negative poorly differentiated chordoma. The patient underwent chemotherapy following Children's Oncology Group AEWS1033 protocol, with vincristine, cyclophosphamide, and doxorubicin, alternating with ifosfamide and etoposide. This compressed regimen was administered every 2 weeks for 13 cycles. Due to excellent response with chemotherapy, surgical local control was then achieved with gross total resection. The patient subsequently received consolidative proton therapy with 63GyE. Currently, the patient is clinically well with normal function and remains in remission 11 months post-completion of therapy.

Conclusion: While INI-1-negative poorly differentiated chordomas are rare in pediatrics, it is a crucial diagnosis that should be considered for any INI-1-negative tumor, particularly if located near the base of the skull. Appropriate diagnosis is essential to direct therapy which should be initiated with neoadjuvant chemotherapy. For our patient, an Ewing's based therapy approach provided an excellent response.

Poster # 850

CIRCULATING TUMOR DNA IS DETECTABLE AT RELAPSE IN FIVE PEDIATRIC PATIENTS WITH SOLID TUMORS

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Background: Circulating tumor DNA (ctDNA) is a noninvasive biomarker that has been utilized in various adult cancers as a marker of minimal residual disease and prognostic tool. While there is evolving evidence that ctDNA may be prognostic in pediatric solid tumors, experience with commercially available assays in pediatric patients is scarce.

Objectives: We describe five pediatric patients with solid tumors enrolled in a ctDNA feasibility study who had detectable ctDNA at or preceding the time of tumor recurrence.

Design/Method: Thirty-three patients treated at Dell Children's Medical Center have been enrolled in a study evaluating the Signatera personalized ctDNA assay. Patients may be enrolled at diagnosis, during therapy, or after completion of therapy. Signatera ctDNA is followed every two to 12 weeks.

Results: Of the 33 patients enrolled thus far, five have experienced tumor recurrence.
A 17-year-old male with Ewing Sarcoma was enrolled after metastasectomy for his second recurrence. ctDNA levels were zero for one year until becoming detectable concurrent with symptomatic and radiographic metastatic recurrence. Following initiation of treatment with chemotherapy and radiation, levels declined to zero.
A 17-year-old male with localized osteosarcoma was enrolled following metastasectomy for first recurrence. ctDNA was initially undetectable until increasing five months later with tumor recurrence. ctDNA levels rose with tumor progression and have decreased to zero, consistent with treatment response.
A 10-year-old female with high risk neuroblastoma was enrolled following completion of initial therapy. ctDNA was initially undetectable but became positive in June 2022 and remained detectable despite no evidence of disease until osteomedullary recurrence one year later. Levels rose with progression on first salvage therapy and have decreased with second salvage regimen.
A 13-year-old male with parameningeal rhabdomyosarcoma was enrolled at initial diagnosis. ctDNA was positive, declined to zero after initiation of chemotherapy and increased during radiation before returning to zero. Nine months after diagnosis, he had leptomeningeal recurrence, and ctDNA at that time was again positive.
A 10-year-old male with osteosarcoma was enrolled at initial diagnosis. ctDNA was positive and decreased with treatment, then was undetectable after resection. ctDNA became detectable after completion of therapy, preceding radiographic detection of relapse.

Conclusion: In our study, the Signatera ctDNA assay was a reliable reflection, or even predictor, of relapse or progression in five pediatric patients with solid tumors. Further investigation is needed to validate the reliability and best utility of this test.
This study was supported by the Natera early adopter program.

Poster # 851

RESISTANCE TO ENTRECTINIB IN A LOW GRADE MYOFIBROBLASTIC SARCOMA WITH ROS1 MUTATION

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Background: Mutations in ROS1, a receptor tyrosine kinase, drives cellular proliferation in a variety of malignancies including non-small cell lung cancer (NSCLC), inflammatory myofibroblastic tumor (IMT), or glioblastoma. Entrectinib, a TRK, ROS1 and ALK tyrosine kinase inhibitor (TKI) has been used successfully to treat NSCLC in adults as well as IMT in pediatric patients. Resistance to Entrectinib has been reported in NSCLC patients. We report a case of Entrectinib resistance in low grade IMT with ROS1 mutation in a pediatric patient.

Objectives: To report a pediatric patient with acquired resistance to ROS1 inhibitor **with** significant tumor progression after an impressive initial response.

Design/Method: Single Subject Case Report

Results: This case describes a 19-year-old female who presented with worsening headaches, nausea, vomiting, and blurred vision. An MRI brain revealed a 9x8x6cm large lobulated heterogenous tumor in the right posterior fossa. Mass effect was present of the right temporal, parietal, occipital lobes, cerebellum, and brainstem. CT head, chest, abdomen, pelvis and MRI spine were negative. Biopsy of the mass was diagnostic for a low grade myofibroblastic sarcoma with ROS1 mutation. Patient was started on Entrectinib. Follow up imaging demonstrated significant reduction in tumor burden and resolution of tumor related symptoms. Patient reported side effects necessitating dose modification. Patient had recurrence of some disease related symptoms, therefore dose was increased back to full dose. With no resolution of disease related symptoms, MRI confirmed significant progression with mass effect on brain stem. Entrectinib was discontinued. The patient underwent debulking of her mass, photon radiation. Due to tumor progression patient transitioned to third generation ALK inhibitor, Lorlatinib. Patient has remained on Lorlatinib for almost two years with continued marked tumor response with ALK inhibition.

Conclusion: Low grade IMTs in the pediatric population have shown to have good response to targeted therapy such as ROS1 inhibition with Entrectinib. This case describes initial response with Entrectinib, but development of resistance leading to significant tumor progression. The patient was salvaged with resection, radiation, and new targeted therapy with ALK inhibitor with continued response to date. Resistance to ROS1, with Entrectinib, should be considered when patients fail first line targeted therapy and novel mechanisms for this resistance should be explored.

Poster # 852

LOCALIZED PRIMARY EWING SARCOMA OF THE TONGUE IN A PEDIATRIC PATIENT – A RARE PRESENTATION

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Background: Ewing Sarcoma (ES) mainly affects children, adolescents, and young adults and generally originates in the bone. Extraskeletal ES (EES) is a primary soft tissue tumor, a rare subtype of ES. Head and neck involvement are rare and estimated to represent about 3% of all cases of ES. Very few reports of primary ES of the tongue are available for review in the literature. Herrin, we discuss the presentation of a 13-year-old female with primary ES of the tongue.

Objectives: This case report demonstrates a patient with ES of the tongue and a literature review.

Design/Method: Single subject case report.

Results: A 13-year-old female presented with a lesion on the ventral right aspect of her tongue. Given the initial small size, no associated symptoms and benign appearance –thought initially to be a pyogenic granuloma – her local medical team decided to continue monitoring the lesion closely. Approximately 18 months later, she noticed that the mass increased in size. Therefore, she underwent excision of the 0.8 x 0.9 cm lesion. Histology revealed small round blue cells concerning ES. Molecular studies confirmed the presence of EWSR1/ERG fusion. There was no evidence of metastatic disease with additional evaluations. Given the diagnosis, she underwent repeat gross resection with negative margins. She then proceeded with adjuvant chemotherapy with vincristine, doxorubicin, cyclophosphamide, ifosfamide and etoposide, with 14 cycles. She tolerated chemotherapy well and has no evidence of recurrence on interval evaluation on imaging.

Our literature review was remarkable for four cases of primary ES of the tongue. All cases were localized primary lesions without distant metastatic disease. Of these cases, most presented as larger lesions or localized to the base of the tongue at diagnosis. Three of the four cases report the presence of an EWSR1 fusion. Treatment included a combination of chemotherapy as well as local control – either surgical resection or radiation therapy.

Conclusion: EES tumors are rare, especially in the head and neck region, and this case highlights a rare presentation of primary ES of the tongue. Despite a prolonged period between initial symptom presentation and diagnosis, our patient did not have any metastatic disease, as was noted in other cases of primary ES of the tongue. Overall, patients with primary ES of the tongue tend to have a favorable prognosis despite no standardized treatment. ES of the tongue may represent a unique biology within the ES family of tumors, given their unique presentation and course.

Poster # 853

METASTATIC UNDIFFERENTIATED SARCOMA WITH A BRD4-NUTM1 FUSION IN AN ADOLESCENT FEMALE

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Background: NUTM1 fusions are historically associated with aggressive Midline Carcinomas found in children and adolescents. Non-carcinoma tumors harboring NUTM1 fusions have rarely been

documented in literature. With increasing utilization of molecular characterization in solid malignancies, these fusions are likely to be recognized more frequently. This stresses the importance of understanding its significance outside of its classic historical context.

Objectives: We present a rare case of undifferentiated sarcoma with BRD4-NUTM1 rearrangement of the right distal femur with diffuse metastases to the bilateral ovaries, pancreas, and intrabdominal lymph nodes.

Design/Method: A 14-year-old female presented with worsening right leg pain and difficulty breathing. Prior to this presentation, a right distal femoral mass was noted on a MRI for which she was being evaluated for osteosarcoma. Pan-CT was performed due to concern for metastatic spread and notable for mid pancreatic lesion, enlargement and heterogeneity of bilateral ovaries, bilateral pleural effusions, and significant ascites. Biopsy obtained from right oophorectomy revealed Grade 3 undifferentiated sarcoma. Immunohistochemistry demonstrated BCOR overexpression and BRD4-NUTM1 fusion.

Results: Treatment was initiated via Children's Oncology Group protocol AEWS1221. Disease reevaluation was performed following 6 weeks of induction chemotherapy with partial response, demonstrating significant decreases in left ovarian and right distal femur tumors and resolution of the pancreatic lesions and lymphadenopathy. She underwent two local control procedures including radical resection of right distal femur with femoral reconstruction with endoprosthesis and left oophorectomy. The patient tolerated therapy and surgery well, however the family elected to discontinue systemic therapy. Three weeks following cessation of systemic therapy, a new mass in the right inguinal area was detected with rapid spread to her abdominal wall and breasts. Her relapse was complicated by severe hypercalcemia of malignancy which was well controlled by oral bisphosphonates. Despite attempts of salvage therapy with radiation at 2500 cGy over 5 fractions and reinitiation of chemotherapy, she passed away from disease progression.

Conclusion: Though there is some commonality in the aggressive behavior among NUT Midline Carcinomas and other documented cases like our patient, the anatomic distribution and morphology varies widely, making treatment planning a challenge. Cases have demonstrated an initial response to anthracycline-based sarcoma therapy, but overall survival is highly dependent on early and complete surgical resection. Clinical trials are underway and have shown some promise, but more information in this age group is needed on this growing class of solid malignancies to improve outcomes in the future.

Poster # 854

LEUKEMIA, LYMPHOMA OR SOMETHING ELSE: CASE OF SPONTANEOUS TUMOR LYSIS SYNDROME AND MEDIASTINAL MASS

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Background: Tumor lysis syndrome (TLS) and presence of a mediastinal mass are two life-threatening manifestations of hematologic malignancies. Rarely, rhabdomyosarcoma can originate from the mediastinum or metastasize to mediastinal lymph nodes. TLS, complicating treatment or occurring spontaneously, has been occasionally described in metastatic rhabdomyosarcoma.

Objectives: This case highlights the diagnostic challenge of recognizing rhabdomyosarcoma mimicking hematologic malignancy.

Design/Method: Case report

Results: Eighteen-year-old male with no past medical history presented to our hospital with cough, shortness of breath, fatigue, dysphagia and vomiting. Upon arrival, his temperature was 35.8°C, heart rate 109, blood pressure 168/92, respiratory rate 20, and oxygen saturation 93% on room air. Physical exam revealed decreased breath sounds and 1cm firm, nontender supraclavicular lymph node. There was no hepatosplenomegaly. Computed tomography (CT) visualized large mediastinal and bilateral hilar lymphadenopathy causing mass effect upon branches of pulmonary arteries, veins and bilateral mainstem bronchi. There was also an extensive pelvic and retroperitoneal lymphadenopathy. Complete blood count was unremarkable. Chemistry panel was significant for elevated creatinine of 1.76 mg/dl, LDH of 1709 U/L, uric acid of 10.9 mg/dl and phosphorus of 5.9 mg/dl. Patient's acute kidney injury (AKI) was attributed to spontaneous TLS, but also partially to intravenous contrast administered earlier. The patient received rasburicase, allopurinol and aggressive hydration, but eventually required continuous renal replacement therapy. Due to the compression of intrathoracic organs, intravenous methylprednisolone was initiated without improvement in patient's dyspnea. A core-needle biopsy of a perirectal lymph node was performed, and revealed presence of small round blue tumor cells, which lacked lymphoid or myeloid markers, but stained positive for desmin and myogenin. We diagnosed the patient with metastatic rhabdomyosarcoma.

Conclusion: Tumor lysis syndrome is a complication feared in hematologic malignancies, but our case illustrates that disseminated rhabdomyosarcoma can also lead to severe spontaneous TLS requiring renal replacement therapy. In the setting of high tumor burden, prophylactic measures including hyperhydration, allopurinol and close monitoring of kidney function and electrolytes should be considered. Attention should be paid to avoiding nephrotoxic agents, such as intravenous contrast. One should also be aware that, in contrast to hematologic malignancies, systemic steroids will not improve the potentially life-threatening mass effect caused by mediastinal involvement of the tumor, and a decrease in disease burden will require prolonged rhabdomyosarcoma-directed chemotherapy.

References
1. Bien E et al, Clin Exp Metastasis, 2010.
2. Sanford E et al, Pediatr Blood Cancer, 2016.
3. Patiroglu T et al, Childs Nerv Syst. 2014.

Poster # 855

PARANEOPLASTIC LEUKEMOID REACTION IN HIGH-GRADE INI1-DEFICIENT EPITHELIOID SARCOMA: A CASE REPORT

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Background: While certain degree of hyperleukocytosis is seen with some solid tumors; a paraneoplastic leukemoid reaction with white blood cell count (WBC) over 50,000u/L is rare. The increase of mature

neutrophils due to a non-hematolymphoid cytokine-secreting tumor is usually associated with a higher burden of disease, tumor activity and worse clinical outcomes.

Objectives: Loss of SMARCB1/INI-1 expression has been linked to several pediatric and adult sarcomas. Epithelioid sarcoma (ES) is a rare mesenchymal tumor, characterized by inactivation of the SMARCB1 gene, with complete loss of expression found in more than 90% of cases. Treatment of localized ES relies on surgery, most often after neoadjuvant chemotherapy and/or followed by adjuvant radiation therapy. Unfortunately, refractory, or progressive disease frequently occur.

Design/Method: A of a 17-year-old female with metastatic INI-1 deficient sarcoma with severe leukemoid reaction and treatment refractoriness. She presented with 2 months of fatigue, anorexia, abdominal pain emesis and night sweats. Exam was remarkable for a painful left chest wall mass and bilateral lower extremity edema and hepatosplenomegaly.

Results: Her WBC 101k, Hb 8, Uric acid 9.6 and LDH 374. CT of neck and chest demonstrated a 6 x 5 cm subpectoral mass, supraclavicular adenopathy, and multiple pulmonary nodules. CT of abdomen/pelvis revealed innumerable hypoattenuating liver lesions including a dominant mass replacing most of the left hepatic lobe, splenomegaly, ascites and peritoneal carcinomatosis. Biopsies of both liver and chest wall mass reported INI nuclear loss/focal CD34 positive staining/focal ERG positive staining/Sall-4 negative/Glypican-3 negative/rare keratin positive cells consistent with high grade INI1- deficient sarcoma. Bone marrow biopsy negative for disease involvement but did show increased cellularity and left shift of granulocytes. Patient started chemotherapy with 2 cycles of VDC/IE. Surveillance scans continue to show aggressive disease with mix response to therapy, so patient was enrolled on PEPN2121 trial with Tiragolumab and Atezolizumab, however after cycle 1 she developed worsening hyperleukocytosis (WBC >150k), severe hypercalcemia, uncontrolled bone pain as well as worsening lung disease on chest CT. Patient was removed from trial and started palliative therapy with oral Tazemetostat. Unfortunately, patient clinical condition continued to deteriorate due to disease progression leading to her demise.

Conclusion: Based on current medical literature this is likely the first case of INI-1 deficient sarcoma presenting with severe leukemoid reaction correlated with an aggressive course and poor outcome. Awareness of soft tissue sarcoma as a possible cause of leukemoid reaction may help improve the early diagnosis and subsequent early intervention in future cases.

Poster # 856

RENAL MEDULLARY CARCINOMA: PEDIATRIC CASES TREATED WITH COMBINATION THERAPY WITH BORTEZOMIB

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Background: Renal medullary carcinoma (RMC) is a rare renal malignancy associated with sickle cell trait and loss of the tumor suppressor gene SMARCB1 that occurs primarily in adolescents and young adults.

Objectives: Because of the rare nature of RMC , most of information comes from the case series and a few recent single institution trials. Here, we report our experience in pediatric patients with a cytotoxic

chemotherapy regimen consisting of platinum-based therapy and bortezomib that we previously published in a series of young adult patients.

Design/Method: We previously published a case series of three patients (2 young adult and 1 pediatric patient) with metastatic RMC treated with alternating cycles of therapy: regimen A consists of cisplatin, doxorubicin, and bortezomib; regimen B consists of carboplatin, paclitaxel, and gemcitabine. Response was assessed with Positron Emission Tomography (PET). All 3 patients had a complete radiologic response following 1 or 2 complete cycles of neoadjuvant chemotherapy. A radical nephrectomy was performed on all three patients. Patients received a total of 4 cycles of this therapy. We present two additional pediatric patients treated with this regimen.

Results: The one pediatric patient in the published cohort remains free of disease now more than 9 years from therapy. Here we report two additional pediatric patients with metastatic RMC treated with this therapy. One of these patients had a complete PET response after 1 complete cycle of therapy but had disease progression during the 4th cycle of therapy. The other patient has just completed 1st cycle of therapy. This therapy was well tolerated with no significant toxicities other than expected myelosuppression.

Conclusion: RMC is a rare renal tumor with most patients presenting with metastatic disease and currently has very grim prognosis. All patients treated with this therapy in both previously published cohort and the additional 2 pediatric patients achieved a complete radiographic response though most relapsed and ultimately succumbed to their disease. One patient remains in complete remission 9 years from diagnosis. We propose that a clinical trial of this or other regimens be undertaken by a cooperative study group to accrue sufficient patients to advance therapies for this rare and devastating malignancy.

Poster # 857

EFFECTIVE USE OF LAROTRECTINIB IN MANAGEMENT OF AN INFANT WITH UNRESECTABLE MESOBLASTIC NEPHROMA

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Background: Mesoblastic nephroma is the most common renal tumor in infants. ETV6-NTRK fusion, which activates the tropomyosin-related kinase (TRK) signaling pathway, is commonly seen. Chromosomal rearrangements involving NTRK1, NTRK2 or NTRK3 genes occur in approximately 1% of solid tumors. Larotrectinib is a highly selective and CNS-active tropomyosin receptor kinase (TRK) inhibitor that has demonstrated efficacy across TRK fusion-positive cancers regardless of the tumor type. In vitro assays with tumors expressing TRK showed that larotrectinib induces cellular apoptosis and G1 cell cycle arrest. This correlated with a dose-dependent tumor response in vivo. Therefore, larotrectinib may complement the standard of care for inoperable mesoblastic nephroma, which is cytoreduction with standard chemotherapy, which has a high rate of failure.

Objectives: We present a case of a patient with mesoblastic nephroma with cystic/necrotic mass involving the right kidney who had a dramatic response to larotrectinib.

Design/Method: Case report with literature review.

Results: A 9-month-old male presented with fever, lethargy, anorexia, and abdominal distension for seven days. A non-tender mass was palpated in the right hemi-abdomen. Imaging confirmed a marginated cystic necrotic mass in the right kidney, measuring 10.8 x 11 x 10 cm. Respiratory decompensation heralded *E. coli* bacteremia and disseminated intravascular coagulation. An initial attempt at resection was aborted due to hemorrhagic shock, but a biopsy was taken. Histologic appraisal revealed mesoblastic nephroma cellular type with positive NTRK 3 gene rearrangement. A second attempt at surgical resection was aborted due to bleeding. Cytoreductive larotrectinib at 100 mg/m^2/dose twice daily was started. After one month of treatment, imaging showed a 90% reduction in tumor volume. Interval right nephrectomy was successfully performed. An adjuvant six month course of larotrectinib was administered due to concerns regarding intraoperative tumor spillage. Interval imaging showed no evidence of recurrence or metastasis.

Conclusion: Radical nephrectomy is the standard of care for mesoblastic nephroma with success of outcome being completeness of resection. Adjuvant chemotherapy is controversial with use being employed for incomplete resections or advanced/refractory disease. Standard of care involves therapies used in sarcomas or Wilm's, specifically vincristine, doxorubicin, and cyclophosphamide. Use of larotrectinib or other NTRK inhibitors as first line agents in NTRK-positive disease can potentially improve outcomes when administered pre- and/or post-operatively especially in inoperable or metastatic cases. Our patient demonstrated a good response to larotrectinib with no obvious toxicities. He remains stable with no evidence of disease one year after initial therapy.

Poster # 858

NOVEL PATHOGENIC DICER1 GENE MUTATION IN A CHILD WITH PLEUROPULMONARY BLASTOMA AND WILMS TUMOR

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Background: Pleuropulmonary blastoma (PPB) is a rare pediatric lung tumor, primarily affecting infants and young children. Over 90% of PPB cases are linked to germline mutations in the *DICER1* gene, critical for RNA interference and gene silencing. This condition, known as *DICER1* syndrome, is a cancer predisposition syndrome with the most common being PPB, cystic nephroma, thyroid carcinoma, multinodular goiter, Sertoli-Leydig cell tumors, embryonal rhabdomyosarcoma and Wilms tumor.

Objectives: To present a rare case of a young child with type III PPB and Wilms tumor in the setting of a novel pathogenic germline *DICER1* gene mutation.

Design/Method: A previously healthy 3-year-old girl presented with 5 days of left-sided chest pain and dyspnea. A chest x-ray demonstrated a large left thoracic mass. Additional imaging studies including MRI, PET-CT, and US were performed to evaluate the thoracic mass which also revealed an incidental left renal mass. A left upper lobectomy via thoracotomy and IR guided left renal mass biopsy were performed. Pediatric solid tumors genetic panel by sequence analysis and deletion/duplication testing was done.

Results: Imaging studies revealed 10.4 cm heterogenous left thoracic mass with pleural involvement

(SUV 7) and a 1 cm left cortical renal mass (non FDG avid). Gross inspection of the lobectomy specimen revealed a 11.0 x 7.5 x 5.5 cm solid, tan, and fleshy mass with areas reminiscent of hyaline cartilage. Microscopically, most of the tumor had a primitive embryonal appearance with tightly packed, moderately atypical nuclei with minimal associated cytoplasm and a small amount of stroma and areas of malignant cartilaginous and rhabdomyosarcomatous differentiation. A sarcoma mutation panel on the tumor sample identified two mutations in *DICER1* gene ((**c.2040dup, p.Gly681Trpfs*11**; **c.5437G>A, p.E1813K**).The renal mass biopsy showed a highly cellular proliferation of small cells with minimal cytoplasm. Areas of epithelial differentiation and a primitive glomerulus were present, diagnostic of Wilms tumor. No anaplasia was present. A germline gene panel identified a pathogenic heterozygous *DICER1* gene mutation (**c.2040dup, p.Gly681Trpfs*11**) which results in premature translational stop signal causing absent/disrupted protein product. The second somatic mutation (second hit, c.5437G>A, p.E1813K, a somatic RNase IIIb hotspot mutation) has been previously reported. The patient started treatment with ifosfamide, vincristine, dactinomycin, and doxorubicin (IVADo). Following two cycles of chemotherapy, imaging studies showed no evidence of disease.

Conclusion: To our knowledge, the pathogenic germline *DICER1* gene mutation in this patient is novel and has not been previously reported in the literature in individuals affected with *DICER1* cancer predisposition syndrome.

Poster # 859

HEPATOBLASTOMA RELAPSE WITH NORMAL ALPHA FETOPROTEIN: ARE CONVENTIONAL MONITORING PRACTICES ENOUGH?

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Background: Hepatoblastoma (HB) is the most common malignant tumor of the liver in children. Despite significant improvements in treatment (nearly 90% survival for non-metastatic cases), relapse after initial therapy remains a serious challenge. For patients with elevated serum alpha-fetoprotein (AFP) at initial diagnosis regular monitoring for relapse is monitoring serum AFP levels alone.

Objectives: We report two patients with elevated serum AFP at initial diagnosis who recurred without an elevation in serum AFP.

Design/Method: Case Report

Results: Case 1: A 13-month old male with a serum AFP of 729,000 ng/ml underwent a left hepatectomy which revealed an epithelial HB. The patient was treated with cisplatin monotherapy and was disease free for 25 months when routine imaging detected an intra-abdominal mass in the previous tumor bed. His serum AFP was normal. The patient was then treated with carboplatin and cisplatin, followed by surgical resection. Following surgery, he received vincristine and irinotecan and then radiation therapy. The patient is continuing in remission at 10 months since relapse and 53 months from original diagnosis.
Case 2: A 13-month old male presented with an abdominal mass and AFP of 71,740 ng/ml. His original pathologic diagnosis was hepatoblastoma, Pretext Stage IV, M+. He was treated with doxorubicin and cisplatin when a second pathology opinion determined this to be a yolk sac tumor. The treatment was

switched to cisplatin, etoposide, bleomycin regimen by an extended right hepatectomy and metastectomy of lung metastases. The patient relapsed with lung lesions at 2.8 years, detected during routine follow-up imaging. The serum AFP at relapse was normal. He was treated with paclitaxel, carboplatin, ifosfamideand doxorubicin. Two lung nodules were resected. The patient relapsed again in the lungs 9.1 years later. Serum AFP at this time was normal. This relapse was treated with Vincristine and Irinotecan. At last contact the patient is alive with disease (11.9 years from original diagnosis) on treatment with pembrolizumab.

Conclusion: We present two cases of HB with elevated serum AFP at diagnosis and subsequent biopsy-proven relapsed disease with normal serum AFP. Both patients had their serum AFP samples at relapse performed at serial dilutions to rule out false normal levels due to the "hook effect". Morphologic, immunohistochemical, and molecular studies will be presented as well as possible mechanisms for these recurrences of HB without elevation of their serum AFP level.

Poster # 860

FILTERING OUT A RENAL CONUNDRUM: WILMS TUMOR WITH LIVER, BONE, AND INTRASPINAL METASTASES

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Background: Wilms tumor (WT) is the most common pediatric renal tumor, comprising 6% of all pediatric cancers.[1] While the overall survival rate for favorable histology WT is 90%, the limited data for patients with bone metastases at presentation demonstrates an overall survival of 13%.[2,3] There is little guidance on optimal strategies for these patients due to the rarity of this presentation. This case illustrates the challenge in prompt recognition of metastatic WT with spinal cord compression and describes a successful, multimodal approach comprising aggressive chemotherapy, surgery, and radiation. Clinicians confronted with a similar conundrum may consider our approach.

Objectives: Describe a rare case of favorable WT with liver, bone, and intraspinal metastases.

Design/Method: Case Report

Results: A 12-year-old girl presented with one day of lower extremity numbness and urinary incontinence preceded by three months of progressive lower back pain. Imaging confirmed a large left renal mass, infiltrating into the neural foramina with compression of the spinal cord and conus medullaris from osseous epidural metastases prompting surgical decompression. She underwent a percutaneous mass biopsy and left T9-L1 hemilaminectomy to remove the extradural intraspinal thoracolumbar tumor. Imaging also revealed liver metastases. Based on her presentation, the initial differential included clear cell sarcoma, rhabdomyosarcoma, and malignant peripheral nerve sheath tumor. Immunohistochemistry was inconsistent with these diagnoses, and histology was initially unrevealing. The patient continued to have symptoms of cord compression with neurogenic bladder and bowel, and therefore emergent chemotherapy was initiated with AREN0321 UH-2 (vincristine, cyclophosphamide, doxorubicin, etoposide, carboplatin). Ultimately next generation sequencing revealed WT1 gene, beta catenin gene, loss of chromosome 7p, and gain of chromosome 7q. Central pathologic review confirmed favorable histology Wilms tumor, LOH negative. Two months post-

diagnosis, imaging showed significant improvement, allowing her to undergo nephrectomy and resection of retroperitoneal disease followed by radiation (total dose 2520 Gy) with resolution of urinary dysfunction and neurological deficit. She has since sustained disease-free remission for 23 months without significant toxicity.

Conclusion: We highlight the diagnostic challenge of metastatic WT with liver, bone, and intraspinal metastases, rare features with poor outcomes. Prompt histopathologic diagnosis and surgical decompression to prevent irreversible neurological deficit are integral to achieving disease control. We suggest consideration of a multimodal approach comprising surgery, radiation, and AREN0321 UH-2 for favorable WT with atypical and aggressive features including metastases.

1. Smith, Cancer, 2014
2. Iaboni, Pediatr Blood Cancer, 2019
3. Gurney, Cancer, 1995

Poster # 861

ADRENAL GANGLIONEUROMA IN A PEDIATRIC PATIENT WITH PIK3CA-RELATED OVERGROWTH SYNDROME

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Background: *PIK3CA*-related overgrowth syndrome (PROS) comprises a rare group of overgrowth disorders caused by somatic mosaic activating mutations in the phosphoinositide-3-kinase-alpha (*PIK3CA)* gene that occur during embryonic development. Somatic *PIK3CA* mutations have also been reported in several cancers, with *PIK3CA* now one of the most frequently implicated genes carrying somatic point mutations associated with solid tumors. These mutations are highly prevalent in many adult cancers including breast (>30%), endometrial (>30%), bladder (>20%), colorectal carcinoma (>17%), and head and neck squamous cell carcinoma (>15%). There have additionally been rare cases of Wilms tumor and nephroblastomatosis reported in pediatric patients with PROS, and exome sequencing has recently identified several previously unrecognized predisposing genes for ganglioneuroma (GN) including *PIK3CA*. However, there have been no cases of GN or other neuroendocrine tumors in the setting of PROS in either children or adults reported in the literature.

Objectives: To present a case of ganglioneuroma in a pediatric patient with PROS.

Design/Method: Single subject case report developed with thorough literature review.

Results: The patient is a 10-year-old female with a clinical diagnosis of PROS who initially presented to the emergency department for painless microscopic hematuria. She had no abdominal or flank pain, gross hematuria, fevers, or weight loss. MRI showed a 5.0 x 3.3 x 3.4 cm solid right adrenal mass consistent with GN. Pathology following right adrenalectomy confirmed the diagnosis of adrenal ganglioneuroma positive for a mosaic mutation in *PIK3CA*.
Of note, a 3.7 x 3.9 cm right adrenal mass had previously been seen on computed tomography of the abdomen when the patient was five months old prior to immigrating to the United States. A biopsy had never been done prior to presentation to our hospital at 10 years of age.

Five months following adrenalectomy, she was started on alpelisib, a PI3Kα-selective inhibitor, for treatment of PROS. She has been on this therapy for almost four years with continual improvement in her segmental overgrowth and without recurrence of her GN.

Conclusion: This is the first case to describe a ganglioneuroma in a pediatric patient with PROS. Our case highlights the need for further characterization of somatic mosaic activating *PIK3CA* mutations in PROS associated with pediatric cancers.

Poster # 862

A NOVEL PATHOGENIC VARIANT IN HEREDITARY PARAGANGLIOMA PHEOCHROMOCYTOMA SYNDROME

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Background: Paragangliomas (PGL) are rare, often catecholamine secreting neuroendocrine tumors originating from the sympathetic or parasympathetic ganglia. They are most often diagnosed around the third to fifth decade of life and are usually benign, although a small percentage may become malignant and metastasize. Thirty to forty percent of cases are familial, usually associated with genetic syndromes such as succinate dehydrogenase (SDH)-related PPGL syndrome, neurofibromatosis 1, von Hippel Lindau syndrome and multiple endocrine neoplasia type 2. Patients with hereditary PPGL syndromes commonly present at a younger age and with metastatic disease compared to those with sporadic disease. Patients who have pathogenic variants in *SDHD* are more likely to have multifocal disease, although the risk of malignancy is 5%.

Objectives: We describe a case of a novel pathogenic variant in the *SDHD* gene in an adolescent with metastatic paraganglioma.

Design/Method: Case report

Results: A 16 year old male was referred to the ear, nose and throat physician for complaints of hearing loss, ear fullness and pulsatile tinnitus for 4 months. MRI of the brain showed a left jugulotympanic mass suspected to be a paraganglioma. He underwent resection of primary mass with diagnosis of paraganglioma confirmed by pathology. Subsequent PET scan showed multiple liver, lung and bone metastases.

Germline testing was sent and he was referred to a genetic counselor for further evaluation. Genetic testing via Invitae Inherited Paraganglioma panel revealed a variant of uncertain significance (c.315-2A>T) in *SDHD*. Variants at this location have been previously reported in individuals with PGL/PCC, but pathogenicity had not been determined. Detailed history revealed distant paternal relatives with head/neck tumors. Re-analysis with additional clinical information and RNA submission was requested given the uncertain variant at a splice site. Invitae's VUS resolution reclassified the variant as pathogenic, the change affecting a splice acceptor causing disruption of function via multiple RNA products. Therefore, the patient was diagnosed with hereditary pheochromocytoma/paraganglioma syndrome.

The patient underwent ablation and resection of metastatic lesions. Due to disease progression, he was subsequently started on lanreotide SQ. Medication has been well tolerated and he has had stable disease for approximately 9 months at the time of this report.

Conclusion: This is a case of a patient with metastatic paraganglioma with a previously unclassified SDHD gene variant, now classified as pathogenic. Findings are consistent with a diagnosis of SDH-related hereditary pheochromocytoma/paraganglioma syndrome and variant is likely responsible for the paragangliomas observed in our patient.

Poster # 863

EVALUATION OF ST. JUDE PATIENTS WITH CONCURRENT NEUROBLASTOMA AND LEUKEMIA

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Background: Neuroblastoma is the most common extracranial solid tumor diagnosed in children and acute lymphoblastic leukemia is the most common pediatric cancer. Leukemia can arise as a second malignancy following treatment for neuroblastoma. However, concurrent diagnoses have not been described.

Objectives: Describe the clinical course of two patients treated at St. Jude Children's Research Hospital with concurrent neuroblastic tumors and leukemia.

Design/Method: Electronic medical records reviewed.

Results: Patient 1: Two-year-old male with a 1-month history of limp, lymphadenopathy and abdominal pain. Imaging identified an abdominal mass. Blasts seen on peripheral blood smear. Bone marrow (BM) with 90% lymphoblasts and diagnosis of low-risk B lymphoblastic leukemia (B-ALL) made. Resection of adrenal mass confirmed non-MYCN amplified neuroblastoma. Post-operative MIBG identified 2 avid lymphnodes near tumor bed. Neuroblastoma was stage L1 and risk classified as low-risk. Therapy for B-ALL was initiated as per the Total XVI protocol [Prednisone, Vincristine, Daunorubicin, PEG-asparaginase, Cyclophosphamide, Mercaptopurine, Cytarabine, and triple intrathecal chemotherapy (Methotrexate, Hydrocortisone, and Cytarabine or "MHA")]. Day 15 BM MRD 0.375% and end of induction MRD negative. Neuroblastoma sequencing resulted and demonstrated segmental copy number alterations including LOH 11q, 17q gain and subclonal deletion in 1p36. Surveillance imaging demonstrated local progressive neuroblastoma. Neuroblastoma treatment was initiated as per POG 3961 (Carboplatin, Etoposide, Doxorubicin, Cyclophosphamide) with concurrent Dexamethasone and intrathecal chemotherapy to maintain leukemia remission. Eight cycles of intermediate-risk neuroblastoma therapy plus abdominal radiation were administered. Vincristine and Dexamethasone (for leukemia) were administered during radiation therapy. After completing neuroblastoma therapy, consolidation for leukemia was initiated, complicated by an inability to tolerate Mercaptopurine (myelosuppression), so received two cycles Blinatumomab. Completed continuation therapy, as per low-risk Total XVI protocol (Dexamethasone, Vincristine, Mercaptopurine, Methotrexate, PEG-asparaginase, and MHA intrathecal chemotherapy). Patient is 34-months off neuroblastoma therapy and 1-year off leukemia therapy without evidence of disease. Germline testing was normal.

Patient 2: Six-year-old female diagnosed with standard-risk B-ALL treated on Total XVII protocol. Asymptomatic hyperbilirubinemia noted near end of induction and abdominal ultrasound identified an abdominal mass. CT showed 6-7 cm well-circumscribed right retroperitoneal mass; MIBG was negative. Mass resected and pathology confirmed ganglioneuroma, maturing subtype. No further treatment needed for ganglioneuroma, so continued with leukemia therapy. Completed Total XVII therapy with no evidence of disease. Germline testing was normal.

Conclusion: Concurrent diagnoses of neuroblastoma and leukemia are rare and clinically challenging. The therapeutic strategies must include a combination of therapies and modalities that target treatment of both malignancies.

CNS Tumors (901-922)

Poster # 901

USING DEEP LEARNING TO IDENTIFY HIGH GRADE LESIONS IN PEDIATRIC BRAIN TUMORS

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Background: Artificial intelligence (AI) and deep learning have come a long way in recent years with increased uses in healthcare. More research is needed to apply this technology to pediatric patients. Studies have shown that it is possible to predict multiple tumor types in adults and children using convolutional neural networks (CNN), a form of deep learning, using MRIs as the input data. This project aims to verify that we can use deep learning models to help predict tumor types and characteristics.

Objectives: This study aims to verify that AI can help diagnose and molecularly classify primary pediatric CNS tumors by validating Recurrent Health's deep learning cloud-first platform on pediatric MRI images. The primary objective is to use AI to predict tumor grade with 95% accuracy. The secondary aim is to validate the AI's ability to predict common genetic alterations with 90% accuracy.

Design/Method: This retrospective study will evaluate pediatric patients (ages 0-21) with histologically confirmed primary CNS tumors to validate AI technology using MR imaging. This study also includes demographic data, including age, location of tumor, HG/LG status, and mutational status. Based on WHO classifications, the goal is for the model to appropriately identify high-grade (HG) vs. low-grade (LG) lesions. The data will be divided into a training and validation set with an 80%/20% split. To determine the viability of the models, we will measure specificity, sensitivity, and F1 Score (Sorenson-Dice coefficient) for predicting tumor classification and genetic alterations. Model score confidence will be achieved through K-fold cross-validation and statistical power analysis with a finite population coefficient to determine the appropriate sample size.

Results: Our retrospective test included 136 patients with multiple scans (including T2, SWI and DWI) for training, model validation, and k-fold testing. The CNN was able to predict high-grade (HG) lesions with >95% recall (sensitivity) and >85% precision (specificity). The model also demonstrated a >90% F1 score (harmonic average), showing that the model performs well across challenging cases. Lastly, the model was learned through relatively low training iterations.

Conclusion: Preliminary data suggests accuracy of the deep learning model in identifying high-grade lesions, providing a potential opportunity to have a non-invasive tool to help decrease diagnosis time and aid in surgical planning. We are expanding our analysis to verify that similar outcomes can be reached when evaluating mutational analysis (BRAF alterations/H3K27 mutations) of these lesions, which could help in identification and targeted therapy initiation in the future.

Poster # 902

CLINICAL ACTIVITY AND SAFETY OF TOVORAFENIB IN PATIENTS WITH OPTIC PATHWAY GLIOMAS IN FIREFLY-1

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Background: Optic pathway gliomas (OPG) are low-grade gliomas (LGG) comprising 3-5% of pediatric brain tumors. Morbidity may include visual loss), hypothalamic/pituitary dysfunction, and/or impaired motor function. Genomic alterations of MAPK/*BRAF* are frequent oncogenic drivers in pLGG.

Objectives: Analyze the activity of tovorafenib, an investigational, oral, selective, CNS-penetrant, type II RAF inhibitor in OPGs.

Design/Method: FIREFLY-1 (NCT04775485) is a phase 2 study evaluating tovorafenib (420 mg/m^2 weekly) in patients 6 months–25 years with *RAF*-altered recurrent/progressive LGG (registrational/arm 1 and extension/arm 2) or *RAF*-fusion solid tumors (arm 3). Independently assessed overall response rate (ORR) by RANO-HGG, RAPNO-LGG, and RANO-LGG criteria, are primary, secondary, and exploratory endpoints, respectively.

Results: Arm 1 had 42 (55%) patients with tumors located in the optic pathway. The median age at enrollment was 8 years (range: 2–16); 37 (88%) harbored a *BRAF* fusion and 5 (12%) a BRAF V600E mutation. Median prior lines of systemic therapy was 3 (range: 1–9); 69% had received prior MAPK inhibitors. Baseline vision (best eye, 36 evaluable patients) was normal in 9 (25%), impaired in 27 (75%): mild, 15 (42%); moderate, 6 (17%); severe or profound, 3 (8%) each. As of June 5, 2023, of the 39 RANO-HGG evaluable patients, the confirmed ORR was 64% (7 CR, 18 PRs) with a median duration of response (DOR) of 16.8 months; 12 (31%) had stable disease (SD), providing a 95%clinical benefit rate (CBR). Per RAPNO-LGG (n=42), the ORR was 50% (12 PRs; 9 MRs) with a median DOR of 13.8 months; 16 (38%) had SD, providing an 88% CBR. Per RANO-LGG (n=42), the ORR was 55% (8 PRs; 15 MRs) with a median DOR of 14.4 months; 15 (36%) had SD, providing a 90% CBR. Vision remained stable (67%) or improved (22%) in 89% of evaluable patients per visual acuity assessment (best eye), even with small decreases in tumor size. Median duration of tovorafenib treatment was 16 months, with 69% still on treatment. Most common treatment-related adverse events (TRAEs) of any grade in all treated patients (arms 1 and 2, n=137) were hair color changes (76%), elevated creatine phosphokinase (56%), anemia (49%), fatigue (44%), and maculopapular rash (41%). Dose reductions occurred in 33 (24%), dose interruptions in 50

(37%), and discontinuations in 9 (7%) due to TRAEs.

Conclusion: Tovorafenib demonstrated antitumor activity in recurrent/progressive *BRAF*-altered OPG and was generally well tolerated. Visual acuity remained stable or improved for the majority with OPGs.

FIREFLY-1 was sponsored by Day One Biopharmaceuticals.

Poster # 903

SPATIAL TRANSCRIPTOMICS REVEAL CELL-TYPE HETEROGENEITY IN MEDULLOBLASTOMA TUMOR MICROENVIRONMENT

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Background: Medulloblastomas are a heterogeneous set of embryonal neuroepithelial tumors of the posterior fossa and represent the most common childhood malignancy in the CNS. Four groups of medulloblastoma are recognized: wingless (WNT), sonic hedgehog (SHH), group 3, and group 4. The tumor microenvironment (TME), consisting of malignant, glial, vascular, and immunological cells along with their extracellular matrix (ECM) influences tumor progression and response to therapy. TME emerged as a target for study and novel therapeutic approaches. Prior single-cell transcriptomics identified distinct cell-types within the TME and their corresponding gene expression profile. TME spatial heterogeneity is infered based on physically isolated biopsies of single tumors, but has yet to be directly visualized.

Objectives: We show the spatial gene-expression architecture of human medulloblastoma through spatial transcriptomics and correlate with patient clinical data.

Design/Method: Spatial Sequencing through 10X Visium was performed on 16 total formalin-fixed paraffin-embedded (FFPE) samples from 14 patients treated at Children's Healthcare of Atlanta representing all groups of medulloblastoma. Metadata obtained for each sample include M stage at diagnosis, tumor histological group, molecular subgroup, and relapse status. Sequencing reads were assessed for quality with fastQC then aligned to human genome build Hg38. Read counts were batch-corrected and normalized. Gene expression clusters were computed and plotted on uniform manifold approximation and projection (UMAP). Differential gene expression is computed across clusters and annotated based on canonical marker expression. Gene-set enrichment analysis (GSEA) is performed in a per-cluster manner using Reactome Pathway Database.

Results: UMAP identifies 16 clusters of distinct gene expression representing cells from different components of the TME, including tumor associated astrocytes, macrophages, and vasculature. Medulloblastoma cells including those expressing neural progenitor gene signatures constitute the majority of cells. Clusters with high expression of genes involved in integrin cell surface interactions, collagen formation, MET mediated cell-motility, and extracellular matrix components are seen on GSEA. Other clusters express pathways known in medulloblastoma including NF-kB, TP53 regulatory genes. Heat-shock transcription factor mediated gene expression is noted to be diminished in samples from patients who later developed relapse disease compared to those who did not. Similarly, expression in of tumor associated astrocyte markers was greater in the same group. Spatial heterogeneity in gene

expression is evident when clusters were spatially mapped on histologic section.

Conclusion: Spatial transcriptomics demonstrates cellular heterogeneity in the tumor microenvironment. Molecular studies for targeted therapy should be interpreted with caution given the spatial dependency of gene expression.

Poster # 904

A CSF LIQUID BIOPSY PLATFORM USING LOW-PASS WHOLE GENOME SEQUENCING FOR MALIGNANT BRAIN TUMORS

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Background: Current methods of monitoring treatment response in pediatric brain tumors rely on imaging and cerebral spinal fluid (CSF) cytology. Low-pass whole genome sequencing (lpWGS) could improve disease monitoring by identifying somatic copy number variants (sCNV) found in cell-free DNA (cfDNA) isolated from the CSF of patients with a variety of brain tumors, without the need for neurosurgical biopsy.

Objectives: To develop and describe a clinical liquid biopsy platform for evaluating CSF in the surveillance of residual disease.

Design/Method: CSF specimens (n=56) were collected from 27 patients with pediatric brain tumors via lumbar puncture (n=50), extra-ventricular drains (n=2), or during surgery (n=4). Samples were collected during routine clinical procedures at diagnosis, staging, on treatment, and at the end of therapy. cfDNA was extracted and lpWGS performed using a validated Illumina NextSeq 500 High Output 75 cycle kit with a 37 bp paired-end read configuration. Results were compared to tumor profiling performed by UW-Oncoplex™, a targeted DNA-based next-generation sequencing panel.

Results: Longitudinal CSF samples were collected from 14 patients with medulloblastoma/embryonal tumors, 3 with ATRT, 3 with high-grade glioma, 5 with low-grade glioma, 1 with ependymoma, and 1 with high grade neuroepithelial tumor. CSF volumes collected averaged 3.13 mL (range 1-8 mL) and contained a mean of 204 pg/ul of cfDNA (range 0.1-5220). Of the 56 CSF samples, 31 yielded sufficient DNA for lpWGS while 25 were insufficient, due to low DNA quantity or absence of tumor DNA. Of the 31 samples, 24 were positive for sCNVs and 7 were indeterminate or negative. Of the 24 samples positive for sCNVs, all 24 (100%) had leptomeningeal metastasis or disease in contact with the ventricles at time of sample collection. CSF cytology was negative for malignant cells in 19/24 (80%) of lpWGS positive cases. lpWGS for one patient identified a previously unknown IDH1 mutation in cfDNA, leading to new therapeutic options and treatment with a targeted IDH1 inhibitor.

Conclusion: CSF liquid biopsy has potential as a minimally invasive method of disease detection for measuring treatment response and longitudinal disease surveillance. lpWGS on CSF-derived cfDNA can identify tumor-derived sCNVs even when CSF cytology is negative for malignant cells. lpWGS can reveal sCNVs that are clinically actionable without need for a tissue biopsy.

Poster # 905

Targeting tumor-infiltrating monocytes in pediatric brain tumors

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Background: Brain tumors in children are a devastating disease in a high proportion of patients despite aggressive multimodal therapy. Because of inconsistent results in early-phase clinical trials in unstratified patient cohorts, the role of immunotherapy in pediatric brain tumors remains unclear. The tumor immune microenvironment of pediatric brain tumors is poorly understood.

Objectives: To determine key drivers that either enhance or suppress anti-tumor immunity, and rationally target these players as novel immunotherapy for optimal efficacy while eliciting minimal toxicity.

Design/Method: We performed an in-depth survey of the single-cell transcriptomes of intra-tumoral immune cells from tumor tissue of children with brain tumors using paired single-cell RNA sequencing and single-cell TCR sequencing.

Results: Our results demonstrate that a large fraction of T cells in the tumor tissue are clonally expanded with potential to recognize tumor antigens. Such clonally-expanded T cells display states linked to anti-tumor immunity, express higher levels of transcripts encoding for molecules linked to T cell activation, effector functions, immune cell recruitment, tissue-residency, immune checkpoints, and importantly, show significant enrichment of signatures linked to neoantigen-specific T cells and immunotherapy response. Notably, we identify several neoantigens in pediatric brain tumors, and show that neoantigen-specific T cell gene signatures are linked to better survival outcomes. We further show that PD1-expressing $CD8^+$ T cells in pediatric brain tumors are indeed functional as evidenced by their capacity for cytotoxicity, cytokine production and proliferation. Our studies suggest that endogenous T cell responses are generated within pediatric brain tumors and have the potential to be reinvigorated by immunotherapy, despite an observed lack of clinical response. Strikingly, we found that tumor-infiltrating monocytes infiltrated high-grade tumors. They displayed pro-tumor functions and impaired T cell responses, thereby contributing to immunotherapy resistance.

Conclusion: Overall, our findings suggest that targeting tumor-infiltrating monocytes in combination with immune checkpoint therapy may potentiate T cell activity and enhance immunotherapy responses, an approach that requires prospective validation in future clinical trials.

Poster # 906

INVESTIGATING DIFFERENTIAL METHYLATION OF EPIGENETIC MARKERS IN PAEDIATRIC HIGH-GRADE ASTROCYTOMA

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Background: Paediatric and adult astrocytoma are notably different. Understanding differentially methylated regions (DMRs) and their association with metastasis have improved prognosis of this lethal disease. We have tried to elucidate the epigenetic modifications in Paediatric astrocytoma (pA) and signify the importance of studying these alterations which may have roles in predicting tumour progression.

Objectives: This project is aimed at understanding the role of differentially methylated epiegentic markers in promoting metastasis of pediatric high grade astrocytomas and identifying poetential targets for drug repurposing.

Design/Method: Methylation analysis was carried out with freely available EPIC and INFINIUM array datasets. Datasets were downloaded from NCBI and were analysed using an R- based differential methylation analysis tool, RnBeads. Differential methylation of CpG islands, CpG sites, promotors and genes were computed individually to correlate the effect of DMRs on DNA with respect to each other following which drug repurposing was done. Each candidate gene with predetermined differential methylation scores was evaluated against potential repurposed drugs and evaluated in monolayer and 3D cultures using cellular viability assays to determine their relative effective concentrations.

Results: Differential methylation analysis (DMA) of CpG sites showed significant hyper-methylation at 211674 sites and significant hypo-methylation at 153807 sites. DMA of CpG islands showed significant hyper-methylation at 3980 sites and significant hypo-methylation at 16595 sites. DMA of promotors showed significant hyper-methylation at 13146 sites and significant hypo-methylation at 13690 sites. DMA of genes showed significant hyper-methylation at 6580 sites and significant hypo-methylation at 4187 sites (Samples having mean p value < 0.8, combined p value < 0.01 were considered hypermethylated and those having mean p value<0.2, combined p value < 0.01 were considered hypo methylated). Drug repurposing was done with the top 5 hypomethylated gene candidates.

Conclusion: This study identified significantly hyper/hypo methylated regions within the genome of patients with pA which are crucial in devising prognostic criteria and in studying the effects in tumour progression. We have also identified repurposed drugs based on these changes.

Poster # 907

ASSESSING SURVIVAL OUTCOMES IN CRANIOPHARYNGIOMA

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Background: Craniopharyngiomas are rare pediatric brain tumors originating from the pituitary infundibulum. Due to this location, patients can present with visual changes, endocrinopathies, hydrocephalus requiring urgent neurosurgical intervention, or hypothalamic dysfunction. Recurrence rates vary, and may be affected by initial treatment, young age at diagnosis, original tumor size, and extent of resection.

Objectives: We aimed to assess 5-year overall survival (OS) and progression free survival (PFS), with secondary aims to assess therapeutic strategies and describe their relationship to PFS.

Design/Method: A single institution, retrospective cohort study of patients treated at Seattle Children's Hospital between 1996 and 2023 was performed. We describe initial surgical approach and extent of resection. Serial, postoperative MRIs were used to survey disease stability. Progression was determined radiographically. 5-year OS and PFS were calculated. Unpaired two-tailed student's t-test was used to compare ages at diagnosis between subgroups.

Results: 90 patients were included in study, of which 53 (58.9%) were male. Average age at diagnosis was 8.74 years (range 1.39-25.17). Surgical approaches included: endoscopic endonasal (n=23), craniotomy (n=63), combined endoscopic endonasal and craniotomy (n=2), unknown (n=2). A total of two patients underwent biopsy, while subtotal, near total, and gross total resections were achieved in 12, 38, and 32 cases, respectively. Five cases had unknown extent of resection.

A total of 48.9% of patients experienced tumor progression in the follow-up period; 10% had no available follow-up imaging (n=9) and were excluded from analyses. 7 patients succumbed to complications from their disease, while 17 patients were lost to follow-up. 5-year OS was 96.1% and 5-year PFS was 51.9%, with median follow-up time of 95 months.

Average age at diagnosis for those with tumor progression was 7.96 years, not significantly different than those without tumor progression (9.67 years, p=0.09). Of those with tumor progression, 61% underwent NTRs (n=27/44) while 14% underwent GTRs (n=6). Excluding patients with unknown disease progression status, 6 patients who underwent surgical resection with the endoscopic/endonasal approach had disease progression (30%), 36 with craniotomy had disease progression (62.1%), and 2 patients who underwent combination of both approaches had disease progression (100%). 34 patients were treated with radiation, 8 as upfront therapy, 25 due to disease progression. 13 patients progressed afterwards despite radiation. 25 patients had radiographic progression multiple times.

Conclusion: Further work to understand specific surgical interventions and other therapeutic strategies and their relationship to disease status and morbidity are important to delineate best practices for craniopharyngiomas.

Poster # 908

POSTOPERATIVE VISION OUTCOMES IN CRANIOPHARYNGIOMA

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Background: Pediatric craniopharyngioma is a rare brain tumor, arising from the infundibulum and often invading the sella, suprasellar space, and third ventricle. Due to its proximity to the optic nerves and chiasm, one of the most common reported symptoms is vision loss. Although visual improvement is a primary goal of treatment, there is limited data on expectation for visual recovery following treatment.

Objectives: To characterize visual outcomes for pediatric craniopharyngioma patients undergoing surgery

Design/Method: We performed a retrospective cohort study of pediatric patients undergoing craniopharyngioma resection at our single tertiary care center from 1995 – 2023. Complete ophthalmic data and neurosurgical treatment were recorded. Inclusion criteria were patients who underwent ophthalmologic evaluation prior to treatment and a follow up visual assessment. Primary outcome was changes in visual acuity from initial presentation to the post-operative period with follow-up at least one year after surgery. Normal visual acuity was defined as vision of ≥20/40, visually impaired defined as 20/50 - 20/150, and legally blind defined as ≤20/200.

Results: 33 patients (66 eyes) were included. Mean age at presentation was 9.8 years old (range 1.6-18.7 years old). Median follow up was 168 months (27-247 months). Initial exam showed optic nerve edema in 18% of patients and optic nerve pallor in 24% of patients. At presentation, 46 eyes (70%) had vision ≥20/40, 9 eyes (%) 20/50-20/150, and 11 eyes (%) ≤20/200 in the better-seeing eye. 75% of patients had evidence of optic chiasm compression on pre-operative MRI.

A total of 20 (61%) patients underwent craniotomy and 13 (39%) patients underwent endoscopic approaches. In patients who underwent craniotomy, in the worse-seeing eye, 4 (20%) patients had visually impaired VA, of which 1 (50%) improved and 1 (50%) worsened. 3 (15%) patients had legally blind VA which all of which improved. 13 (65%) craniotomy patients had normal VA in their worse-seeing eye and all vision remained stable postoperatively.

For patients who underwent endoscopic approach, in the worse-seeing eye, 2 (15%) patients had visually impaired VA, of which 50% remained stable and 50% worsened. 4 (30%) patients had legally blind VA, of which 1 (25%) improved and 3 (75%) remained stable. In the endoscopic group, 7 (55%) patients had normal VA in their worse-seeing eye, of which 71% remained stable and 29% worsened.

Conclusion: Visual function after surgery can be unpredictable. Future studies describing risk factors and different treatment strategies are ongoing and will be helpful to prevent further vision changes.

Poster # 909

TRACHEOSTOMY REQUIREMENT IN PEDIATRIC BRAIN TUMOR PATIENTS

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Background: Brain tumors are the leading cause of cancer related deaths in childhood. The anatomical location of these tumors can affect neurologic brain stem control of breathing as well as management of secretions leading to respiratory failure, nasopharyngeal insufficiency and need for prolonged mechanical ventilation for airway protection.

Objectives: To characterize the population of pediatric brain tumor patients who have undergone tracheostomies and their outcomes.

Design/Method: A single-center, retrospective chart review of all pediatric patients with brain tumors who received tracheostomies was performed from 2004 to 2023. Univariate analysis was performed on variables collected.

Results: Eighteen patients with brain or spinal cord tumors who had undergone tracheostomies were identified. The most common diagnoses were ependymoma (n=5, 28%) and medulloblastoma (n=3, 17%) with the most common locations of the primary tumor being in the posterior fossa (n=9, 50%) and brainstem (n=3, 17%). Out of 16 patients who received oncologic therapy for their tumor, 83% (n=15) had the tracheostomy placed while receiving oncologic treatment with the most common indication being sialorrhea and dysphagia as well as neurological dysfunction manifesting as central apnea, vocal cord paralysis or cranial nerve palsies. Mortality was 33% (n=6). All patients experienced progression of disease and two of these patients also had infectious complications which contributed to their death. All of these patients still had a tracheostomy at time of death however no patients had tracheostomy related mortality. Five of the surviving 13 patients (38%) were able to be decannulated. For these patients, the average duration of tracheostomy was 353 days. When comparing patients who underwent early tracheostomy (< 30 days of mechanical ventilation) or late tracheostomy (> 30 days), there was no statistical difference in decannulation rates (13% vs 33%, p = 0.42) or mortality (38% vs 67%, p=0.38).

Conclusion: Neurologic dysfunction, sialorrhea and dysphagia were the common indications for tracheotomy requirement in pediatric brain tumors. Decannulation rates were not associated with timing of tracheostomy. Mortality in our cohort of patients was due to underlying disease progression and related infectious complications rather than complications of tracheostomy.

Poster # 910

IMPACT OF SELUMETINIB TREATMENT IN NF1-PN PEDIATRIC PATIENTS: PERSPECTIVES FROM PATIENTS/CAREGIVERS

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Background: Plexiform neurofibromas (PNs) affect approximately 20% to 50% of patients with NF1 and can lead to pain, disfigurement, and compression of vital structures (Nguyen et al., 2011; Tchernev et al., 2016; Miller et al., 2019). Selumetinib, a MEK1/2 inhibitor, is the first and only FDA-approved pharmacological treatment licensed for the treatment of symptomatic, inoperable PNs in children with NF1.

Objectives: The aim of this study was to assess the drivers for initiation of treatment as well as the impact of selumetinib treatment on the patient's quality of life from the perspective of both patients and their caregivers

Design/Method: This was a qualitative study of children and their caregivers who were prescribed selumetinib for the treatment of their PN(s). Participating patients were age $\geq$ 9 years and taking Selumetinib for > 6 months; caregivers were a parent or primary caregiver of a patient aged 2–18 who had been taking selumetinib for $\geq$ 6 months. Demographic and clinical background information were summarized using descriptive statistics.

Results: The study included 10 patients (mean age of 13.2; range 9-17 years) and 19 caregivers (mean patient age of 11; (range 3 – 17 years)) with an average selumetinib treatment duration 30.6 months

(range 7 to 96 months). Reported treatment goals mainly focused on tumor size reduction (N=8, 42.1%); stabilization of PN(s) (N=7, 36.8%); and a decrease in PN-associated pain (N=6, 31.5%). In terms of treatment response, most caregivers (n=17, 89.4%) reported either stabilization or a reduction in size of PNs. Of the 11 caregivers reporting pain pre-treatment, all (100%) reported pain reduction post selumetinib initiation. All caregivers (N=19, 100%) reported some form of physical improvement, and over one third (N=7, 36.8%) reported improvements in the emotional, social, and learning domain following treatment initiation. Patients less frequently reported pre-treatment burden of PN but reports of post-treatment improvement was consistent with that of their caregivers.

Conclusion: Children with NF1 and PNs and caregivers are concerned about the presence of PNs and associated morbidities. Treatment goals primarily focused on tumor shrinkage/stabilization and reduction in PN-associated pain. Most caregivers reported tumor stability and/or shrinkage, reduction in pain, as well as well improvement in psycho-social aspects following selumetinib therapy initiation, and their children's responses were generally consistent regarding treatment benefits, despite understatement of pre-treatment burden of PN.

Poster # 911

METRONOMIC AND REPURPOSED DRUG REGIMEN IN A METASTATIC RECURRENT CHOROID PLEXUS CARCINOMA

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Background: Choroid plexus carcinoma (CPC) are WHO grade 3 neoplasms commonly associated with LFS and historically poor outcomes. Treatment approaches are varied and consist of surgery, irradiation, and chemotherapy, including marrow ablative chemotherapy and autologous stem-cell rescue.

Objectives: We report a case of a metastatic choroid plexus carcinoma treated with antiangiogenic metronomic therapy plus a repurposed multidrug regimen with metformin, mebendazole/albendazole, doxycycline, ivermectin, valgancyclovir, grape seed extract, vitamin D, turmeric, and omega 3 with a durable response.

Design/Method: Relevant papers were selected for literature review regarding terminology including guidance protocols, latest treatments, outcomes.

Results: 5-year-old male presented at 6 months of age with macrocephaly and left-sided gaze palsy. Brain MRI demonstrated a large ventricular mass with resultant hydrocephalus. He underwent right craniotomy with total resection of the lesion. Pathology showed a choroid plexus carcinoma with a TP53 germline mutation. Received chemotherapy followed by myeloablative conditioning regimen chemotherapy and autologous stem cell rescue as per the Head Start II protocol. A distant lesion was seen in lumbosacral spine consistent with leptomeningeal progression on his one year of surveillance. He was then treated with triple intrathecal chemotherapy (thiotepa, topotecan and etoposide), followed by an antiangiogenic metronomic therapy (thalidomide, celecoxib and fenofibrate with alternating oral etoposide and cyclophosphamide), plus bevacizumab. An Ommaya reservoir was placed and subsequently underwent radiolabeled Omburtamab therapy at 3 years of age. Further imaging demonstrated worsening metastatic disease in the brain and spine. Subsequently, proceeded standard

dose CSI to 23.4 Gy RBE, boost to brain disease to 54Gy and Spine disease to 50.4 Gy. He was then restarted on the repurposed multidrug regimen including metformin, mebendazole/albendazole, doxycycline, ivermectin, valgancyclovir, grape seed extract, vitamin D, turmeric, and omega 3. His imaging studies have been stable after one year on this regimen.

Conclusion: CPC continues to present treatment challenges particularly in TP 53 mutated tumors/LFS. Further studies are required to explore safety and impact of long-term effects of these drugs in pediatric patients.

Poster # 912

A HEMORRHAGIC BRAIN MASS IN A CHILD WITH ENCEPHALOCRANIOCUTANEUOUS LIPOMATOSIS

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Background: Encephalocraniocutaneous lipomatosis (ECCL) is a rare neurocutaneous genetic condition associated with missense mutations of FGFR1, N546K or K656E, which presents with skin, eye, and central nervous system findings. Here we report on a novel *FGFR1* mutation found in the brain tumor of a patient with ECCL by way of retrospective chart review.

Objectives: To report a case of a novel *FGFR1* mutation found in a low grade glioma of a pediatric patient with ECCL.

Design/Method: Literature review and retrospective chart review with consultation of pathology, genetics, radiology, and the patient's oncology team.

Results: The patient presented at age 9 with known clinical diagnosis of ECCL to the emergency room with altered mental status, headache, and right sided hemiparesis. The initial computed topography (CT) head without contrast demonstrated a large deep left cerebral hemisphere hemorrhagic mass with moderate surrounding edema and rightward midline shift. He underwent emergent decompressive left hemicraniectomy and magnetic resonance imaging (MRI) which showed a complex signal in the left hemorrhagic mass without other suspicious intracranial lesions. Molecular testing on the tumor sample tested positive for a likely pathogenic mutation in *FGFR1* (N546D) by UW Oncoplex assay Next Generation Sequencing version 6. The patient's germline saliva was negative for *FGFR1* N546D. Pathology review showed a glial neoplasm containing largely non-neoplastic neuroglial tissues with ischemia, hemorrhage, scattered inflammatory and other reactive changes. His final tumor diagnosis was diffuse low-grade glioma, MAPK pathway altered per the 2021 WHO Classification of CNS tumors. After resection, the patient continued undergoing surveillance imaging; MRI brain 16 months following resection demonstrated a stable, nonspecific left thalamic non-enhancing focus and no tumor growth or recurrence. Clinically, the patient demonstrated significant progress since the initial injury; his right hemiparesis remains, but he has adapted well to his motor limitations, including transitioning to left-handed dominance. He continues to have ongoing challenges related to understanding, reasoning, and memory.

Conclusion: This case introduces a not previously detected FGFR1 variant detected in a patient with ECCL. It raises a question as to whether the presence of an *FGFR1* mutation in patients with ECCL may be

associated with the likelihood of developing a low-grade CNS tumor, which may guide clinical management for these patients. High coverage genetic testing of multiple affected tissues specific to *FGFR1* and long-term follow-up of known patients with ECCL are needed to determine the connection with low grade CNS tumors and to inform ongoing screening in these patients.

Poster # 913

SOMATIC VERSUS GERMLINE- A CASE SERIES OF THREE CHILDREN WITH ATM-MUTATED MEDULLOBLASTOMA

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Background: Medulloblastoma is the most common malignant brain tumor in childhood, and current standard treatment includes resection, craniospinal irradiation with boost (CSI + boost) to tumor bed, and adjuvant chemotherapy. *ATM* encodes for ATM kinase, involved in homologous repair. Aberrations in *ATM* have been implicated in radiosensitivity.

Objectives: To describe the outcomes of three pediatric patients with *ATM*-mutated medulloblastomas by way of retrospective chart review.

Design/Method: All three patients selected for this case series were treated with proton CSI + boost to a total dose of 54 CGE and adjuvant chemotherapy. Resected tumors and paired blood samples were evaluated for *ATM* aberrations with next generation sequencing and targeted variant analyses.

Results: Patient A is an 8-year-old female with stage M0, WNT, average risk medulloblastoma. While she tolerated treatment well, MRI showed signs of tissue necrosis nine months after proton radiotherapy. Despite treatment with steroids, bevacizumab, and focal laser ablation, she succumbed to progressive respiratory failure six months later. Her tumor was found to have a truncating mutation in *ATM*. Concurrent peripheral blood targeted DNA analysis confirmed the *ATM* variant was germline. Patient B is a 26-year-old male with stage M0, SHH, high risk medulloblastoma. While his resected tumor was positive for an *ATM* frameshift mutation and loss of heterozygosity, paired blood sample was negative for *ATM* variants. He tolerated treatment with no concerns for necrosis. Patient C is a 3-year-old male with stage M0, anaplastic/large cell, average risk medulloblastoma. NGS of his tumor revealed a truncating mutation in *ATM* with associated loss of heterozygosity, but targeted variant analysis in peripheral blood was negative for germline *ATM* variants. He tolerated radiation with no evidence of delayed radiation-induced necrosis.
All three tumors harbored loss-of-function *ATM* mutations and all three patients initially tolerated radiation well. However, Patient A subsequently developed devastating neurologic damage secondary to radiotherapy-induced necrosis. In this patient, the same pathogenic mutation found in tumor was found in the germline, which hypothetically contributed to the significant delayed radiosensitivity in normal tissue. The other two patients with somatic biallelic inactivation of ATM responded well to treatment with radiation and chemotherapy with no evidence of residual disease on follow-up.

Conclusion: This series highlights the potential of precision oncology in determining the best therapeutic

approach for each individual patient. As next generation sequencing becomes more widely accessible, clinicians could consider incorporating screening to evaluate.

Poster # 914

LONG-TERM REMISSION OF RECURRENT METASTATIC MEDULLOBLASTOMA WITH 131-I OMBURTAMAB-8H9 AND VISMODEGIB

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Background: Medulloblastoma is the most common pediatric posterior fossa tumor (WHO grade IV), representing 60% of childhood intracranial embryonal tumors. Approximately 75% of children diagnosed with medulloblastoma will survive into adulthood, however, the prognosis is influenced by genetic risk. High-risk and recurrent MB is associated with significant mortality. The likelihood of long-term survival decreases substantially in the setting of recurrent disease after initial therapy.

Objectives: We report a case of long term remission of recurrent medulloblastoma SSH-type with leptomeningeal disease status post treatment with 131-I Omburtamab-8H9 radioisotope intra-Ommaya therapy and Vismodegib.

Design/Method: Literature and chart review.

Results: A 17-year-old female presented with headaches, dizziness and an unsteady gait. Brain MRI demonstrated a posterior fossa mass with no metastasis. The tumor was grossly resected with classic medulloblastoma sonic-hedgehog (SSH) type by immunohistochemistry and a pathogenic mutation of the PTCH1 gene was revealed in further studies. She received craniospinal radiation 2340 cGy with a boost to the posterior fossa, followed by 5 cycles of chemotherapy as per the SJMB trial with cisplatin, cyclophosphamide and vincristine. Two years later, she presented with left shoulder pain radiating to the arm. Cervical spine MRI showed a new lesion at C5 intradural-extramedullary involving the neural foramen. She underwent a C5-C6 laminectomy with resection of a 1 cm lesion along the nerve roots, pathology consistent with recurrence of the medulloblastoma. MRI showed leptomeningeal disease in the spine for which she completed 2 cycles of topotecan/cytoxan with intra Ommaya methotrexate, with stabilization of the disease. Proton radiation (32.4 CGE) to the spine was then given. Two months later, an MRI demonstrated mets isolated to the foramen magnum prompting radiation to that lesion, started on 5 oral metronomic antiangiogenic chemotherapy plus Avastin. Chemotherapy resumed with temozolomide/irinotecan plus intrathecal etoposide and thiotepa. Nonetheless, an MRI demonstrated progressive leptomeningeal disease in the brain requiring cranial irradiation with oral etoposide. Subsequently, the patient received Vismodegib for several years, she received 2 doses of 131-I Omburtamab (8H9) radioiodine antibody intra-Ommaya. Patient is now 27 years old and has been disease free for almost 5 years.

Conclusion: Recurrent primary CNS tumors have few curative treatment options. Medulloblastomas continue to present treatment challenges for care providers. Close long-term monitoring is required to ensure long-term spontaneous oncologic remission with this proposed approach. Moreover, the identification of a cancer predisposition gene has important implications for the patient and family members with regards to future risk, screening, and reproductive decision-making.

Poster # 915

A RARE CASE OF BRCA2-ASSOCIATED HIGH-GRADE PONTINE EMBRYONAL TUMOR AND CONCERN FOR FANCONI ANEMIA

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Background: Embryonal tumor with multilayered rosettes (ETMR) is a rare, high-grade embryonal pediatric central nervous system tumor most commonly found in the supratentorial region of young children. The vast majority show C19MC alteration. There are multiple reports highlighting BRCA2-associated Fanconi anemia (FA) and predisposition to (among other malignancies) medulloblastoma, another high-grade embryonal brain tumor of childhood. Our case is unique as BRCA2 association with ETMR is essentially unreported. This is an important factor to consider during diagnostic/pathologic work-up of high-grade embryonal tumors (including whether to include germline testing) and therapy recommendations, given the association with FA. It is vitally important to have this information initially, as FA can result in overly severe, prolonged, and even fatal complications from standard chemotherapy regimens that clinicians may not otherwise expect.

Objectives: To discuss a rare pediatric case of a brainstem primary ETMR with confirmed BRCA2 germline mutation.

Design/Method: Case Report

Results: A 17-month-old female presented with a one-week history of new-onset head tilt, diplopia, difficulty walking, and increased oral secretions. MR brain revealed a 2.8 x 2.9 x 3.0 cm mass involving the right pons without evidence of obstructive hydrocephalus. MR spine done at the same time was normal. Biopsy revealed ETMR with C19MC amplification and gain of chromosome 2. Molecular analysis identified a pathogenic, maternally inherited, BRCA2 loss of function variant. Due to worsening symptoms, therapy was urgently started as per COG ACNS0334, which includes vincristine, etoposide, cyclophosphamide, and cisplatin, followed by high-dose chemotherapy with stem cell rescue. At the discovery of the BRCA2 mutation, in preparation for transplant, further FA-directed genetic testing and subsequent diepoxybutane (DEB) assay revealed no FA (but confirmed BRCA2 mutation). Of note, DEB testing had to be repeated due to prior exposure to cyclophosphamide. She received 4 cycles of induction chemotherapy (an additional cycle was added due to delay from the required additional FA testing). Unfortunately, her disease quickly metastasized widely to her spine while on therapy, resulting in withdrawal of treatment, and death soon after.

Conclusion: ETMR is a very rare type of embryonal tumor with an as-of-yet undocumented association with BRCA2. The association with BRCA2 is an important consideration during initial diagnostic decisions for patients with rare high-grade embryonal tumors, and when deciding therapy, given its association with Fanconi anemia and the subsequent delay in therapy additional testing could cause.

Poster # 916

PEDIATRIC GLIOBLASTOMA ASSOCIATION WITH GERMLINE BRCA1 ALTERATION

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Background: The underlying pathogenesis of glioblastoma (GBM), rare in children (0.17 per 100,000 in the 0-14 age group), commands attention due to its high mortality. Recent studies have expanded the relevance of BRCA1 and BRCA2 variants beyond breast and ovarian cancers to other malignancies, including pancreatic and prostate cancers. Alterations in DNA repair genes are known to be linked with the pathophysiology of glioblastoma in adults; however, the specific role of BRCA1 in the development of pediatric glioblastoma has not been reported.

Objectives: To explore the association between BRCA1 somatic and germline variants in pediatric glioblastoma. Focused on uncovering predisposition factors, prognostic indicators, and therapeutic implications, this study was prompted by the intriguing case of a 13-year-old female with family history of a germline BRCA1 variant who was found to have pediatric glioblastoma, as well as BRCA1 positivity of the tumor.

Design/Method: A literature review was performed utilizing PubMed search engine, and retrospective chart review was performed on a pediatric patient with germline BRCA1 variant-associated glioblastoma.

Results: A previously healthy 13-year-old female presented to the ED with nausea, vomiting, headache, and syncope and was found to have a post-gadolinium enhancing right parieto-occipital tumor. Pathology from gross total resection revealed a high-grade diffuse astrocytoma with low positive MGMT methylation, IDH-1 negative, ultimately classified as WHO Grade IV glioblastoma. NGS of resected tumor tissue revealed several sequence variants, including H3F3A, RB1, TP53, ATRX and BRCA1 (c2193del, p.Glu732Lysfs*4). Later, germline testing revealed the same pathogenic heterozygous variant of BRCA1 (c.2193del, p.Glu72Lysfs*4). Treatment involved focal proton beam irradiation with concurrent temozolomide, followed by CCNU and temozolomide as per ACNS0423. The patient has remained disease-free for 5 years since diagnosis. Literature review of BRCA1 association with glioblastoma (reported in adults only) revealed possibly increased radiosensitivity of GBMs with somatic BRCA1 alterations leading to prolonged survival; however, no data on pediatric GBM was found.

Conclusion: This report sheds light on the pathogenic role of BRCA1 variations in pediatric glioblastoma, as well as a direct link between the germline and somatic variant type. The positive outcome for our patient may demonstrate a possible link between BRCA1-altered tumors and more favorable outcomes in pediatric cases. These findings prompt further exploration into the genetic underpinnings of pediatric GBM and may possibly advocate for earlier screening in individuals with known BRCA1 variants. This case contributes to the small but growing body of literature associating BRCA alterations with gliomagenesis.

Poster # 917

PIK3CA-ALTERED GLIONEURONAL TUMOR IN A CHILD WITH MACROCEPHALY-CAPILLARY MALFORMATION SYNDROME

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Background: PIK3CA-related overgrowth spectrum (PROS) refers to a group of rare genetic disorders characterized by tissue and organ overgrowth due to gain-of-function alterations in *PIK3CA*, a member of the PI3K/AKT/mTOR pathway, leading to uncontrolled cell proliferation. One PROS phenotype is macrocephaly-capillary malformation (MCM), characterized by hemimegaloencephaly, cortical dysplasia, developmental delay, hypotonia, and seizures. Treatment of PROS-related manifestations can be challenging. The FDA recently approved the use of alpelisib, a phosphoinositide-3-kinase (PI3K) inhibitor, in patients aged two years and older with severe or life-threatening manifestations of PROS.

Objectives: Describe the case of a young child with MCM syndrome found to have a multifocal low-grade glioneuronal tumor harboring a *PIK3CA* variant, treated with alpelisib for more than 30 months.

Design/Method: Case report.

Results: The patient is now a 4-year-old male with history of an antenatal diagnosis of complete right hemimegaloencephaly and severe right facial lipomatosis, resulting in loss of vision in the right eye, poor oropharyngeal coordination and feeding, developmental delay, and seizure disorder. Due to refractory seizures, he underwent functional right hemispherectomy at three months of age, subsequently weaning off anti-epileptic medications. Germline genetic testing performed on a buccal swab identified a *PIK3CA* p.His1047Arg pathogenic variant (allele frequency 15%, Baylor Genetics Overgrowth Syndrome Panel, Houston, TX), consistent with PROS.

In consideration of the severe manifestation of PROS and the expectation for ongoing asymmetric overgrowth, the patient started alpelisib at 24 months of age in an effort to mitigate progression and morbidity. After four months of therapy, the right facial lesions appeared slightly smaller and softer, and at later follow-up, he began to make gradual developmental gains (interacting with sounds, sitting independently, grabbing toys). After the right facial lipomatosis was stabilized with medical therapy, he proceeded to right face debulking to improve oropharyngeal function and quality of life. During surgical planning, an MRI of the brain/face unexpectedly revealed multifocal right posterior cerebral tumors (largest 1.3 cm in diameter). Biopsy of the largest lesion was consistent with a low-grade glioneuronal tumor harboring the same *PIK3CA* p.His1047Arg variant (allele frequency 38%). All tumors have remained stable after 15 months of monitoring. He continues to tolerate alpelisib without adverse effects.

Conclusion: This is the first report of multifocal glioneuronal tumors identified in a 3-year-old patient with *PIK3CA*-positive MCM, receiving long-term therapy with alpelisib.

Poster # 918

ANGIOCENTRIC GLIOMA, AN UNEXPECTED PRESENTATION

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Background: Angiocentric glioma (AG) is a rare benign neuroepithelial neoplasm that primarily affects children and young adults. Current prevalence of AG is unknown due to few cases reported. Clinical and imaging data is limited due to relatively few reported cases. However, the majority of AG cases reported a history of intractable seizures. Diagnosis of AG currently relies on histologic and molecular characteristics of the tumor.

Objectives: To report a rare diagnosis of AG with a remarkable and unusual presentation.

Design/Method: This case report highlights a rare diagnosis of AG and an unexpected finding on imaging.

Results: This case involves a 10-year-old boy who presented to an outside hospital (OSH) due to a brief amnestic episode after hitting his head in a slip n' slide incident. He was unable to recall details of the incident after hitting his head but did not lose consciousness. His only complaint upon arrival was a headache. His review of systems was otherwise negative. An initial OSH computed tomography (CT) scan revealed an incidental 11 x 5 cm arachnoid cyst in the anterior and middle cranial fossa causing significant mass effect. The patient was subsequently transferred to the University of Mississippi Medical Center pediatric emergency department. Routine labs were unremarkable and a repeat CT scan also revealed a 2.8 x 2.7 cm intra-axial lesion in the right frontotemporal region. Further imaging with magnetic resonance (MR) redemonstrated the mass. The patient underwent a right frontotemporal craniotomy for resection and biopsy acquisition. Tissue histology revealed low-grade glial cells with an angiocentric infiltrative pattern. Immunohistochemistry revealed cells were positive for glial fibrillary acidic protein (GFAP) and epithelial membrane antigen (EMA) in a perinuclear dot pattern. Next-generation sequencing confirmed tumor cells were positive for myeloblastosis quaking (*MYB-QKI*) fusion protein.

Conclusion: AG diagnostic criteria is limited due to relatively few cases reported. Further diagnostic workup must be made by histopathology, immunohistochemistry and molecular characterization. The World Health Organization (WHO) classifies AG based on several molecular and morphological characteristics, including an angiocentric infiltration of tumor cells on microscopy and positive GFAP and dot-like EMA immunostaining. A *MYB-QKI* gene fusion is detected in most cases. This fusion protein is a specific finding as it has been reported as a recurrent tumor driver in AG. Children with AG usually present with a history of intractable seizures, unlike this case. The incidental findings of a congenital cyst and a rare neoplasm with an asymptomatic presentation make this case unique.

Poster # 919

CHEK2 GERMLINE MUTATIONS IN TWO PEDIATRIC BRAIN CANCER PATIENTS

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Background: Checkpoint kinase 2 (Chk2) is a protein kinase encoded by gene CHEK2, is activated in response to DNA damage, is involved in cell cycle arrest, and is a probable tumor suppressor gene. In adults, CHEK2 mutations predispose to various cancers including some missense variants in brain

tumors. CHEK2 mutations found in pediatric brain tumors haven't proven a causative association and risk of relapse or secondary malignancies due to the mutation is unknown. Overall, pediatric CHEK2 mutations confer unexplored risks.

Objectives: We present two patients with brain tumors found to have heterozygous missense variants in the CHEK2 gene to compare patient characteristics and diagnoses.

Design/Method: After presentation and surgical resection, pathology confirmed the diagnosis of each patient. Enhanced exome sequencing was then performed to determine the molecular genetics of the tumor.

Results: Case 1 is a 5-year-old female who presented after three weeks of headaches found to have a cerebellar vermis mass on imaging. She underwent total mass resection with temporary external ventricular drain (EVD) placement. Her postoperative course was unremarkable. Pathology confirmed a WHO grade 1 pilocytic astrocytoma; molecular genetics revealed unmethylated MGMT and a heterozygous missense variant in the CHEK2 gene (Gly167Arg). There were no somatic mutations, but had a gene fusion of SRGAP3::RAF1 often seen in the setting of pilocytic astrocytoma. The patient's mother underwent genetic testing and was found to also have the same CHEK2 mutation.
Case 2 is a 4-year-old male who presented with one week of headaches and vision changes. On imaging, a posterior fourth fossa ventricle mass was found, and he underwent total mass resection with EVD placement. Pathology confirmed a WHO grade 3 posterior fossa ependymoma. The patient underwent 30 fractions of proton beam radiation with minimal complications. Molecular genetics revealed unmethylated MGMT and a heterozygous missense variant in the CHEK2 gene (Ile157Thr).

Conclusion: Currently, there is no standard CHEK2 germline mutation testing in pediatric cancers. Given the adult oncology risks and emerging evidence of mutations in pediatrics, there is an argument for standard evaluation of pediatric tumors for CHEK2 germline mutations in the hopes of generating future therapies.

Poster # 920

KIF5B-ALK FUSION HISTIOCYTOSIS OF THE CENTRAL NERVOUS SYSTEM IN A 2-YEAR-OLD: A CASE REPORT

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Background: KIF5B-ALK fusion positive histiocytosis is a new clinicopathologic entity, it has recently been documented pediatric CNS tumors. In a recent study by Kemp et al (2022) ALK inhibitor therapy was offered to patients with diagnosis of progressive KIF5B-ALK fusion positive histiocytosis of the CNS and demonstrated durable response with 100% of patients having an objective response and 0% with disease progression at 6 months, suggesting ALK inhibitors may be an option for patients with unresectable tumors and spare them the toxicity of traditional chemotherapy.

Objectives: To report a case of a pediatric patient with an KIF5B- ALK fusion positive histiocytosis of the CNS successfully treated on ALK inhibitor monotherapy.

Design/Method: Case Report

Results: A 2-year-old, Caucasian male with complex past medical history that presented to an outside hospital following a prolonged apneic episode requiring cardio-pulmonary resuscitation (CPR). After admission, episodes defined as “paroxysmal neurologic symptoms” increased in frequency. Magnetic resonance imaging (MRI) of the brain demonstrated a posterior medullary mass 1.8 x 2.3 x 2.5 cm in size. Patient was then transferred for neurosurgical intervention. Biopsy revealed KIF5B-ALK fusion positive histiocytosis. Following biopsy patient rapidly decompensated with acute respiratory distress syndrome requiring tracheostomy, cardio-pulmonary resuscitation, and veno-arterial ECMO support. Patient was successfully weaned off hemodynamic support after 18 days but continued to be ventilator dependent. On 10/2 he was consented to a non-protocol treatment plan consisting of daily lorlatinib at 95 mg/m2/day by mouth. Over 2.5 weeks of therapy, spells decreased and ultimately ceased. Patient was weaned to trach collar ventilatory support and returned to neurologic baseline. MR imaging repeated 10/20 with a decrease is size of mass to 1.2 x 1.3 x 1.8 cm, with further decrease on 11/27 to 1.5 x 1.1 x 1.3 cm.

Conclusion: We report a rare case of a pediatric patient with an KIF5B-ALK fusion positive histiocytosis of the CNS with response to treatment on ALK inhibitor monotherapy. While duration of disease control and long-term side effects are unclear, this case report highlights the need for an integrated pathological diagnosis as recommended by WHO criteria and targeted monotherapy with ALK inhibitors is a potential therapeutic option in similar clinical settings. This case report adds to the growing literature of infantile brain tumors being recognized as an emerging entity amenable to targeted therapy.

Poster # 921

UNILATERAL PERIPHERAL EDEMA SECONDARY TO SELUMETINIB IN A PATIENT WITH NF1 : A CASE REPORT

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Background: Neurofibromatosis type 1 (NF1) is an autosomal dominant disorder that predisposes to benign and malignant tumors. Plexiform neurofibromas (PNs) seen in approximately 50% of NF1 patients are histologically benign peripheral-nerve sheath tumors manifesting with pain, functional impairment, disfigurement, with a risk of malignant transformation. Selumetinib, a selective mitogen-activated extracellular kinase inhibitor, is a commonly employed FDA approved treatment option for patients 2 years and older with symptomatic, inoperable PNs. Its adverse reactions mainly include gastrointestinal (diarrhea, hepatic impairment), dermatologic (maculo-papular and acneiform rash, paronychia, mucositis) symptoms, cardiomyopathy, ocular toxicity, and creatine kinase (CK) elevations. Unilateral peripheral edema, not found in selumetinib prescribing information, is an extremely rare side effect which may warrant drug interruption or discontinuation.

Objectives: Report unilateral peripheral edema as an extremely rare side effect of selumetinib in a NF1 patient with PNs

Design/Method: Clinical case report identified via retrospective chart review.

Results: A 20-year-old female diagnosed with NF1 at age 6 months presented with 1 year history of severe right thigh pain interfering with routine activity and sleep. Patient was deemed inoperable due to the location and extent of multilevel spinal foraminal neurofibromas (MRI spine: multilevel spinal foraminal neurofibromas – largest right L4-L5 neural foramina measuring 2.2 x 1.8 cm). Treatment with selumetinib 25 mg/m^2 twice daily showed significant pain improvement within 6 months. Routine surveillance MRIs showed no shrinkage in the foraminal neurofibromas; however, functional improvement continued as pain resolved and activity improved. 3 years after treatment, progressive left lower extremity (LLE) swelling was noted. Physical examination revealed a neurovascularly intact LLE with non-pitting edema, significantly enlarged as compared to right (LLE vs RLE circumference – mid-thigh: 59.5 vs 56 cm, mid-calf: 37 vs 34 cm, mid-foot: 26 vs 22 cm). No organomegaly or lymphadenopathy was noted. CK was elevated grade 4 (1756 U/L). Echocardiogram was normal. LLE Doppler study showed no deep venous thrombosis. MRI abdomen and pelvis showed no masses. MRI LLE revealed lower calf and foot edema. Lymphoscintigraphy was normal. As all the potential causes were excluded, LLE swelling was presumed to be drug related. Selumetinib was held for 6 weeks with significant improvement in LLE edema. Patient remained off Selumetinib for cosmetic reasons.

Conclusion: While treating NF-1 patients with PNs, it is important that the clinician identifies unilateral peripheral edema as a potential but an extremely rare side effect of selumetinib given this may have important implications for medication continuation or dosage adjustments.

Poster # 922

IDIOPATHIC HYPERTROPHIC PACHYMENINGITIS - A DIAGNOSTIC DILEMMA

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Background: Hypertrophic Pachymeningitis is an uncommon chronic inflammatory disorder that is characterized by focal or diffuse thickening of cranial and/or spinal dura mater. It can be idiopathic or secondary to infection, autoimmune disease, malignancy, or trauma, and treatment of the underlying disease is critical. We present a case that posed a diagnostic challenge in a 17-year-old male presenting with spinal cord compression.

Objectives: To report a case of idiopathic hypertrophic pachymeningitis in a pediatric patient and raise awareness for its inclusion in the differential for spinal cord compression.

Design/Method: Case report.

Results: A 17-year-old male with a history of autism spectrum disorder was admitted to our hospital with three months of worsening loss of sensation in his legs. This progressed to difficulty walking along with urinary retention. He reported weight loss but denied night sweats, pain, recurrent fevers, abnormal swellings, and rashes. There were no complaints of headaches, visual changes, or vestibular changes. His physical examination demonstrated loss of light touch below the xiphoid process, with similarly distributed decreased pain sensation, and strength 2/5 in bilateral lower extremities. His cranial nerve examination and the rest of the physical examination were appropriate. Magnetic Resonance

Imaging (MRI) of the spine displayed a lobulated dorsal intradural extra-medullary mass from T2 to T12 with spinal cord compression. MRI of his brain showed abnormal thickening and enhancement of the falx cerebri concerning for metastasis. His laboratory investigations showed a normal complete blood count and liver/renal function tests. Inflammatory markers were normal. Thyroid function tests were normal and the screen for rheumatologic antibodies (C-ANCA, P-ANCA, ANA) was also negative. Infectious evaluation yielded a negative QuantiFERON gold and no evidence of any viral infections. He had an emergent posterior laminectomy and debulking of the spinal lesion with duraplasty which relieved his symptoms. Pathology showed a monotonous lymphocytic infiltrate composed of B and T cells. The proliferative rate was extremely low and there were no clonal rearrangements for IG and TCR gamma and beta. There was no demonstration of clonality when evaluated by Clonoseq testing and a lymphoproliferative process was ruled out. He was started on steroids and this was tapered over 3 months with resolution of his imaging findings and good neurologic recovery. Surveillance scans showed recurrence of his disease and he has been started on a combination of steroids and rituximab.

Conclusion: In conclusion, idiopathic hypertrophic pachymeningitis can present in children and should be considered in the differential for intradural masses.

PTCTC Abstracts

Advanced Practitioners

1. **Title:** Scrubbing Olympics

Katilyn Kusnier, MSN, APRN, FNP-C, BMTCN, Kathi Spears, MSN, CNL, RN, Chelsea S. Goodin, BSN, RNIII, BMTCN, Rachel Meyer, BSN, RNII, BMTCN, CPN, David Haslam, MD, Dr. Christopher E. Dandoy, MD, MS, Stella M. Davies, MBBS, PhD, MRCP and Priscila Badia, MD: **Cincinnati Children's Hospital Medical Center**

Theme: Advanced Practitioners

Background:
Patients undergoing hematopoietic stem cell transplant require a central venous catheter (CVC). Central line associated bloodstream infections (CLABSI) are associated with increase morbidity, mortality, and healthcare costs. Maintenance and disinfection of needleless connectors (NC) require significant efforts to prevent CLABSI and current guidelines are based on limited evidence.

Objective:
Evaluate factors involved in NC care including disinfectant, scrubbing material, scrubbing time and human factors.

Design/Methods:
One hundred NC were used for each study phase. A negative NC control group (10/100) were flushed with saline. A positive NC control group (10/100) and study groups were contaminated for 30 minutes with Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus mitis, Escherichia coli, and Pseudomonas aeruginosa. Positive control group had no scrubbing prior to flushing with saline. Two milliliters of saline were used to flush each group's NC into a sterile tube and 10 microliter loops inoculated the blood agar. For the study groups, 40/80 NC (group 1) was disinfected with 2% chlorhexidine gluconate (CHG) plus 70% isopropyl alcohol frepp; and 40/80 NC (group 2) was disinfected with 3.1% CHG plus 70%

isopropyl alcohol swab. For both groups, NC were subdivided into four different scrubbing times: 15, 30, 45, and 60 seconds. After 24hrs cultures were analyzed. Three experienced nurses scrubbed NC for both groups and during the different scrubbing times. The same nurses repeated the study at a different date.

Results:
In phase 1, group 1 had 8/40 (20%) positive cultures, group 2 had 3/40 (7.5 %), p=0.107. Nurse pink had two positive cultures 2/14 (14%), nurse blue had two positive cultures 2/34 (5%) and nurse green had 7/32 (22%) positive cultures. P=0.173. In phase 2, group 1 had 4/40 (10%) positive cultures, group 2 had 2/40 (5%), p= 0.402. Nurse pink had one 1/24 (4%), nurse blue had 2/24 (8%) and nurse green had 3/32 (9%) positive cultures, p= 0.759. In phase 3, group 1 had 7/40 (17%) positive cultures, group 2 had 5/40 (12%) p= 0.537. Nurse pink had 7/24 (29%), nurse blue had 4/24(16%) and nurse green had 1/32 (3%), p=0.024. Scrubbing time did not impact disinfection in either group. Scrubbing with 3.1% CHG plus 70% isopropyl alcohol appears to have better disinfection p= 0.075 (95% CI -0.158 to 0.008).

Conclusions:
Scrubbing time and disinfectant does not appear to impact disinfection. Human factors were the only statistically significant factor that showed to affect disinfection results.

2. **Title:** A Program within a Program: Optimizing operational workflow during a period of growth for patients with sickle cell disease seeking hematopoietic stem cell transplant

Authors: Kelly Lyons Snelling CPNP-AC/PC, Robert Sheppard Nickel MD, Allistair Abraham MD, Ana Ortiz, Sandra Andrade, Sam Berhane, David Jacobsohn MD BMTCN

Theme: Advanced Practitioners
Institution: Children's National Hospital, Washington D.C
Topic: Hemoglobinopathies; Allogenic Transplant, Quality Improvement, Advanced Practice Providers

Background
Over the past decade, the application of hematopoietic stem cell transplant (HSCT) for sickle cell disease (SCD) has increased through improved overall transplant outcomes, increased use of haplo-identical familial donors, and the development of less toxic conditioning regimens. During this time of growth, our hospital has supported an increased number of consultations and patients transplanted with an underlying diagnosis of SCD. The team following this population set in place several process improvements to improve the management of these patients from initial referral to long term follow up.

Design/Method
Utilizing the model for improvement as a conceptual framework, in 2017 the healthcare team set out to accomplish a comprehensive program for the care of patients with SCD considering HSCT. The primary goals were program growth and improving patient outcomes. The operational workflow changes consisted of routine meetings with internal referring providers and community hematologists, optimization of dedicated HSCT-SCD staffing, efforts to increase turnaround time with referred patients for HLA typing, and a standardized consultation process. The standardized consultation approach included a rapid identification of patients after HLA typing and/or referral and attending provider intake consultation. Standard approaches for follow up consultations with a BMT Team member (nursing, psychologist, or social worker) and other disciplines (transfusion medicine, pulmonology, neurology, psychology, urology, and gynecology) were put in place.

Findings & Interpretation.
Our program has seen an increase in patients referred from HLA typing, most recently with 46 patients referred from Jan 2023 to Sept 2023 and ultimately 27 patients undergoing HLA typing revealing 5 patients with HLA-matched siblings. The mean number of new patients transplanted was 7.2 in the 5 years before the study period, which increased to 10.7 new patients transplanted per year since the study period. Outcomes have improved as well with a 100% overall survival during the study period, increased from 87.2% from 1996 to 2011.There is also a shared understanding of the process within our program which aids in the care of these complex patients.

Discussion & Implications:
This outlined process has been able to support growing numbers of patients referred for consultation and HSCT at our center. In addition to increased transplant numbers, our program has supported increased referrals for HLA typing, consultations, and study enrollment on sickle cell-based protocols all while maintaining outstanding results. This operational workflow can help other institutions model their process improvement to adequately support a growing number of referrals for curative therapies for sickle cell disease.

Allogeneic HSCT

1. **Title:** Towards early detection of post-allogeneic bone marrow transplant bronchiolitis obliterans syndrome (BOS) – The use of portable airway oscillometry.

Eleanor Cook MBBS 1 Richard Cooper 1 Jane Koo 1 Kas Myers 1 Sam Goldfarb 4 Stella Davies MBBS 1 Christopher Towe MD 3
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Theme: Allogeneic HSCT

Background
Bronchiolitis obliterans syndrome (BOS) is a devastating complication of allogeneic bone marrow transplantation (BMT). Early detection of small airway disease may allow earlier BOS diagnosis and improved long term outcomes. Spirometry can be technically difficult for young and/or ill children. Oscillometry is novel pulmonary function assessment technology which superimposes pressure waves on normal tidal breathing and measures the alterations in flow and pressure. It is not effort dependent, and can be used in younger children than spirometry.

Methods
Portable airway oscillometry was performed using the Tremoflo oscillometer on eleven BMT patients with established BOS. The portable device was brought to the patient's clinic room during routine follow up. The patient performs tidal breathing through a mouthpiece for 20-60sec, for 3 tests (Fig.1). The procedure has been successfully completed by BMT patients as young as 3 years in our other clinical studies.

Results
Eleven BOS patients have completed portable airway oscillometry. The median age is 18 years (10-25yo), and median time post BMT is 4.1 years (1.7-15). Six patients had malignant disease (50%), four immunodeficiency (33%), one bone marrow failure and one hemoglobinopathy. Formal spirometry was performed on the same day per routine clinical care. Patients had significantly abnormal spirometry, with mean FVC z-score -2.11 (0.3 to -5.58), mean FEV1 z-score -4.40 (-2.35 to -6.45) and mean FEV1/FVC 0.52 (0.4-0.62).

Oscillometry results: Reactance at 5Hz (X5) reflects elastic recoil and compliance of the peripheral airways and is a marker of respiratory system stiffness. The X5 was dramatically reduced in this cohort, with a mean X5 z-score -4.86. X5 strongly correlates with FEV1, with correlation coefficient of 0.8091, p=0.0039.
Resistance at 5Hz (R5) provides a measure of total airway resistance, and R19 reflects proximal airway resistance. R5-19 therefore reflects peripheral airway resistance. Most BOS patients (8 of 11, 73%) had normal range R5-19; mean R5-19 z-score 1.21 (-0.16-3.99). The R5-19 z-score correlates with the FEV1/FVC ratio (r=0.88, p=0.0007).

Conclusion
Our work defines the unique oscillometry characteristics of BOS, which now allows screening for early detection. This technique is portable, not effort dependent and relatively inexpensive. We have shown a dramatic reduction in reactance in BOS patients, reflecting stiff and poorly compliant lungs; these oscillometry findings may help to better understand the pathophysiology of BOS.

2. **Title:** A Case Report of Rapidly Progressive Interstitial Lung Disease with Persistent Air Leak after HCT

Authors: Katherine T Lind, MD, Rohini Chakravarthy, MD, MPH, M Eric Kohler MD PhD University of Colorado School of Medicine/Childrens Hospital Colorado

Theme: Allogeneic HSCT

Background: Bronchiolitis Obliterans Syndrome (BOS) is the most common manifestation of pulmonary chronic graft-vs-host disease (GVHD). Interstitial Lung Disease (ILD), once considered a separate entity, has demonstrated histopathological overlap with BOS suggesting it may be a rare variant of pulmonary GVHD.

Objective: To highlight a rare case of pulmonary GVHD manifesting as ILD

Methods: Case Report

Results: A 19-year-old male underwent maternal haploidentical peripheral blood stem cell transplant with myeloablative conditioning and post-transplant cyclophosphamide for relapsed acute myelogenous leukemia. While his initial course was relatively unremarkable, he presented approximately 130 days after transplant with new onset neutropenia, thrombocytopenia, and moderately elevated transaminases followed several days later by headache, fatigue, and cough. Despite an extensive evaluation, no infectious etiology was identified. Evaluation of his bone marrow was negative for evidence of leukemia. He progressed to acute hypoxemic respiratory failure with a chest CT noting diffuse ground glass opacities and thus was treated for idiopathic pneumonia syndrome with systemic

steroids. After a brief clinical improvement, he developed bilateral pneumothoraxes, an extensive pneumomediastinum with interstitial emphysema, and rapidly progressive interstitial lung disease without air trapping or other typical features of BOS. He had no other systemic signs or symptoms suggestive of GVHD. His pulmonary status precluded pulmonary function testing, bronchoscopy or biopsy, and he was followed by serial imaging. He developed persistent air leak syndrome, necessitating a chest tube under negative pressure for over two months. High resolution chest CTs demonstrated worsening ILD with reticulation and fibrosis. During this period, he had worsening cytopenias and marrow testing was consistent with secondary graft failure. Taken together, he was empirically treated for chronic GVHD with systemic steroids, Belumosidil, FAM therapy, and an anti-fibrotic, Nintedanib. While on immunosuppression, he underwent a CD34 selected stem cell boost without conditioning and had subsequent count recovery. After six weeks of GVHD-directed and antifibrotic therapies, his air leak ceased, and his chest tube was removed without re-accumulation of extra-pulmonary air. He has been stable on nasal canula oxygen as an outpatient while undergoing a prolonged steroid taper while continuing on Belumosidil and Nintexanib.

Conclusion: This patient's acute rapidly progressive ILD with persistent air leak ultimately responded to aggressive treatment for pulmonary GVHD. Although BOS is the only diagnostic manifestation of pulmonary GVHD, this case adds to the accumulating literature to describing ILD as a presentation of pulmonary GVHD.

3. **Title:** OUTCOMES OF ALLOGENEIC HEMATOPOIETIC CELL TRANSPLANTATION (ALLOHCT) WITH POST-TRANSPLANTATION CYCLOPHOSPHAMIDE (PTCy) FOR ADOLESCENT AND YOUNG ADULT (AYA) PATIENTS WITH MYELODYSPLASTIC SYNDROME (MDS) OR ACUTE LEUKEMIAS

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Theme: Allogeneic HSCT

Background:
In adults with myelodysplastic syndrome (MDS) or acute leukemia, nonmyeloablative (NMA) and reduced intensity conditioning (RIC) HCT regimens are associated with lower treatment related mortality (TRM). In contrast, myeloablative conditioning (MAC) regimens are mainly used for pediatric acute leukemias/MDS. AlloHCT with PTCy outcomes for hematologic malignancies are not well described for AYA patients (ages 13-39); thus, it is unclear what conditioning intensity leads to the best outcomes.

Methods:
This is an IRB-approved retrospective analysis of 226 AYAs with MDS or acute leukemia who received their first alloHCT with PTCy at the Johns Hopkins Hospital from 2010-2020. Cox proportional hazards models or Fine-Gray's regression models were used for multivariable analysis (MVA) to assess the associations between alloHCT conditioning intensity and outcomes.

Results:
Diagnoses included AML (122), ALL (83), MDS (17), and mixed lineage leukemia (4). AYA patients received NMA (n=89, Flu/Cy/200cGy TBI), RIC (n=53, Flu/Cy/400cGy TBI), or MAC (n=84, Bu/Cy or Cy/TBI) conditioning. Median follow-up was 4.5y. MAC patients were younger than RIC or NMA patients (24y vs. 30y and 31y, p<0.001). All patients who received RIC or NMA received planned post-HCT immunosuppression with PTCy, mycophenolate mofetil (MMF), and a calcineurin (CNI) or mTOR inhibitor. 35% of MAC patients received PTCy alone (HLA-matched donors), and 65% received PTCy with MMF and a CNI or mTOR inhibitor (haplo donors). Median recovery of engraftment for neutrophils and platelets was significantly earlier in RIC (17d/22d) and NMA (19d/23d) vs. MAC (24d/26d) (p<0.0001 and p<0.005 for neutrophils and platelets, respectively). Primary graft failure was significantly higher in NMA vs. RIC vs. MAC (10% NMA vs. 0% RIC vs. 4% MAC, p=0.02). MAC had more VOD as compared to RIC or NMA (12% MAC vs. 4% RIC vs. 2% NMA, p=0.02) and fungal infections within 6m of HCT (35% MAC vs. 9% RIC vs. 22% NMA, p=0.003), along with a higher cumulative incidence (CuI) of NRM at 1y (16% MAC vs. 4% RIC vs. 1% NMA, p=0.06, Figure 1), CuI of Grade III-IV aGvHD at 6m (8% MAC vs. 2% RIC vs. 0% NMA, p=0.009, Figure 1), and incidence of at least one readmission post-HCT (48% MAC vs. 19% RIC vs. 31% NMA, p=0.002). There were no differences among groups in OS, Gr II-IV aGVHD, cGVHD, or GRFS. On multivariable analyses, higher CuI of relapse was associated with NMA and minimal residual disease (MRD+) pre-BMT, lower EFS was associated with NMA, and lower OS and EFS was associated with MRD+ pre-BMT and increasing donor age (Figure 2). In most subgroup categories, OS, EFS, and relapse were quantitatively improved with MAC vs. NMA, with no differences between RIC vs. MAC. NRM was lower with RIC compared to MAC (p=0.031).

Conclusions:
These data support using RIC and younger donors for AYA patients. Further analysis of patient and donor characteristics benefiting from a certain conditioning intensity is ongoing.

4. **Title:** Outcomes after allogeneic hematopoietic cell transplant in patients with GATA2 deficiency

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Theme: Allogeneic HSCT

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Background: GATA2 deficiency syndrome is an inherited immune and bone marrow failure disorder with predisposition to myeloid malignancies. Allogeneic hematopoietic cell transplantation (allo-HCT) is a potential curative treatment. However, patients usually enter transplant with significant comorbidities rendering them at a high risk for early transplant complications. Available reports on outcomes following HCT are scarce.

Design/Methods: The Center for International Blood & Marrow Transplant Research (CIBMTR) registry was used to evaluate outcomes of patients with GATA2 deficiency who received allo-HCT. Primary outcome was overall survival (OS) at 1 and 3-years post-HCT. Causes of death were described. Frequency of acute graft versus host disease (aGVHD) and cumulative incidence of chronic GVHD (cGVHD)was assessed. Regression analysis was performed to determine factors associated with developing aGVHD and cGVHD.

Objective: To evaluate outcomes of patients with GATA2 deficiency who received allo-HCT.

Results: We identified 127 patients that received allo-HCT at 46 centers [median age 23 years (0.7-61) 63% were adults]. Most (64%) had a high comorbidity index (HCT-CI > 3) with infection (40%), prior solid tumor (35%) and moderate/severe pulmonary disease (26%) being the most common comorbidities. Immune deficiency and bone marrow failure were the indications for transplant in 76% of patients, with the remaining indication being MDS or leukemia. Most received myeloablative conditioning regimen (76%) and received HCT from unrelated donors (56%).
The median follow-up was 4 years (0.3-12 years). OS was 93% (95%CI 89-97%) at 1 year and 82% (95%CI 77-91%) at 3 years. OS didn't differ when stratifying for age or transplant indication. Main cause of death was organ failure followed by infection. Subgroup analysis of 40 patients with post-HCT infectious data, showed a high frequency of post-HCT infectious complications (87%), the majority being viral (67%). Endothelial complications (TA-TMA (2%) and VOD (5%)) were rare. All patients had primary engraftment. GVHD was frequently observed post-HCT: 60% of patients developed aGVHD, of which 60% were grade II-IV; cumulative incidence of cGVHD was 44% (95%CI 34-54%) at 1 year, with the majority (84%) experiencing extensive disease. GVHD was a contributing cause of death in 6 patients. Regression analysis did not identify any variables that significantly affected development of GVHD.

Conclusions: In patients with GATA2 deficiency, mortality related to transplant was low. However, the incidence of GVHD was high, adding to post-HCT related morbidity. Future research should be directed towards assessing risk factors for GVHD and optimizing prevention strategies.

5. **Title:** INVESTIGATING THE EXPERIENCE OF PAIN IN CHILDREN AND YOUNG ADULTS WITH SICKLE CELL DISEASE FOLLOWING HEMATOPOIETIC STEM CELL TRANSPLANTATION IN CANADA, A NATIONAL STUDY.

Authors: Hailey Zwicker, Greg Guilcher, Melanie Noel, Aisha Bruce, Nur El Huda Abu-Saris, Gurpreet Singh, Jenny Duong, Brianna Henry, Caitlin Forbes, Ufuoma Muwhen, Fiona Schulte

Location: University of Calgary, Calgary, Alberta, Canada

Theme: Allogeneic HSCT

Background: Hematopoietic stem cell transplantation (HSCT) is the only known curative treatment for sickle cell disease (SCD), a severe genetic form of anemia. While HSCTs have been performed for 40 years for SCD, many survivorship outcomes post-transplant remain poorly studied, including pain. Pain is a hallmark symptom of SCD that has been extensively investigated, however, very little research has been conducted to understand if survivors of HSCT experience pain, and what this pain may look like.

Objective: This work aims to explore pain interference in children and young adults who have undergone non-myeloablative HSCT for SCD.

Design/Method: This research is part of an ongoing cross-sectional study aimed to examine the wellbeing of youth with SCD post-HSCT. Eligibility criteria include: a minimum of one-year post-HSCT for SCD; age between 8-25 years; able to read and speak English; absence of any acute medical injury at the time of survey completion, or a diagnosed developmental disability. Questionnaires completed by the participants include a demographics form to obtain clinical information, and the Patient-Reported Outcomes Measurement Information System (PROMIS) pain interference subscale, as well as questions regarding pain duration and presentation. The PROMIS measure is scored on a T-score metric based on a reference sample of the general population with mean of 50 and standard deviation of 10. Data collection is currently ongoing.

Results: Sixteen youth who have undergone HSCT (current mean age 16.31 years old, 9 females) who were on average 4.94 years post-HSCT were included in this preliminary analysis. Fifty percent of this sample report experiencing no pain (N=8). Of the participants who reported experiencing pain (N=8), four reported experiencing chronic pain or pain that persisted for a minimum of three months straight. Average PROMIS pain interference scores across the pain-experiencing subsample were 55.91 (SD=3.39), suggesting scores within the normal range.

Conclusion: Preliminary results from the current study indicate optimistic outcomes suggesting pain interference post-HSCT is comparable to levels of the general population. However, 25% of our sample experience chronic pain. This study is an important first-step in understanding pain in those who have undergone HSCT for SCD. Future priorities should include long-term surveillance of those who undergo HSCT to ensure they receive appropriate chronic pain management in survivorship, if required. And to explore the impact of acute and chronic pain in this population.

6. **Title:** Systemic inflammatory response post low-dose total body irradiation in pediatric patients with sickle cell disease: a case series

Authors: Rozalyn Chok[1], Robert S Nickel[2], Gregory MT Guilcher[3].

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Theme: Allogeneic HSCT

Background:
HLA-matched sibling donor hematopoietic stem cell transplantation (HSCT) for pediatric sickle cell disease (SCD) has traditionally involved chemotherapy-based conditioning with acute and late toxicities, including graft versus host disease (GvHD). A novel nonmyeloablative (NMA) regimen of alemtuzumab, total body irradiation (TBI), and sirolimus has achieved successful engraftment without serious GvHD in adults. This approach is being prospectively evaluated in the phase II multicenter clinical trial "Sickle Transplant Using a Nonmyeloablative (SUN) Approach" (NCT 03587272). After a protocol amendment changing alemtuzumab administration from intravenous (IV to subcutaneous, we observed systemic inflammatory response syndrome (SIRS) after TBI in three patients enrolled on study.

Objective:
To describe the presentation and management of pediatric patients with SCD experiencing SIRS after TBI as part of a nonmyeloablative conditioning regimen.

Design/Method:
Case series. Patients received subcutaneous alemtuzumab 0.2 mg/kg with methylprednisolone premedication from day -7 to -3 and 300 cGy TBI as a single fraction on day -2.

Results:
Affected patients were an 11-year-old female with HbSS complicated by recurrent acute chest syndrome (ACS) and vaso-occlusive episodes, 17-year-old female with HbSβ^+ complicated by chronic pain, and 14-year-old male with HbSS complicated by ACS and red blood cell (RBC) alloimmunization. Patients were afebrile with normal vital signs at time of TBI. Tachycardia and hypotension developed post TBI on day -2 in all three patients. Two patients had concurrent fever. All patients received fluid resuscitation with crystalloid and/or RBC transfusion. Two patients required intensive care unit (ICU) admission; one required vasoactive medication for less than 24 hours. Both patients admitted to ICU received systemic corticosteroids. All patients had negative blood cultures and normalization of vital signs within 24 hours. This complication was not observed in 38 patients receiving IV alemtuzumab but in 3/11 (27.3%) of patients receiving subcutaneous alemtuzumab (p=0.009).

Conclusion:
We observed SIRS with cardiovascular dysfunction in patients with SCD receiving subcutaneous alemtuzumab and TBI. The absence of infection and rapid onset and recovery post TBI in all three cases suggests an inflammatory response akin to cytokine release syndrome (CRS). We hypothesize that the combination of immune-modulating therapy and TBI in the context of chronic inflammation uniquely predisposes patients with SCD to this serious complication.
Our observations underscore the need for careful monitoring of patients receiving this combination of therapy. Measuring inflammatory cytokines at different timepoints may help elucidate the mechanism of this response. Surveillance and enhanced supportive care on the SUN study are ongoing.

7. **Title**: Impact Of Human Herpesvirus 6 Peri Engraftment Post Umbilical Cord Stem Cell Transplantation

Shaikha Alqahtani, Faraz Afridi, Irtiza Sheikh, Jeremy Conners, Priti Tewari, Demetrios Petropoulos, Ramia Zakhour ,Natalie Dailey Garnes, Elizabeth Shpall, Dristhi Ragoonanan

Theme: Allogeneic HSCT

Background:
Human herpesvirus 6 (HHV6) reactivation post umbilical cord blood (UCB) stem cell transplant (SCT) can lead to significant morbidity such as infection, delayed neutrophil and platelet engraftment, and graft rejection. This occurs most often within 2-4 weeks post SCT during the peri-engraftment period.

Objective:
To present three patients post UCB SCT with complications secondary to HHV 6 infection.

Design/Method:
Case series. A review of the chart and literature was completed. Patient demographics and SCT details are included in table 1.

Results:
Patient 1 initially neutrophil engraftment on day (D)+14. She later developed hemophagocytic lymphohistiocytosis (HLH) secondary to disseminated HHV6 infection in the CSF (96,600 counts/ml) and bone marrow (309 counts/ml) resulting in secondary graft failure by D+26 post UCB SCT. She was treated with foscarnet and weekly IVIG until she had negative HHV 6 on D+38. She also received anakinra and rituximab for her HLH. She subsequently underwent conditioning with fludarabine, cyclophosphamide, TBI, followed by haplo- allogeneic SCT, with post-transplant cyclophosphamide. She successfully neutrophil engrafted on D+15 and remains in remission 18 months post SCT. (Figure 1a)
Patient 2 had neutrophil engraftment on D+18, however had delayed platelet engraftment and required frequent platelet transfusions. On further evaluation, he was found to have HHV 6 viremia (76,100 copies/ml) present on D+24. He did not have any other concomitant infections. He was treated with foscarnet and weekly IVIG and cleared the HHV6 viremia on D+34.He achieved platelet engraftment shortly thereafter on D+39 and remains in remission 10 months post SCT. (Figure 1b)
Patient 3 initially achieved neutrophil engraftment on D+17, however, her neutrophil count started to decline shortly thereafter, raising concern for developing secondary graft failure. She was found to have HHV6 viremia (14,100 copies/ml) on D+16 and began treatment with foscarnet and weekly IVIG. Her HHV6 infection was cleared on D+35 and neutrophils subsequently recovered. She remains in remission 2 months post SCT. (Figure 1c)

Conclusion:
Patients post UCB are at high risk for viral reactivation due delayed immune reconstitution and recovery. Screening and prophylaxis guidelines for HHV6 in UCB SCT recipients are not well established. HHV6 infection in this population can potentially result in increased morbidity and may warrant routine screening for HHV6 reactivation during the peri-engraftment period. Further larger studies are needed to inform future guidelines.

Table 1: Patients characteristics

Patient No.	Age /Gender	Primary disease	Conditioning regimen	Cell Dose TNC/Kg	Match grade	HHV 6 first detected	Neutrophil engraftment
1	10 years Female	tAML (Inv16)	Bu/Flu/Clo/ATG /low dose TBI	2.8/kg x 10^7	5/6	D+23	D+14
2	6 years Male	Relapsed AML (KMT2A)	Bu/Cy/ATG	7.28 x10^7/kg	5/6	D+24	D+18
3	5 years Female	AML (TP53)	Bu/Cy/ATG	12.53 x 10^7/kg	5/6	D+14	D+17

Abbreviation: Busulfan (Bu). Fludarabine (Flu), Clofarabine (Clo), Antithymocyte Globulin (ATG), Total body irradiation (TBI), cyclophosphamide (Cy).

Figure 1a shows absolute neutrophil count trend post transplant with HHV6 in patient 1

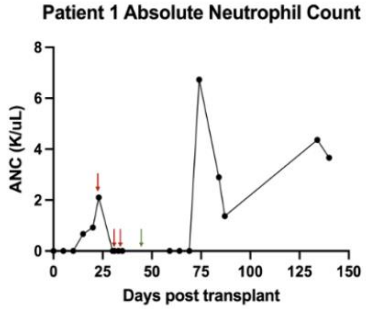


Figure 1b shows platelet count trend post transplant with HHV6 in patient 2

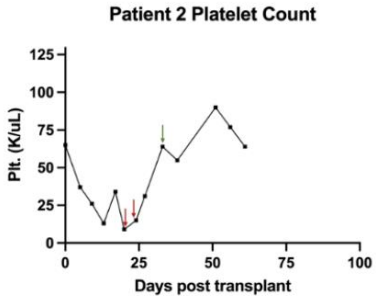
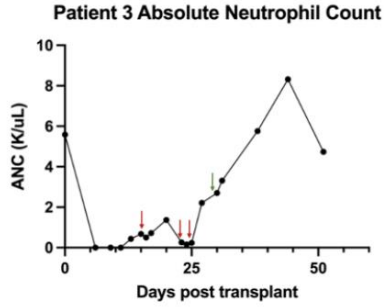


Figure 1c shows absolute neutrophil count trend post transplant with HHV6 in patient 3



Red arrows indicated HHV6 detected
Green arrow indicated HHV6 clearance

8. **Title**: Comparison of Late Effects After Hematopoietic Cell Transplantation for Non-Malignant Diseases by Conditioning Regimen

Neel S. Bhatt, Courtney Vandervlugt, Jenny Tseng, Paul Carpenter, James Connelly, Debra Friedman, Madhavi Lakkaraja, Adam Kidwell, Aleksandra Petrovic, Rachel Phelan, Julie Talano, Monica Thakar, Hesham Eissa, K. Scott Baker, Lauri Burroughs
Fred Hutchinson Cancer Center

Theme: Allogeneic HSCT

Background: Allogeneic hematopoietic cell transplantation (HCT) is curative for many patients with non-malignant diseases. Although effective at establishing the graft, chemoradiotherapy-based conditioning regimens can be associated with undesirable late effects.

Objective: To examine the incidence of late effects associated with treosulfan-based versus low-dose total body irradiation (TBI)-based conditioning in patients with non-malignant diseases

Methods: A multi-center retrospective analysis of patients with non-malignant diseases who underwent HCT with either TREO (treosulfan, fludarabine, anti-thymocyte globulin ± thiotepa) or TBI-based (200-400 cGy TBI, fludarabine, with either cyclophosphamide or ± alemtuzumab) conditioning regimens between 2006-2023 was performed. The incidences of the following late effects were compared between TREO vs TBI groups using chi-square testing: echocardiographic ejection fraction <50%, serum cholesterol >200 mg/dL, serum triglycerides >150 mg/dL, blood glucose > upper limit of normal, bone mineral density Z-score ≤-2.0 using dual X-ray absorptiometry, forced expiratory volume in 1-second <80% predicted (as a surrogate for obstructive defects), total lung capacity <75% predicted (for restrictive defects), and diffusion defect defined as diffusing capacity for carbon monoxide corrected for hemoglobin <75% predicted.

Results: A total of 143 survivors (TREO N=108, TBI N=35) were included. The median age at HCT was 6.1 (range 0.2-32.4) years for the TREO group and 4.4 (0.4-46.9) years for the TBI group. Median follow-up post-HCT was 5.4 (interquartile range 3.4-9.1) years for the TREO group and 7.3 (3.9-11.7) years for the TBI group. Immune deficiency was the most common diagnosis in both groups. The incidence of grade 3-4 graft-vs.-host-disease (GVHD) was 7% and 20% for TREO and TBI groups respectively; the incidence of extensive chronic GVHD was 19% and 46%, respectively. The proportion of patients with at least one long-term complication was similar between both groups (TREO 79% vs. TBI 69%, p=0.22). No significant differences in the incidence of late effects by conditioning regimen were noted. The most common complication in both groups was hypertriglyceridemia (TREO 62%, TBI 69%, p=0.26) followed by hyperglycemia (TREO 43%, TBI 49%, p=0.53). Six percent of patients developed systolic dysfunction in the TBI group and none in the TREO group.

Conclusion: No significant differences in late effects were noted in patients with non-malignant diseases after HCT with either TREO or TBI-based conditioning. Additional work is underway to compare the late effects with other conditioning agents (e.g. busulfan).

9. **Title:** Assessment of Clinician Adherence to Screening and Prevention Guidelines for Pediatric, Adolescent, and Young Adult Allogeneic Hematopoietic Cell Transplant Survivors
Elizabeth M. Hellewell, K. Scott Baker, Paul A. Carpenter, Catherine J. Lee, Neel S. Bhatt

Fred Hutchinson Cancer Center

Theme: Allogeneic HSCT

Background: Prior studies have reported variable adherence to screening and prevention guidelines from hematopoietic cell transplant (HCT) survivors' perspective (Khera N et al. Biol Blood Marrow Transplant. 2011 Jul;17(7):995-1003). However, no prior study has assessed clinician adherence to these guideline recommendations.

Objective: To examine clinician adherence to the 2011 screening and prevention practice guidelines (Majhail NS et al. Biol Blood Marrow Transplant. 2012 Mar;18(3):348-71).

Methods: A retrospective, single-center cohort study of pediatric, adolescent, and young adult patients who underwent allogeneic HCT for hematologic malignancies between January 1, 2016 and December 31, 2016 was conducted. Patients who were alive and disease free for at least 3 years post-HCT were included. Data on key screening practices or tests focusing on cardiovascular, metabolic, endocrine, renal systems, re-vaccination, and subsequent neoplasm screening were abstracted from electronic medical records (EMR). "Non-adherent" was defined by no evidence of an order or test result for each screening test between 1-3 years post-HCT. Descriptive statistics were used for the analysis.

Results
Thirty-four patients were included, with a median age at HCT of 25.5 (range 1-39) years; 59% were females and 79% were of white race. Acute lymphoblastic leukemia (38%) and acute myelogenous leukemia (38%) were the most common HCT indications. Twenty-four percent of patients had severe acute GVHD and 18% had chronic GVHD. Among pediatric survivors, 14% demonstrated non-adherence to echocardiographic cardiovascular screening. In contrast, there was 6% non-adherence among the 32 patients old-enough to complete dual X-ray absorptiometry and 3% for checking serum vitamin D levels. All patients underwent fasting lipid and blood glucose testing (100%). Assessment of thyroid (94%) and renal (97%) function was also completed for most survivors. Completion rates for skin cancer screening (32%) and age-appropriate cervical cancer screening (73%) were lower. Fifty-nine percent completed dental screening. Lastly, at least one post-HCT vaccination was ordered for 94% of patients.

Conclusions:
To our knowledge, this is the first report of EMR-based clinician adherence to screening and prevention guidelines for HCT survivors in the United States. Overall, the adherence was more than 90% for most of the studied tests and procedures, which is reassuring. Our next step is to conduct a multi-center analysis to understand the clinician adherence across HCT centers and assess factors associated with lower adherence to specific tests and procedures. The findings will provide an opportunity to develop and test interventions to improve clinician adherence to screening and preventive practice guidelines.

10. **Title**: Hematopoietic Stem Cell Transplant for Blastic Plasmacytoid Dendritic-cell Neoplasm in an Adolescent Male in Third Remission

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Theme: Allogeneic HSCT

BACKGROUND: Blastic Plasmacytoid Dendritic-Cell Neoplasm (BPDCN) is a rare hematologic malignancy. BPDCN presents with cutaneous tumors in virtually all cases and is typically seen in older men (median age 70). BPDCN confers a poor prognosis (overall survival <1 year) with relapse common in those untreated with hematopoietic stem cell transplant (HSCT).

OBJECTIVE: Case report of refractory BPDCN who underwent HSCT following third remission.

METHODS: A 16-year-old AA male presented with painless lesions on his face and torso. Workup demonstrated 60% blasts on peripheral blood, prompting bone marrow (BMBx) and skin biopsies. Pathology confirmed sheets of CD123, CD56, and TDT positive cells, consistent with BPDCN. CSF was CNS2.

RESULTS: Induction chemotherapy was initiated via a modified AALL1732 4-drug regimen including PEG-Asparaginase weekly. Skin lesions resolved and end of induction BMBx showed minimal residual disease (MRD) negative remission (MRD <0.01%). Donor selection for HSCT was poor, so 3 cycles of Tagraxofusp, a CD123 directed cytotoxin, were given. He developed marrow relapse during cycle 3. He entered CR2 following one cycle of cyclophosphamide/etoposide and 3 cycles of high dose methotrexate. A MUD was identified, however HSCT was delayed due to donor illness and availability. Subsequently, he had a third marrow relapse. Following FLAG-Ida as salvage therapy, he developed *Cryptococcus neoformans* bacteremia and pneumonia. He recovered following treatment with multi-agent therapy. CR3 was achieved following count recovery. HSCT from a 7/8 HLA MUD was performed using TBI 1200cGy (days –8 to -6), etoposide 1500mg/m^2 (day–5), and cyclophosphamide 60mg/kg (days –4 to –3). GVHD prophylaxis included tacrolimus, abatacept, and methotrexate. Day +30 BMBx resulted MRD-negative. He developed rapidly progressive EBV infection Day +51 causing cardiac tamponade and multi-organ failure. He died Day +56, 5 days following EBV detection on PCR and one dose of rituximab.

CONCLUSION: There is currently no consensus for treatment of BPDCN, though studies have shown more success incorporating aspects of both lymphoid and myeloid leukemia treatment over lymphoma protocols. Despite initial responses, duration of remission is variable and survival is best when HSCT is achieved following CR1. Here, HSCT was repeatedly delayed due to difficulty identifying an acceptable donor, primarily because of limited availability of donors for minority patients in the National Marrow Donor Program. This led to extended pre-HSCT treatment and infections which increased risk of post-HSCT complications. Though we eventually proceeded with transplant, our case highlights the aggressive nature of this disease and the need for a more diverse donor pool.

11. **Title** The Impact of Distance from Hematopoietic Cell Transplant (HCT) Center on Acute Graft versus Host Disease and Death in Long Term Survivors- A Secondary CIBMTR Analysis

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Theme: Allogeneic HSCT

Background: Hematopoietic cell transplantation (HCT) is a potentially curative therapy for numerous malignant and non-malignant conditions but confers risk of significant morbidity and mortality from

complications. There are conflicting data regarding the impact of proximity to HCT center on graft versus host disease (GVHD) and mortality.
Objective: We hypothesized that increasing distance between patient's home and HCT center is a barrier to care and would be associated with higher rates of both mortality and GVHD in the post-transplant period.

Methods: We performed a secondary analysis of existing Center for International Blood and Marrow Transplant Registry (CIBMTR) data (PMID: 31726205). Inclusion criteria included two-year survivors of first allogeneic or autologous HCT for malignant and non-malignant indications between 2003 and 2013. Distance from HCT center was dichotomized as <100 miles or >/100 miles. Sub-distribution, time dependent cox proportional hazard models were used to determine the association of patient and transplant characteristics and grade 2-4 acute GVHD (aGVHD), treating death as a competing risk. Cox proportional hazard models were used to calculate risk factors for death. SAS 9.4 (Cary, NC) was used for analysis.

Results: 21,991 patients were included in the study. The median age was 45 years (IQR 19,57), 87 % underwent HCT for hematologic malignancy, and the median distance from HCT center was 38 miles (IQR 15,112). Univariable risk factors for grade 2-4 aGVHD included age, race, insurance type, distance to HCT center, Karnofsky score, HCT indication, peripheral blood stem cell (PBSC) transplant, HLA mismatch, sex-match of donor and recipient, preparative regimen intensity, and aGVHD prophylaxis. In multivariable analysis, distance from HCT center (≥100 miles) remained a significant risk factor for grade 2-4 aGVHD (HR 1.1, 95% CI 1.02-1.18). Univariable risk factors for death included HCT indication, insurance type, distance from HCT center, HLA mismatch, PBSC transplant, age, sex, preparative regimen intensity, recipient CMV status, acute GVHD prophylaxis, grade 2-4 aGVHD, and year of HCT. In multivariable analysis, distance from HCT center was not a significant risk factor for death (HR 0.98, 95% CI 0.89-1.08).

Conclusion: In this large secondary CIBMTR analysis, we found that increased distance from transplant center was associated with an increased adjusted risk for the development of grade 2-4 aGVHD, but not death. Patients receiving care >100 miles from home may have additional challenges in the diagnosis and treatment of acute GVHD that contribute to this association, though additional studies are needed.

12. **Title** Timing and Dosing of Alemtuzumab Effects on Graft-Versus-Host-Disease, Viral Reactivations, Mixed Chimerism, Graft Failure, and Overall Survival in Pediatric Patients: A Single-Center Retrospective Study and Review of the Literature

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4Mayo Clinic Alix School of Medicine

Theme: Allogeneic HSCT

Background
Alemtuzumab is a humanized monoclonal antibody that can be administered prior to hematopoietic cell transplantation (HCT) in patients with malignant or non-malignant disorders. Alemtuzumab provides in vivo lymphodepletion to mitigate the risk of graft-versus-host-disease (GVHD) and graft failure.

However, many studies have shown that both the timing of administration and dosing of alemtuzumab affect the rates of GVHD, viral reactivations, mixed chimerism, graft failure, and overall survival. Our institution administers alemtuzumab to patients undergoing matched unrelated donor (MUD) transplants via a specific weight-based nomogram and proximal schedule.

Objective
The primary objective of this study is to describe key clinical outcomes associated with our institutional alemtuzumab dosing strategy in patients receiving MUD transplants.

Design/Method
We conducted a retrospective chart review at Mayo Clinic in Rochester, MN. Patients age 21 years or younger undergoing a MUD transplant from January 2003 – December 2023 who received alemtuzumab dosed by the proximal weight-based nomogram were eligible for inclusion. Patients were excluded if they received an alternative dosing scheme or if the dosing information was not available. The weight-based nomogram is as follows: 3 mg if 5-15 kg, 5 mg if 15-30 kg, and 10 mg if greater than 30 kg. All doses were administered proximal to the transplant (e.g. after day -12). Reports of acute GVHD, chronic GVHD, viral reactivations, mixed chimerism, graft failure, and overall survival were extracted from the medical record for analysis.

Results
From 2003 – 2023, 58 patients with malignant and non-malignant disorders received alemtuzumab, with a total of 62 MUD transplants. Malignancy was the most common indication for transplant. Median age at transplant was 11.4 years. Acute GVHD developed in 27.4% and chronic GVHD in 9.7% transplants. CMV reactivation occurred in 22.5%, EBV reactivation in 6.3%, and adenovirus reactivation in 7.9% transplants. Mixed chimerism at day +30 was noted in 4.9% and graft failure in 8% (3 of these 5 patients had non-malignant disorders). There were 15 deaths total in the cohort.

Conclusion
We describe our institutional experience with a proximal weight-based dosing nomogram of alemtuzumab in pediatric patients undergoing MUD HCT. This dosing strategy conferred relatively low rates of acute GVHD, chronic GVHD, and mixed chimerism. Graft failure and viral reactivation were comparable to historical controls. Overall, our results compare favorably to other published reports of proximally-dosed alemtuzumab and support the need for prospective evaluation to ascertain the optimal alemtuzumab dosing approach in children undergoing MUD HCT.

13 Title: Plasma Proteome Analyses Identify Predictors of Graft Rejection Prior to Stem Cell Infusion and Support Interferon-Mediated Ferroptosis as a Novel Mechanism of Graft Rejection

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Theme: Allogeneic HSCT

Background: No established biomarkers or effective interventions exist for graft rejection. We previously reported that CXCL9, a downstream marker of interferon, differentiates graft rejection from other complications but is only useful at the time of rejection. We hypothesized that biological differences in the host proteome exist prior to HSCT and that interferon-mediated pathways drive host elimination of donor cells during graft rejection.

Objective: We sought to identify novel graft rejection mechanisms, biomarkers and therapies.

Design/Methods: We studied the plasma proteome of 21 HSCT recipients prior to stem cell infusion (day -2 to day 0) and at the time of rejection (or timepoint matched days for controls) using an aptamer-based proteomics analysis (SomaScan). Twelve patients suffered graft rejection with associated fever and 9 (matched for age and diagnosis) developed fevers after HSCT but not graft rejection (febrile controls).
Results: A total of 723 proteins were significantly different in graft rejection patients at the time of rejection vs controls. CXCL11 was the most differentially expressed protein during rejection ($p=5.2e-8$, log2 fold change= 12.9) but did not differ from controls at baseline. In contrast, LAG3, an interferon regulated protein involved in activated T-cell expansion, was different in rejection patients both prior to stem cell infusion ($p=0.009$) and during rejection ($p=0.007$, Fig.1C). A total of 158 proteins were different prior to stem cell infusion in patients with later rejection vs controls.
Ingenuity pathway analysis (IPA) of proteins differentially expressed prior to stem cell infusion found differences in interferon-γ pathways that promote leukocyte recruitment, suggesting some recipients are primed for rejection by interferons before donor stem cells are infused. IPA of differentially expressed proteins at time of rejection shows a combination of interferon-γ, α, and β pathways resulting in cell death and leukocyte activation. Ferroptosis signaling was also significantly increased in rejection patients at the time of rejection vs controls ($p=1e-3$). The ferroptosis database (FerrDB) identified 32 genes corresponding to proteins differentially expressed in rejection patients. Our data suggest interferon activation during rejection induces ferroptosis-mediated cell death of donor cells.

Conclusion: This is the first study to establish significant differences in biologically relevant plasma proteins prior to stem cell infusion. Our findings suggest early intervention with targeted therapies may prevent impending rejection and identifies measurable proteins for graft rejection surveillance. Our findings strongly validate the integral role of interferons in graft rejection and identify a novel mechanism of interferon-mediated cell death in graft rejection, ferroptosis.

Autologous HSCT

1. Title: Invasive Fungal Infections Are Rare in Pediatric and Young Adult Autologous Hematopoietic Stem Cell Transplant Patients

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Theme: Autologous HSCT

Background

Invasive Fungal Infections (IFI) have a reportedly lower incidence in autologous hematopoietic stem cell transplant (auto-HSCT) recipients compared to their allogeneic counterparts, especially in pediatric and adolescent populations. This study aimed to evaluate the incidence of IFI in pediatric auto-HSCT recipients at our center between 2013-2023.

Methods
A retrospective cohort study was conducted on 150 consecutive pediatric and young adult patients who underwent auto-HSCT at Cincinnati Children's Hospital Medical Center (CCHMC) from January 2013 to January 2023. Data collected included patient demographics, transplant characteristics, and fungal infection diagnoses within the first 100 days post-transplant. Only proven and probable invasive fungal diseases (IFD), as per the European Organization for Research and Treatment of Cancer definitions, were considered, excluding tinea and onychomycosis cases.

Results
Among 150 patients (240 transplant episodes), neuroblastoma was the predominant indication for auto-HSCT (37.3%), and micafungin was the most utilized antifungal prophylaxis (82.7%). None had a history of IFI prior to HSCT, and neutrophil engraftment occurred at a median of 10 days (range 8-22 days). No proven or probable IFD cases were identified within 100 days post-HSCT. Sub-analysis for late infections also showed negligible incidence of fungal infections within the first year post-transplant.

Conclusions
The incidence of IFI, particularly from mold species, is notably rare in this auto-HSCT recipient cohort. No early fungal infections were observed post-HSCT, highlighting a potentially low-risk cohort that might not require aggressive antifungal prophylaxis during HSCT.

2. Title: Route of Nutrition Impacts Outcomes after Autologous Stem Cell Transplant for High-risk Neuroblastoma

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Theme: Autologous HSCT

Background:
Neuroblastoma is the most common extracranial solid tumor of childhood. Treatment of high-risk neuroblastoma includes autologous stem cell transplant (ASCT), including myeloablative conditioning that can lead to malnutrition, pancytopenia, ulcerative mucositis, and infections. The effect of differing nutrition routes (enteral versus parenteral) on nutritional outcomes and adverse events in this population is understudied.

Objective:
Primary objective was to determine whether there are differences in nutritional outcomes in patients with high-risk neuroblastoma undergoing ASCT who are supported with enteral nutrition, parental nutrition,

or a combination of both. Secondary objective was to determine if there are differences in the incidence of adverse or harmful events as well as the time to engraftment.

Design/Methods:
Thirty-six transplants (27 patients) at American Family Children's Hospital from 2011-2021 were selected for retrospective chart review following IRB approval. Primary endpoints measured were nutritional parameters (height, weight, BMI, z-score, type of feeding tube). Secondary endpoints included a variety of clinical outcomes including length of stay, mortality, time to engraftment and transfusion needs. Standard descriptive statistics stratified by nutritional intervention group and time for the primary endpoint of the study were utilized. Secondary endpoints were analyzed with a generalized linear mixed effects model with patient specific random effects and a logit link function to evaluate the association incidence of treatment related adverse events and nutritional intervention.

Results:
Patients were analyzed within 3 groups: enteral (n = 6), parenteral (n = 7), and combined enteral plus parenteral (n = 14) nutrition. Statistically significant increases in weight (+0.8kg, p=0.0006) and BMI z-scores (p=0.0003) were found in the parenteral group compared to enteral. Mean number of days of diarrhea and vomiting were reduced in the enteral group compared to parenteral (5.8 vs. 20.8, p=0.0001; 6.2 vs. 12.7, p=0.0075, respectively). Mean mucositis severity pain scores were reduced in enteral group compared to parenteral (2.1 vs. 4.5, p=0.0022). Time to platelet engraftment was shorter in enteral group compared to parenteral (9.4 vs. 25.8 days, p=0.0001), and lower mean pRBC transfusions were administered (2.2 vs. 6.2, p=0.0023). No differences in length of stay, or mortality at 100 or 365 days post-transplant were seen.

Conclusions:
High-risk neuroblastoma patients supported with parenteral nutrition during ASCT transplant had improved nutritional outcomes compared to those supported with enteral nutrition. However, recipients of enteral nutrition showed less complications (decreased duration of diarrhea/vomiting and lower mucositis severity) while showing faster time to engraftment of platelets and fewer blood transfusions.

Theme: Cellular Therapies

1. Title: Treatment of Refractory Cytomegalovirus (CMV) Infections using CMV-specific Cytotoxic T-lymphocytes (CTLs) in Children, Adolescents and Young Adults (CAYA) Post Allogeneic Hematopoietic Stem Cell Transplantation (AlloHSCT) or Solid Organ Transplant (SOT), or with Primary Immunodeficiency (PID)

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Theme: Cellular Therapies

Background: CMV, is a cause of significant morbidity and mortality in patients post-transplant, or with PID, secondary to decreased CMV specific T-cell immunity, delayed immune reconstitution and/or continued immunosuppression. The use of virus-specific (vs) CTLs offers an opportunity to restore temporary immunity.

Objective: Determine the safety and efficacy of familial CMV specific CTLs for the treatment of refractory systemic CMV infections.

Design/Methods: Patients were deemed eligible if they had evidence of CMV DNAemia after 7 days or persistent quantitative RT-PCR DNA copies after 14 days of appropriate anti-viral therapy or known resistance and/or intolerance to anti-viral agents. Donors were required to be matched≥3 HLA (A/B/DRB1) loci and have an adequate T-cell CMV response. vsCTLs were isolated using the CliniMACS® Prodigy following stimulation with viral specific GMP PepTivator®, generously provided by Miltenyi-Biotec®. CMV specific CTLs were enriched using a Cytokine Capture System. The target cell dose was $0.5x10^4$ CD3+ cells/kg (recipient-weight). Repeated doses were permitted every 2 weeks to a maximum of 5 doses in the absence of a complete response (CR) and adverse events. The following were used to define response: CR, undetected CMV PCR, partial response (PR), at least one log decrease from baseline, progressive disease (PD), at least one log increase from baseline, and patients with stable disease (SD).

Results: Fifteen patients were enrolled: 10 males and 5 females; aged 0.7-19 years. Thirteen patients were post-AlloHSCT, 1 patient was post-SOT, and 1 PID patient. All vsCTLs donors were haploidentical: 5 were the original HSCT donors and 10 were third party donors (8 maternal, 1 paternal and 1 grandmother). The mean number of CMV CTL infusions was 2.26 (range: 1-5). None of the patients experienced cytokine release syndrome, Graft-versus-host disease, or an infusion reaction. One patient experienced respiratory distress 12hrs post infusion, possibly related to vsCTLs. Three patients were taken off study by physician discretion. Ten patients achieved CR, 1 patient had PR, 3 had SD, and 1 had PD. The overall response (OR) was 69%. The median time to CR was 43.4 days (range 6-81 days). Day 100 and 365 overall survival (OS) post-enrollment was 100% and 85.5% (CI95: 38.9-96.2), respectively. For patients who achieved CR, day 365 post-enrollment probability of viral-associated mortality was 0%.

Conclusion: Our preliminary data demonstrate that haploidentical CMV specific CTLs manufactured by direct selections are safe, rapid, well-tolerated, and efficacious in patients with refractory/persistent CMV infections in immunocompromised patients. Accrual is ongoing. Grant #:1R01FD006363.

2. Title: Combinatorial immunotherapy with IL-15 superagonist N-803 and anti-ROR1 Chimeric Antigen Receptor-Engineered Natural Killer Cells Significantly Enhances *in-vitro* Cytotoxicity against $ROR1^+$ Neuroblastoma and *in-vivo* Survival of Xenografted Immunodeficient NSG Mice

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Theme: Cellular Therapies

Background: Neuroblastoma (NB) is the third most common malignancy in childhood, and the most common malignancy in infancy. Children with recurrent and/or metastatic NB have a dismal event-free survival rate (<25%). Natural killer (NK) cells have a unique role in immunosurveillance and tumor cell killing. Receptor tyrosine kinase like orphan receptor 1 (ROR1) is highly expressed on the surface of NB cells. Engineering NK cells to target ROR1 represent a potential novel immunotherapy for NB. The efficacy of this approach may be enhanced by use of the interleukin-15 superagonist IL-15RαSu-Fc fusion molecule N-803. We previously demonstrated that N-803 increased the viability, proliferation and ADCC of expanded peripheral blood NK (exPBNK) cells in combination with dinutuximab against solid tumors.

Objective: We investigated the *in-vitro* and *in-vivo* anti-tumor effects of anti-ROR1 chimeric antigen receptor (CAR) modified NK cells with or without N-803 against NB cells.

Methods: Anti-ROR1 CAR NK cells were generated by electroporating anti-ROR1 CAR mRNA into exPBNK cells using the MaxCyte GT® electroporation System; mock-transfected exPBNK cells were used as controls. The cytotoxicity of anti-ROR1 CAR NK cells with or without N-803 was assessed *in-vitro* using ROR1$^+$ NB cells. CD107a, perforin, granzyme B and IFN-□ levels were determined by intracellular flow cytometry or ELISA assays. The phenotypic and functional effects of N-803 activation on anti-ROR1 CAR NK cells were evaluated by mass cytometry. Human NB xenografted NOD/SCID/IL2r□null (NSG) mice were utilized to investigate *in-vivo* anti-tumor effects.
Results: Compared to mock exPBNK cells, the *in-vitro* cytotoxicity of anti-ROR1 CAR NK cells against ROR1$^+$ NB cells was significantly enhanced ($p<0.001$). The anti-ROR1 CAR NK cells expressed significantly higher levels of intracellular CD107a, IFN-□, and granzyme B. N-803 significantly enhanced anti-ROR1 CAR NK *in-vitro* cytotoxicity against ROR1$^+$ NB cells compared to controls ($p<0.05$). High Dimensional Analysis revealed that N-803 significantly enhanced Stat5 phosphorylation and Ki67 levels in exPBNK and anti-ROR1 CAR NK cells with or without NB cells SKNFI ($p<0.05$). Additionally, N-803 enhanced the expression of activating receptors NKG2D and NKp30 on both exPBNK cells and anti-ROR1 CAR NK cells. *In-vivo*, anti-ROR1 CAR NK cells plus N-803 significantly enhanced survival of NB xenograft NSG mice compared to anti-ROR1 CAR NK alone ($p<0.05$).

Conclusion: Our results provide the rationale for further development N-803 in combination with anti-ROR1 CAR NK cells as a novel immunotherapeutic for patients with recurrent or metastatic ROR1$^+$ NB. The genomic and immunologic mechanisms studies are ongoing. (Funded by U54 CA232561).

3. Title: Clinical response to virus-specific T-cells is not impacted by T-cell co-stimulation inhibition

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Theme: Cellular Therapies

Background: Patients undergoing allogeneic hematopoietic stem cell transplant (HSCT) are at increased risk of viral infections. Virus-specific T cells (VSTs) have been successfully used in the treatment of viral infections that are unresponsive to antiviral therapy. Abatacept is used in the prevention of graft-vs-host disease (GVHD). Abatacept inhibits T cell activation, decreases T cell proliferation, survival and cytokine secretion in vivo. The impact of abatacept on VST outcomes has not been previously studied.
Objective: Analyze the effect of abatacept on VST outcomes.
Methods: We reviewed medical records of allogeneic HSCT patients who received donor derived (DD) or third party (TP) VSTs for treatment. Clinical response was evaluated at 4 weeks after each infusion. Complete response (CR) was defined as the resolution of viremia by blood PCR quant and/or resolution of associated symptoms, partial response (PR) was defined as >50% reduction in viremia and associated symptoms, no response (NR) was defined as worsening viremia or associated symptoms. Interferon-γ enzyme linked immunosorbent assay (ELISpot) was performed by pulsing patient peripheral blood mononuclear cells with the viral pepmix.
Results: Thirty-four patients who received abatacept received a total of 50 VST infusions for treatment of viral disease. Forty-four (88%) infusions were DD and 6 (12%) were TP VSTs. VSTs were infused at a median post-transplant day of +62 (range +21 to +280). The average number of infusions per patient was 1.8. The median time between most recent abatacept dose and VSTs was 29 days. Overall response rate to at least one virus was 88% (CR: 30 (60%), PR: 14 (28%)). No response was seen after 5 (10%) infusions and one was unevaluable due to high dose steroid use. The timing of abatacept infusion did not affect the clinical response. Interferon-γ ELISpot obtained in a patient who received abatacept showed T cell expansion leading to decrease in viral load.
Conclusion: In this data we show that the clinical response to VSTs in patients who received abatacept for GVHD prophylaxis is comparable to previously published data for all comers. Use of abatacept does not appear to modify clinical response to VSTs in patients undergoing allogeneic HSCT and can be safely administered at any time in patients who require VSTs for treatment. This retrospective analysis is limited by the small sample size and will be reinvestigated in the future with further accrual.

4. Title: Utilization of Machine Learning to Develop a Pediatric B-cell Acute Lymphoblastic Leukemia (B-ALL) CAR T-cell Comorbidity Index (CAR-CI)

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Theme: Cellular Therapies

Background: The ability to predict severe CAR T-cell associated toxicities can inform risk mitigation strategies to improve outcomes. While such predictive parameters have been developed and validated in adults receiving CAR T-cells, this is less well established in children and young adults (CAYA) receiving CAR T-cells for B-ALL. Incorporation of machine learning across a host of pre-infusion clinical variables may offer a novel way to predict toxicities in CAYA.

Methods: We sought to develop a pediatric CAR-CI to predict severe cytokine release syndrome (CRS) (>grade 3) using a training cohort of CAYA with relapsed/refractory B-ALL treated on 1 of 4 Phase I CAR Tcell trials at the NCI targeting CD19 and/or CD22 (NCT01593696, NCT02315612, NCT03448393, NCT05442515). In total, 32 key pre-CAR variables were tested, including baseline cytopenias, inflammatory markers, markers of organ function, indicators of disease severity, demographic information, as well as clinical factors such as medication use and prior therapy. Individual variables were assessed for association with severe CRS at the univariate level ($p<0.1$), using Wilcoxon, Spearman correlation, or Fisher's exact testing. Independently, a machine learning method of Least Absolute Shrinkage and Selection Operator (LASSO) regression (glmnet R-package) was performed using the full set of variables to ascertain features that may be used in combination to predict severe CRS.

Results: The training cohort consisted of 158 patients with a median age of 15.8 years (range 4.3-38.7). Of these patients, 122 (77.2%) had any grade CRS, and 30 (19.0%) had severe CRS. Using univariate analyses, severe CRS independently associated with age, creatinine, lactate dehydrogenase, bone marrow (BM) disease, prior stem cell transplant (SCT), prior CAR, ejection fraction (EF), and C-reactive protein ($p=0.0002$, $p=0.003$, $p=0.02$, $p=0.02$, $p=0.04$, $p=0.06$, $p=0.08$, $p=0.09$; respectively). Six of these univariate features were also selected by LASSO for multivariable prediction of severe CRS including age, creatinine, prior SCT, prior CAR, BM disease, and EF, and LASSO additionally identified hemoglobin as a predictive variable.

Conclusion: These initial findings demonstrate the feasibility of developing the CAR-CI using machine learning methodologies that utilize pre-infusion variables to identify risk for severe CRS. The next steps will involve model cross-validation of the seven features identified by LASSO, assignment of high versus low-risk scores based on receiver operating characteristic curves, followed by external model validation in a second pediatric cohort. Future efforts will be directed towards building additional LASSO models to predict other key outcomes (e.g., remission rates, neurotoxicity, and survival).

Disease-Specific, Transplant-Related

1. Title: CD34 Selected Haploidentical Stem Cell Transplant for Severe Combined Immunodeficiency Secondary to pre-T cell Receptor Maturational Arrest in a Patient with Multiple Congenital Anomalies

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Theme: Disease-Specific, Transplant-Related

Background: Severe combined immunodeficiency (SCID) is a relatively rare immune deficiency with well-known mutation dependent phenotypes. SCID is diagnosed by measuring T cell receptor excision circles (TRECs) formed by the genetic rearrangement of the T cell receptor (TCR). Here we describe a case of NK+/B Cell+ SCID with low T cells, without known phenotypically associated genetic aberrations.

Case: Our patient was a 2-month-old male born at 38 weeks to a 28yo G1P1 mother with a history of pregestational diabetes. At birth he was found to have horseshoe kidney, congenital renal calculus, bony cranial abnormalities, multiple vertebral anomalies, mild right ventricular dilation, and abdominal muscle wall defects. Newborn screening showed low TRECs confirmed with a second newborn screen. Lymphocyte subsets showed normal NK and B cells with low T cells, with a chimerism ruling out maternal engraftment of T cells. Thymic shadow was absent on chest x-ray and ultrasound. Whole exome sequencing was negative. Microarray showed a very small heterozygous deletion on chromosome 16, however this was non-contributory. A TCR maturation defect similar to pre-TCR-alpha deficiency was diagnosed using artificial thymic organoid testing. His mother's T cells were negative for this defect in TCR maturation.

At 4 months old he underwent a haploidentical CD34 selected peripheral blood stem cell transplant. His course was complicated by pulmonary hypertension, respiratory distress, hyperphosphatemia, hypocalcemia, hypoparathyroidism, and severe xeroderma. He engrafted neutrophils on D+13, platelets on D+34, and had a 100% peripheral blood donor chimerism at D+30. He was discharged on D+93 but re-admitted on D+103 due to NG tube dysfunction. During this admission he had an episode of Staphylococcus epidermidis bacteremia. Donor chimerism on D+126 was found to have decreased to 5%, indicating secondary graft failure. Lymphocyte subsets within the first 100 days consistently showed low T cells.

Discussion: Testing to confirm the presence or absence of thymic tissue was not available at the time of our patient's SCID diagnosis, however we postulate that a lack of thymic tissue could have contributed to his inability to fully engraft and ultimately led to secondary graft failure. He ultimately reverted to his baseline immune-phenotype and was continued on infectious prophylaxis. He is currently awaiting whole genome sequencing and possible thymic transplant referral in preparation for repeat stem cell transplant. We highlight this case due to his complex congenital anomalies, lack of identifiable genetic defect, complicated clinical course, and graft failure in the setting of probable athymia.

2. Title: TRANSPIRE: Lung injury in a longitudinal cohort of pediatric hematopoietic stem cell transplant patients

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Theme: Disease-Specific, Transplant-Related

Background: Hematopoietic stem cell transplantation (HSCT) is an effective treatment for malignant and non-malignant diseases in pediatric patients but comes with significant risk of short and long-term toxicity. Pulmonary morbidity affects as many as 25% of children receiving transplant. Better diagnosis and treatment of pulmonary complications are urgently needed as survival after HSCT improves.

Objective: To describe a longitudinal, prospective cohort of allo-HSCT recipients with lung injury.

Methods: TRANSPIRE is a multi-institutional prospective, uniformly screened cohort of pediatric and young-adult patients receiving allogeneic-HSCT (allo-HSCT). Through the collection of biological samples and clinical and research pulmonary assessments, we aim to identify specific risk factors and mechanisms of lung injury.

Results: We have enrolled 229 patients across all sites since study opening in September 2021. The most common indication for allo-HSCT is malignancy (n=82, 40.6%). Median age at HSCT was 8.2 years old (range 0.2-24.8 years). Across all sites we have collected 94.5% of baseline blood samples, 93.6% of day 30 samples and 90.2% of day 100 samples. To date, we have identified 124 pulmonary injury related events across all sites. The most common events included: new viral pathogen identified on nasopharyngeal testing (n=44, 35.4%), clinically significant oxygen supplementation (n=33, 26.7%), and radiologic evidence of pulmonary injury (n=18, 14.5%). We have 108 (95.4%) eligible patients with baseline PFTs, 69 eligible (85.5%) patients with day 100 PFTs and 21 (95.2%) eligible patients with 1-year PFTs. Three sites are currently performing FO. We have 60 (84%) patients who have completed FO at baseline, 32 (82%) patients at day 100 and 14 (74%) patients at 1-year post-HSCT. We have three sites performing MBW. Fourteen (62.3%) patients have completed MBW testing at baseline, 13 (62.3%) patients at day 100 and 3 (75%) patients at 1-year post-HSCT. Three sites are performing home spirometry, and we have 37 patients who were eligible and initiated at the day 100 timepoint. Twenty-two (81.4%) patients have completed home spirometry requirements, and 3 (11.1%) patients are still actively completing study requirements. Currently, one site is actively performing ^{129}XeMRI imaging. Fifteen patients have completed at least one ^{128}XeMRI imaging protocol. We have completed 12 (80%) at baseline, 11 (73.3%) at day 100 and 6 (40%) at the one-year post-HSCT time point.

Conclusions: We have enrolled a large number of pediatric and young adult allo-HSCT patients on this prospective, multi-institutional study. We are currently 16.9% of our original target enrollment (1350 patients total). Completed research pulmonary assessments and imaging are currently being analyzed and will be compared to clinical testing to determine optimal imaging and pulmonary function metrics for the diagnosis and treatment of pulmonary injury in this patient cohort.

3. Title: Breathing New Life into an Old Problem: Pulmonary Complications after Autologous Hematopoietic Stem Cell Transplant

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Theme: Disease-Specific, Transplant-Related

Background: Pulmonary complications are a major cause of morbidity and mortality in children undergoing autologous and allogeneic hematopoietic stem cell transplant (HSCT). Pulmonary

complications are likely underreported in pediatric patients. Our goal was to describe the incidence and spectrum of pulmonary complications after autologous HSCT in a large cohort of pediatric patients.

Methods: We completed a retrospective cohort analysis cohort study evaluating a consecutive cohort of pediatric patients who completed autologous HSCT at the University of Minnesota (UMN) and Cincinnati Children's Hospital Medical Center (CCHMC) between January 2012 and June 2022. Patient records were reviewed to determine the incidence of non-infectious and infectious pulmonary complications after autologous HSCT.

Results: We identified 252 patients who completed autologous HSCT at UMN and CCHMC. Fifty-three (29.4%) patients had abnormal findings in their chest imaging prior to their first autologous HSCT. Only 71 (31.5%) patients had baseline pulmonary functional testing (PFT), with the most common reason for not completing PFTs due to age. Twenty-six (11.9%) of patients had any baseline pulmonary issues preceding first transplant. The majority of patients had no abnormal findings (n=106, 50.2%) seen on baseline pulmonary imaging before first transplant. Twenty-eight (11.1%) patients required intensive care unit admission for respiratory failure and distress. Mechanical ventilatory support was required by 26 (10.3%) patients. Pulmonary hypertension was identified in 9 (3.6%) of patients with all cases being diagnosed after day 100 from last transplant. Diffuse alveolar hemorrhage was identified in 7 (2.8%) patients, with the majority of cases identified as a late complication (n=5, 71.4%). Cryptogenic organizing pneumonia was identified in five (2%) of patients and idiopathic pneumonia syndrome seen in four (1.6%) of patients. Pulmonary veno-occlusive disease was diagnosed in 13 (5.2%) of patients with all cases occurring in the early period. We identified numerous respiratory viral pathogens within this cohort. Rhinovirus was the most frequent viral pathogen diagnosed (n=44, 34.6%), followed by influenza (n=14, 11%). Bacterial infections were less common in this cohort (n=8, 6.2%). Fungal infections were frequent in the early period after last transplant (n=18, 31.6%).

Conclusions: Pulmonary complications are common in pediatric patients after autologous HSCT. Patients receiving auto-HSCT require consistent routine baseline and follow-up pulmonary surveillance after auto-HSCT, similar to patients who complete allogeneic-HSCT.

4**. Title:** Measurement of respiratory system function by airwave oscillometry (AOS) in a cohort of children undergoing hematogenous stem cell transplant (HSCT)

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Theme: Disease-Specific, Transplant-Related

BACKGROUND. Respiratory complications are common following HSCT in children. The most sensitive tests to evaluate these complications are unknown. Airwave oscillometry has been proposed to be a sensitive test of disorders of the mechanics of the respiratory system, including large and small airway dysfunction and elevated respiratory system stiffness due to pulmonary parenchymal or chest wall damage.

OBJECTIVE: We performed oscillometry (Tremoflo©C100, Thorasys, Montreal, CA) at baseline and following HSCT in a cohort of 56 children at 3 of 4 centers to date: Cincinnati Children's Hospital, Children's Hospital of Philadelphia, University of Minnesota Children's Hospital, and Boston Children's Hospital.
METHODS. Children between the ages of 4 and 21 years were eligible for study. Following ERS 2020 Guidelines, the following parameters were measured between 5 and 37 hz: R5 (measure of total resistance), R5-R19 (measure of peripheral airway obstruction), X5 (measure of respiratory system stiffness), and AX (measure of stiffness and small airway function). Results were compared to 1. predicted values of Ducharme (2019) and 2. a cohort of 80 CHOP control subjects. A result was considered abnormal if it deviated from the predicted Ducharme mean by > 1.64 standard deviations.
RESULTS. AOS was well tolerated, and technically interpretable in most children. Of 92 separate studies in the first 56 children studied, the overall number (percentage) of abnormal results when compared to Ducharme normal values were as follows: R5: 5(5%); R5-R19: 1 (1%); X5: 7(8%); AX: 12 (13%). When AX data from studies pre-transplant were compared to studies post-transplant there were no clear changes in the proportion of abnormal studies by $\Psi 2$ test. However the power of this analysis may not have been sufficient in this early phase of the study. The proportion of abnormal reactance tests (X5 and AX) (10%) was significantly greater than the proportion of abnormal resistance tests (R5 and R5-R19) (3%) ($p < 0.005$ by $\Psi 2$ test).
CONCLUSIONS. We provide an overview of a multicenter study of respiratory oscillometry in a cohort of children undergoing HSCT. We conclude: 1. AOS is well tolerated and simple. 2. While most children fell within the Ducharme predicted normal range, there were clear outliers when assessing respiratory system stiffness and small airway function. 3. Different outcome measures have different degrees of ability to detect abnormalities of respiratory mechanics. Outcomes that include measures of respiratory system stiffness (X5, AX) may have better ability to screen abnormalities than measures of resistance (R5, R5-19) alone. 4. Comparison with biologic controls from the same laboratory or multicenter study are an important part of confirming abnormalities in a HSCT cohort and may be more sensitive in detecting abnormalities than comparison with published values alone.

5**. Title:** Vulnerable Vessels: Microvascular Disease in Post-Transplant AYA Patients with Diamond-Blackfan Anemia

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Theme: Disease-Specific, Transplant-Related

Background: Diamond-Blackfan anemia (DBA) is an inherited disorder of erythroid hypoplasia necessitating chronic transfusions and an increased risk for myelodysplastic syndrome (MDS). Hematopoietic stem cell transplant (HSCT) can be curative, though not without risks. Few publications

have reported on severe transplant-related complications among DBA patients, in particular microvascular disease and transplant-associated thrombotic microangiopathy (TA-TMA).
Objective: This case series presents four adolescent and young adult (AYA) patients who underwent HSCT either for transfusion dependence or MDS, three of whom developed severe microvascular disease.
Methods: A retrospective chart review was performed for these patients cared for at Nemours Children's Hospital – Delaware, in Wilmington, DE, USA.
Results: Patients 1 and 2 are fraternal twin brothers with DBA and MDS who received 10/10 fully matched unrelated donor stem cell transplants. They did not have an identified genetic cause of their erythroid hypoplasia. Patient 1 was transfusion dependent prior to HSCT while patient 2 was not. Patient 1 received defibrotide prophylaxis to prevent sinusoidal obstructive syndrome (SOS) and had an uncomplicated clinical course post-transplant. Patient 2 developed severe SOS treated with defibrotide, steroids, and a portosystemic shunt; he subsequently developed gastrointestinal bleeding requiring embolization thought to be secondary to TA-TMA. Patient 2 met criteria for a diagnosis of TA-TMA with anemia, thrombocytopenia, elevated LDH, elevated sC5b-9, and schistocytes on peripheral blood smear. He was treated with eculizumab and ultimately expired secondary to pulmonary disease. Patients 3 and 4 are identical twin sisters with transfusion-dependent DBA who enrolled in the ASCENT trial and received 9/10 and 8/10 mismatched unrelated donor transplants, respectively. These sisters shared a translocation on the RPS19 gene (c.185G>A p.R62Q). Both patients met criteria for TA-TMA given hypertension, anemia, thrombocytopenia, proteinuria, elevated LDH, and elevated sC5b-9. TA-TMA treatment with eculizumab was followed by narsoplimab administration due to an unsatisfactory clinical response. Patient 3 developed acute graft-versus-host disease of the gastrointestinal tract prior to her TA-TMA diagnosis, and patient 4 suffered from multiple viral infections/reactivations surrounding her TA-TMA diagnosis which culminated in death from pulmonary disease.
Conclusion: We present four AYA patients who underwent HSCT for DBA. Three patients (75%) developed severe microvascular disease and two (66%) succumbed to this complication. In addition, genetic mutations were only identified in 50% of the patients. These cases raise the question of whether an underlying vascular difference in DBA patients may predispose to the development of microvascular complications after HSCT, a question which merits further research.

6. Title: Lower levels of the vitamin A transporter serum amyloid A1 (SAA1) are associated with improved HSCT outcomes in children and young adults.

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Theme: Disease-Specific, Transplant-Related

Background: We have previously shown in a randomized controlled trial (RCT) that vitamin A supplementation can reduce acute and chronic graft-versus-host disease (GVHD). Serum amyloid A1 (SAA1) is a vitamin A transporter protein that delivers vitamin A during periods of stress such as hematopoietic stem cell transplantation (HSCT).
Objective: We evaluated the role of SAA1 in HSCT.
Design/Method: Plasma SAA1 levels were measured by ELISA (R&D Systems) in a consecutive cohort of 130 children and young adults receiving allogeneic HSCT. SAA1 levels were measured longitudinally at baseline (prior to the start of the preparative regimen) and days 0, +7, +14, +21, +42, and +100. In a

separate experiment, we performed SAA1 immunohistochemistry (Fisher Scientific, MAB30191SP) on an independent cohort of patients with (n=10) and without (n=10) gastrointestinal (GI) GVHD.
Results: SAA1 levels were dynamic with a marked peak at day +7, nadir between days +21 and +42, and further increase by day +100. Importantly, SAA1 levels were associated with HSCT outcomes. Higher SAA1 levels conferred inferior outcomes as early as day +7 (HR 2.48, p=0.001) and day +14 (HR 2.04, p=<0.001), however the impact on non-relapse mortality was also seen as late as day +100 (p=<0.0001). Higher SAA1 levels at day +7 (HR 1.62, p=0.017), day +14 (HR 1.42, p=0.007), and day +42 (HR 2.13, p=0.005) were seen in patients with thrombotic microangiopathy (TMA), with a higher cumulative incidence (CI) of TMA seen in patients with SAA1 levels above the median at day +7 (p=0.005) and day +42 (p=0.04). Higher SAA1 levels at baseline (HR 1.53, p=0.061), day +21 (HR 1.46, p=0.055), and day +100 (HR 7.90, p=0.049) were associated with acute GVHD. SAA1 IHC revealed that SAA1 was strongly upregulated in the GI epithelium of patients with acute GI GVHD, suggesting an active role of SAA1 in GVHD pathogenesis. Higher SAA1 levels at day +21 were associated with chronic GVHD (HR 1.57, p=0.04), with a higher CI of chronic GVHD in patients with SAA1 levels above the median at day +100 (p=0.03).
Conclusion: Our data show a significant impact of SAA1 levels on both early and late outcomes of HSCT. In our RCT, patients that received vitamin A supplementation had lower SAA1 levels, suggesting an easy way to manage SAA1 and improve HSCT outcomes. Additional studies are underway to elucidate the role of SAA1 during HSCT.

This research was performed at Cincinnati Children's Hospital in Cincinnati, OH, USA.

7. **Title:** Clinical outcomes of pediatric patients with high-risk neuroblastoma following tandem transplant

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Theme: Disease-Specific, Transplant-Related

Background: Treatment for high-risk neuroblastoma (HRNB) typically includes a multimodal approach with tandem high-dose chemotherapy and autologous stem cell transplant (ASCT). Despite the COG0532 trial showing improved event-free survival (EFS) with tandem transplant compared to single transplant, there is still a lack of comprehensive knowledge about the long-term outcomes and toxicities of this regimen.
Objective: Define the treatment related outcomes and toxicity of tandem ASCT for patients with HRNB.
Methods: We conducted a 14-center retrospective review of records for pediatric patients with HRNB who were to receive tandem ASCT between January 2014-June 2021. Data including disease information, Grade 3 or higher organ toxicities (per CTCAE v5.0) and transplant-related outcomes including relapses and death were collected. We report our preliminary analysis on a subset of 196 pediatric HRNB patients and describe their clinical outcomes.
Results: In a study of 196 patients with HRNB, 120 patients (61%) were male with a median age at diagnosis of 38.6 months (range 4-455). Neuroblastoma was the predominant histology in 95% of cases. MYCN was amplified in 40% (78 patients), had a gain of 3-4 copies in 3% (6 patients), non-amplified in 53% (103 patients) and unknown in 5% (9 patients). At diagnosis, 91% (178 patients) had metastatic disease.

ASCT #1 with cyclophosphamide and thiotepa conditioning was performed at a median age of 45 months (range 9.6-464.3). Eleven percent (22 patients) experienced bacteremia, 1 patient developed thrombotic microangiopathy (TMA), 4% (7 patients) had veno-occlusive disease (VOD), and 12% (23 patients) required intensive care unit (ICU) admission during ASCT #1. Respiratory failure necessitating intubation or non-invasive mechanical ventilation occurred in 4.1% (8 patients). One patient had an early relapse on Day 124.
Out of 195 patients, 188 underwent ASCT #2 with carboplatin, etoposide and melphalan at a median age of 48.3 months (range 11.4-466.3). In ASCT #2, 15% (28 patients) experienced bacteremia, TMA was reported in 15% (28 patients), VOD in 8.5% (16 patients) and 13% (25 patients) required ICU admission. Respiratory failure was seen in 19% (36 patients), with 11% (20 patients) requiring endotracheal intubation. By day 100 post-transplant, 5% (9 patients) had died, mainly due to respiratory or multiorgan failure. Disease relapse was observed in 16% (28 patients) of the remaining 179, with a fatality rate of 9.5% (17 patients).

Conclusion: The cumulative toxicity of tandem ASCT may be underappreciated and requires further prospective investigation. Improvements in institutional screening practices may prevent excessive organ toxicity.

8. Title: Clinical implications of the interactions between total body irradiation and central nervous system disease in pediatric acute myeloid leukemia.

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Theme: Disease-Specific, Transplant-Related

Background: The clinical ramifications of previous central nervous system (CNS) involvement in children with acute myeloid leukemia (AML) undergoing hematopoietic cell transplantation (HCT) remain inadequately elucidated. Of particular interest is the role of total body irradiation (TBI) in children with CNS-positive AML, considering the presumed advantages in enhanced tissue penetration, juxtaposed with well-established long-term late effects.

Objective: To bridge this knowledge gap, we conducted an analysis of pediatric AML patients in the Center of International Blood and Marrow Transplantation Research (CIBMTR) registry.

Design/Methods: The study dataset was obtained from the CIBMTR data repository. Patients age ≤21 years old undergoing an initial allogeneic HCT with myeloablative conditioning for de novo AML in the first or second complete remission between 2008 and 2016 and who provided consent for research were included. Patients with mismatched related donor transplant, non-calcineurin inhibitor graft-versus-host disease (GVHD) prophylaxis regimens, missing disease site data, or those with non-CNS extramedullary disease were excluded. Patients were categorized as CNS-positive or -negative AML based on the disease status at diagnosis (AML-CNS(+) and AML-CNS(-), respectively). Cox regression model and Fine Grey methods were employed to quantify the effects of TBI and CNS disease on key HCT outcomes ($p < 0.05$).

Results: The study cohort comprised 550 pediatric de novo AML patients; 25% (n = 136) of whom had CNS involvement. CNS disease was more prevalent in patients aged 0-3 years, those with favorable cytogenetic risk, and those who achieved second complete remission status prior to HCT. In comparison to AML-CNS(-), AML-CNS(+) demonstrated a lower relapse rate (hazard ratio [HR]: 0.51, 95% confidence

interval: 0.34-0.77) but comparable disease-free survival (DFS) and overall survival (OS) (p values 0.10 and 0.20, respectively). In the AML-CNS(+) cohort, the use of TBI based regimens were associated with lower relapse rate, but with increased risks of non-relapse mortality and grade 3-4 acute GVHD (p values 0.001 and 0.04, respectively). Both CNS(+) and (-) cohorts exhibited an association between TBI use and elevated risks of Grade 2-4 acute GVHD, bacterial infection, and endocrine dysfunctions.

Conclusion: In this cohort of pediatric patients with de novo AML, no associations were revealed between CNS involvement at diagnosis and unfavorable outcomes. Regardless of CNS disease status, TBI-based conditioning regimens did not demonstrate superior disease-free survival (DFS) or overall survival (OS) compared to non-TBI regimens. However, the use of TBI-based conditioning regimens was associated with an increase in both acute and late comorbidities.
Title: Validation of Elevated D-Dimer as a Prognostic Marker in Children with Transplant- Associated Thrombotic Microangiopathy Following Hematopoietic Cellular Therapy
Joel K Ofori, Satheesh Chonat, Muna Qayed, Kirsten M Williams, Taylor Fitch, Elyse Bryson, Kathleen Spencer, Adrianna Westbrook, Michelle L Schoettler

9. Title: Validation of Elevated D-Dimer as a Prognostic Marker in Children with Transplant-Associated Thrombotic Microangiopathy Following Hematopoietic Cellular Therapy

Joel K Ofori, Satheesh Chonat, Muna Qayed, Kirsten M Williams, Taylor Fitch, Elyse Bryson, Kathleen Spencer, Adrianna Westbrook, Michelle L Schoettler

Theme: Disease-Specific, Transplant-Related

Introduction:
Transplant-associated thrombotic microangiopathy (TA-TMA) is a common, severe complication of hematopoietic cellular therapy (HCT) with significantly high morbidity and mortality rates even post-treatment. We recently identified that elevated D-dimer (>574 ng/dL) was associated with a significantly increased risk of multi-organ dysfunction (MOD) and non-relapse related mortality (NRM) (Schoettler et al., AJH 2024). Our objective was to validate these findings and cut-off point in a second cohort of pediatric autologous and allogeneic HCT recipients.
Methods:
In this IRB approved prospective study, serial autologous HCT recipients with a diagnosis of TA- TMA (Jodele Criteria) were enrolled from August 2019 – December 2023 and allogeneic HCT recipients from August 2022 – December 2023. The sensitivity, specificity, positive predictive value, and negative predictive value of elevated D-dimer and MOD and NRM were calculated. Patients who developed MOD prior to TA-TMA diagnosis were excluded from predictive models.
Results:
Twenty-five patients were diagnosed with TA-TMA at a median of 26 days after HCT (range 0- 301 days), of whom 5 had autologous HCT and 20 allogeneic. Of those with TA-TMA, 21/25 (84%) developed MOD, with 11/21 (52%) developing MOD at a median of 9 days (range 1-100 days) after TA-TMA diagnosis. The estimated cumulative incidence of MOD in those with high D- dimer levels 30 days after TA-TMA diagnosis was 83% (95% CI 40.3-96.4) versus 0% in those with low D-dimer values (p=0.02). The sensitivity of elevated D-dimer levels at diagnosis predicting later MOD was 100%, specificity 91.67%, PPV 75.00%, and NPV 100%. The estimated NRM 100 days after TA-TMA diagnosis was 28.9% (95% CI 9.3- 50.4) in those with elevated D-dimer and 0% in those with lower levels (p=0.32). High D-dimer had a sensitivity of 100%, specificity 27%, PPV 15.8%, and NPV 100% for predicting NRM.
Discussion:

In a cohort including both autologous and allogeneic HCT pediatric recipients, we have validated elevated D-dimer as a poor prognostic marker. Using our previously determined cut- off point, the sensitivity and specificity for predicting MOD were both >90%, indicating excellent performance to predict severe disease. While there were no significant differences in NRM in the high and low D-dimer group, consistent with prior literature, overall mortality rates were lower in this study which included autologous HCT recipients. Thus, the inability to detect statistical differences may be due to limited power in a smaller sample size. Multi-institutional studies including adults to further investigate the prognostic implications of D-dimer, a widely available and inexpensive test, are warranted.

Supportive Care

1**. Title:** Administration of human milk oligosaccharide (2'-fucosyllactose) reduces dysbiosis and increases short chain fatty acids in children and young adults following HSCT: a prospective, single-center study.

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Theme: Supportive Care

Introduction: Gut dysbiosis is implicated in the pathophysiology of graft-versus-host disease (GVHD). We have previously shown that human milk administration favorably modifies the gut microbiome and metabolome by virtue of human milk oligosaccharides (HMOs) that are known prebiotics.
Objective: We evaluated the utility of oral supplementation of the most abundant HMO, 2-fucosylactose (2'-FL), in children and young adults undergoing allogeneic HSCT.
Design/Method: We performed a prospective, single-center study to assess the safety and feasibility of 2'-FL administration in HSCT patients. Patients 0-30 years of age received oral 2'-FL supplementation once daily (according to an age-based dosing regimen) from 1 week prior to the start of their preparative regimen until day +30 following HSCT. Stool samples were collected at baseline and days +7, +14, and +28 for microbiome and NMR-based metabolomic analyses. Urine 3-indoxyl sulfate (3-IS) was measured by NMR spectroscopy prior to HSCT and at day +7 as a secondary measure of dysbiosis, with low urine 3-IS levels associated with dysbiosis1. An independent cohort of age- and prep-matched HSCT recipients with available stool samples in our institutional biorepository served as controls.
Results: Twenty-five patients were prospectively enrolled and received oral, once daily 2'-FL supplementation. Twenty independent age- and prep-matched controls were selected for comparison. No patients experienced gastrointestinal (GI) intolerance or developed bloodstream infections from a presumed GI etiology during 2'-FL administration. One 2'-FL patient developed acute skin GVHD and no 2'-FL recipients developed acute GI GVHD in comparison to five control patients that developed acute GVHD (GI, n=3; skin, n=5; liver, n=1) (p=0.07).
Preliminary analysis of a limited subset of patients demonstrated increased fecal acetate from baseline to day +7 in 2'-FL recipients (p=0.02). Additionally, fecal hydroxyphenylacetate (p=0.02), fumarate (p=0.02), and phosphocholine (p=0.006) were higher at day +7 and fecal isobutyrate was higher at day +28 (p=0.08) in 2'-FL recipients compared to controls, reflective of favorable fecal metabolomic profiles. Urine 3-IS was higher at day +7 in 2'-FL patients compared to controls (p=0.003), suggestive of reduced

dysbiosis in 2'-FL recipients. Microbiome studies are ongoing, but preliminary analyses show preserved Shannon diversity in 2'-FL recipients longitudinally.
Conclusion: Oral 2'-FL supplementation reduces dysbiosis and increases short chain fatty acid production in children and young adults following HSCT. Ongoing phase II studies of 2'-FL supplementation are in progress.
This research was conducted at Cincinnati Children's Hospital in Cincinnati, OH, USA.
References: Weber et al., Blood, 2015.

2. **Title:** Feasibility of Home Spirometry for Early Identification of Pulmonary Dysfunction after HSCT in the TRANSPIRE Research Study

Christopher Towe, Jessica Patti, and Carrie Stevens, Kasiani Myers, Jane Koo, Eleanor Cook, Richard Cooper, Matthew Abts, K. Scott Baker, Sheri Ballard, Fernando A. Urrego, Alexis Melton, Sana Noori, Jason C. Woods, Stella M. Davies, Samuel B. Goldfarb

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Theme: Supportive Care

Background: Bronchiolitis obliterans syndrome is a devastating complication following hematopoietic stem cell transplant (HSCT) which can be treated once detected. Spirometry offers the opportunity for earlier detection of lung function decline in at risk patients, but many patients do not live near their HSCT center and may not be able to return for frequent spirometry monitoring.

Objective: As part of the TRANSPIRE research study, we are evaluating the feasibility of home spirometry as a remote monitoring strategy in pediatric and young adult HSCT recipients.

Methods: TRANSPIRE is an ongoing multicenter prospective cohort study of pulmonary complications in pediatric and young adult HSCT recipients. Home spirometry is being studied at three sites in eligible participants, defined as those with the ability to do acceptable and repeatable, or at least consistently usable, spirometry by American Thoracic Society standards in the clinical pulmonary function laboratory. Subjects were provided with a home spirometer (GoSpiro, Monitored Therapeutics, Dublin, OH) that connects to their blue tooth capable device via a free proprietary app and are trained in its use. Data is transmitted electronically directly to a HIPAA compliant server and then downloaded by study staff. If a subject was noted to not be performing home spirometry consistently, study staff reached out and provided reminders. Home spirometry was initiated at Day 100 post-HSCT and actively monitored for 6 months. Data collected for this interim feasibility analysis included patient demographics and the frequency of home spirometry use.

Results: Forty-seven subjects were eligible for home spirometry across all 3 sites, and 37 subjects were successfully initiated with a mean age of 14.9 years, 26 (70%) are male. Of those, one subject died, 2 electively withdrew, and 12 are still actively being monitored. Of the remaining 22 (59%) subjects who have completed the study monitoring period, 21 (95%) had at least one use during month 1, 11 (50%) during month 3, and 10 (45%) during month 6. In subjects with at least one use during the month, they used it on average 4.1 days during month 1, 3.5 days during month 3, and 3.1 days during month 6.

Conclusions: Home spirometry monitoring of pulmonary function is feasible in pediatric post-HSCT patients with adherence rates similar to other home interventions in medically complex children. However, further efforts directed towards increasing longitudinal adherence rates are necessary.

3. Title: Avascular Necrosis Following Hematopoietic Cell Transplantation in Pediatric Patients with Sickle Cell Disease

Authors: Robert Lisac, Elizabeth Stenger, Ann Haight, Benjamin Watkins and Kirsten Williams and Muna Qayed
Institution: Aflac Cancer & Blood Disorders Center at Children's Healthcare of Atlanta, Emory University, Atlanta, Georgia, United States

Theme: Supportive Care

Background: Avascular necrosis (AVN) is a common morbidity of sickle cell disease (SCD) due in part to recurrent vaso-occlusion and bone ischemia. Hematopoietic cell transplantation (HCT) is a curative treatment for SCD and reduces vaso-occlusive events. However, limited literature on AVN post-HCT for SCD exists. We hypothesized that pediatric patients undergoing HCT for SCD have stabilization of pre-existing AVN and limited development of de novo AVN post-HCT, except when exposed to high-dose steroids for the treatment of graft-versus-host disease (GVHD).
Objectives: To describe the progression of AVN following HCT for pediatric SCD and examine the association of post-HCT steroid exposure with de novo AVN.
Design/Method: In this IRB approved retrospective study, consecutive pediatric recipients of HCT for SCD at a single institution between 2011 to 2019 were included and analyzed for appendicular AVN. One patient with graft failure within 100 days was excluded.
Results: Seventy eligible patients were identified with a median age of 8 years old (range 2-20) at HCT. Median follow-up post-HCT was 5 years (IQR 3-7). Seven (10%) patients had pre-HCT AVN; 2 had progression of pre-existing AVN neither of whom were exposed to steroids post-HCT, 1 developed de novo AVN having received 392 mg/kg prednisone equivalents (PE) post-HCT, and 4 without progression or de novo AVN received a median of 5 mg/kg PE (range 0-44) post-HCT. Five (8%) patients developed de novo AVN post-HCT without pre-HCT AVN and received a median of 175 mg/kg PE (range 62-678) post-HCT. Steroid exposure post-HCT was significantly higher in patients with de novo AVN (median: 243 mg/kg PE, IQR 117-372) compared to those without de novo AVN (median: 0 mg/kg PE, IQR 0-5; $p<0.001$). Among all 12 patients with AVN, the median number of joints involved was 3 (range 1-6). Median time to first de novo AVN was 9 months (IQR 4-20) post-HCT and 3/6 patients developed de novo AVN in >3 joints. Five out of 8 patients with progressive or de novo AVN required at least 1 surgical intervention and 2/5 required >2 with a median time to first surgical intervention 26 months (IQR 24-43) post-HCT.
Conclusion: While the effect of HCT on pre-existing AVN in pediatric patients with SCD remains unclear, our findings suggest steroid exposure is a significant risk factor for the development of de novo AVN post-HCT. This study highlights the need to mitigate steroid exposure post-HCT and utilize steroid-sparing agents for the treatment of GVHD to avert this HCT-related morbidity.

4. Title: HSCT Support Resource Delivery Gaps: An Interview Based Study
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Theme: Supportive Care

Background: Hematopoietic stem cell transplantation (HSCT) is a complex medical treatment associated with a lengthy inpatient stay and significant long-term side effects, lasting for months to years. The transplant process takes an enormous financial, mental, physical, and emotional toll on the entire family, as even siblings report PTSD-like symptoms. The healthcare system struggles to connect families to support resources as both awareness and sufficient health literacy are required to take advantage of the available opportunities. In 2022, We initiated a study to identify gaps in our support delivery system to understand how families discover, utilize, and compensated for these gaps.
Objective: We hypothesize that gaps exist in the system providing support to and that families respond to these gaps creatively, developing personal strategies to fulfill family needs.
Methods Interviews of primary caregivers of patients undergoing HSCT were performed at Cincinnati Children's Hospital Medical Center (Cincinnati, Ohio, USA), a 654-bed academic pediatric hospital. This study was deemed exempt under IRB 2022-0646. A convenience sample of adult patients and caregivers of pediatric patients were approached to participate in a single interview during their inpatient stay. The interviewer used a script to guide the conversation through a series of inpatient topics. All interviews were conducted in person on the inpatient floor and recorded using a digital audio recorder. Recordings were transcribed and analyzed by the study team for thematic content and illustrative quotes. Each interview was coded by at least one team member and then reviewed by another. Team conversation resolved any differences.
Results: 11 interviews (2 patients, 9 caregivers; 3 male, 8 female; mean age: 38) were conducted between November 2022 and August 2023. 90% of interviews referenced at least one delivery system failure where existing resources were not communicated to the family and, when provided, were often offered in a format least preferred by families (as written materials). Families did mitigated gaps in support, often in creative ways, with strategies to improve sleep being the most reported support domain.
Conclusions: Our interviews offer evidence supporting our hypothesis that gaps in our support delivery system do exist, and many families faced with these gaps are finding creative solutions on their own. Future work will continue the analysis of interview response patterns and begin the work to improve both the support materials available and the delivery system.

5. Title: Chronic graft versus host disease adversely impacts school performance and quality of life in children and young adults.

Theme: Supportive Care

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Introduction: Chronic graft-versus-host disease (cGVHD) adversely affects return to work for adult allogeneic hematopoietic stem cell transplant (HSCT) patients, but no data exist on children with cGVHD returning to school.

Objective To evaluate the impact of cGVHD on broad aspects of education in children and young adults.

Methods: We enrolled 40 allogeneic HSCT patients of school/college age prospectively and administered a 42-item patient/parent reported questionnaire investigating academic performance after HSCT, targeting grades, attendance, special accommodations, and social-emotional aspects focusing on peer and educator relationships. Responses were compared between patients with and without cGVHD.

Results: Twenty patients had cGVHD while 20 age and gender matched allogeneic HSCT patients without cGVHD served as controls. Two cGVHD patients did not return to school due to cGVHD, while all controls resumed/commenced school post-HSCT. Seven cGVHD patients missed ≥4 days of school/month post-HSCT compared to 0/20 controls (p=0.004). Seven cGVHD patients subjectively reported not performing at expected grade level compared to 2 controls (p=0.05). Likert-scale based questions assessing the patients' interaction at school along with peer and teacher support, identified comparable responses towards school, teachers and friends between both groups. However, in response to the statement "My teachers know I went through a bone marrow transplant", more cGVHD patients disagreed than controls. Additionally, 4 cGVHD patients highlighted lack of awareness of cGVHD among teachers and school nurses, identifying an area of intervention. No cGVHD patients self-reported positive experiences at school compared to 9/20 controls. Three cGVHD patients reported negative psychological effects due to inability to continue school or selected area of study, while no controls experienced similar challenges. Open-ended questions regarding interactions with classmates and teachers identified more unsupportive statements experienced by cGVHD patients compared to controls. These statements involved themes of bullying, identifying physical limitations and negative comments on physical appearance.

Fifteen patients in cGVHD cohort had severe GVHD with predominant ocular (n=12) and skin (n=13) involvement. Profound barriers specific to cGVHD were appreciated with cGVHD respondents identifying an average of 3 concomitant barriers (range 1-7) related to physical appearance, ocular GVHD, difficulty with concentration and hand contractures despite comparable 504 plans/individualized education plans between cGVHD (n=6) and controls (n=4), highlighting a gap in services. Four cGVHD patients identified clothing related barriers, indicating that textural challenges and temperature dysregulation affected ability to participate in school.

Conclusions: The social-emotional impacts of cGVHD on school experiences are extraordinary and underappreciated, highlighting several specific areas of intervention.

Funding: Incyte Ingenuity Award in GVHD.

6. Title: Low Vitamin C levels are associated with Transplant-associated Thrombotic Microangiopathy

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Theme: Supportive Care

BACKGROUND
Vitamin C is an essential nutrient known for its antioxidant properties. Additionally, Vitamin C has also been shown to play a role in maintaining immune and endothelial function and could impact outcomes in allogeneic hematopoietic stem cell transplant (HSCT).
OBJECTIVE
To investigate the association between blood vitamin C levels and transplant-associated thrombotic microangiopathy (TMA).
DESIGN/METHOD
We performed a retrospective chart review of patients who underwent HSCT at Cincinnati Children's Hospital Medical Center (CCHMC) in Cincinnati, Ohio, USA from 2020 to 2022 and had vitamin C levels measured before or up to 3 months after HSCT. The incidence of TMA including assigned risk stratification was also collected. In patients where vitamin C levels were obtained after HSCT, the incidence of TMA was collected if it occurred after timepoints of vitamin C levels.
RESULTS
Two hundred and seventy-eight consecutive pediatric and young adult patients underwent HSCT at CCHMC between 2020 and 2022. Of these 278 patients, 64 had evaluable vitamin C levels measured either before HSCT (n=53) or after HSCT but before measured outcome of interest (n=11). Median age of the 64 patients was 8.53 years (range 0.48 - 34.56 years). Twenty-four out of 64 patients had low levels of Vitamin C (37.5%) while 40/64 (62.5%) had normal vitamin C levels. Of the 24 children with low vitamin C levels, 15 had low vitamin C levels before HSCT. Additionally, of the 24 children with low vitamin C levels, an underlying malignancy was the most common diagnosis (13/24) followed by bone marrow failure (8/24). Patients with low Vitamin C levels showed a greater incidence of TMA, with 11/19 patients (58%) developing TMA compared to 12/38 patients (32%) with normal Vitamin C levels (p=0.056). Within TMA, 7/13 with low vitamin C had high-risk TMA compared to 4/11 with normal Vitamin C levels showing a notable trend.
CONCLUSION
Pre-HSCT vitamin C deficiency is a surprising finding in children who are otherwise without obvious risks for nutritional deficiencies. Low Vitamin C levels are associated with a greater incidence of TMA, consistent with its known role in endothelial function and could be a modifiable risk factor to screen and supplement pre-HSCT. Larger prospective studies are needed to study this association further.

7. Title Fertility Counseling in Pediatric Hematopoietic Cell Transplant and Cellular Therapy Patients

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Children's Hospital Colorado

Theme: Supportive Care

Background: Pediatric, adolescent, and young adult patients who receive a hematopoietic cell transplant (HCT) and/or cellular therapies (CT) are at risk for significant gonadal dysfunction secondary to preconditioning therapies. Patients should therefore be offered appropriate counseling on these risks and possible fertility preservation options. Children's Hospital Colorado established the Fertility Preservation and Reproductive Late Effects (FPRLE) Program in January 2020; However, referrals to the FPRLE team have been underutilized in HCT/CT patients.

Objective: We aim to increase the number of patients who receive counseling from the FRPLE team prior to HCT or CT by 15% by incorporating a fertility bundle into the existing workflow. We also seek to understand common fertility preservation methods that are pursued.
Design/Methods: All patients 0-30 years who received a HCT, CT and/or gene therapy between January 2020 and August 2023 were identified using electronic medical records. A retrospective chart review identified those who had a documented FRPLE team consult prior to implementation of the intervention. A fertility bundle, consisting of a pre-selected fertility referral order and a fertility counseling reminder in the pre-transplant workup checklist, was included in the transplant workflow in August 2023. Prospective data were then collected. Descriptive statistics with Chi-squared test and Fisher's exact p-value were used for analysis.
Results: A total of 182 patients met inclusion criteria pre-intervention. 43% [N=79] of patients (autologous=36% [N=18], allogeneic=50% [N=54], CAR T=26% [N=6], gene therapy=100% [N=1]) had a documented fertility consult prior to therapy. Of patients who received a consultation, 59.4% [N=47] (autologous=54.5% [N=10], allogeneic=62.9% [N=34], CAR T=33% [N=2] gene therapy=100% [N=1]) pursued fertility preservation prior to therapy, with testicular tissue cryopreservation being the most common method. Following implementation of the fertility bundle, 13 patients have thus far met inclusion criteria. 84.6% [N=11] had a documented fertility consultation prior to receiving HCT or CT [Risk Ratio=1.95; 95% Confidence Interval 1.47 – 2.59; p=0.004]. Of those who received a consultation, 63.6% [N=7] pursued fertility preservation. Ovarian tissue cryopreservation and sperm banking were equally common preservation methods.
Conclusion: Implementation of the fertility bundle has shown initial success with a significant increase in the number of patients who are being referred to the FRPLE team; however, this does not seem to have a significant impact on the number of patients who pursue fertility preservation. Further data are being collected on disparities based on race/ethnicity and barriers to patients pursuing fertility preservation.

8. **Title: Implementation of a Bone Marrow Transplant Managed Iatrogenic Adrenal Insufficiency Protocol**

Authors: Jessica Cooper, DNP, CPNP-AC/PC; Amanda Strommen, PharmD, BCOP; Erin Barthelmess, PharmD, BCOP; Katherine Lind, MD
Children's Hospital Colorado

Theme: Supportive Care

Background
Long and repeated courses of corticosteroids for management of hematopoietic stem cell transplantation (HSCT) complications, such as graft versus host disease (GVHD) and idiopathic pneumonia syndrome (IPS), place patients at risk of iatrogenic adrenal insufficiency (AI). Chronic glucocorticoid therapy (CGT) suppresses the hypothalamic-pituitary-adrenal axis causing decreased synthesis of adrenocorticotropic hormone and inadequate cortisol production. Failure to identify and manage these patients promptly can lead to an adrenal crisis. At our institution, HSCT patients on CGT would not always be identified as being at risk for AI and may not be able to see an endocrinologist in a timely manner due to availability. A standardized protocol allows for proactive identification, intervention, and management of pediatric HSCT patients at risk of AI.
Objective
This quality improvement (QI) project's aim was to standardize treatment and capture all patients with iatrogenic AI and appropriately treat and manage them.

Design/Method
Using Plan-Do-Study-Act QI methodology, a multidisciplinary team was created to develop an AI management protocol. The team identified two major limitations with the current practice: proactively identifying patients who may develop AI, and timely follow-up with endocrinology prior to stress dose precautions being required. In collaboration with endocrinology, it was determined that management of iatrogenic AI by the bone marrow transplant (BMT) team would allow for patients to be treated promptly. Current literature and guidelines were reviewed to develop a treatment algorithm. After a patient was identified with AI, the BMT provider would prescribe stress dose and if needed physiologic hydrocortisone, and the BMT pharmacist would educate patients and their caregivers. The guideline also outlined how to taper off physiological steroids and when to discontinue stress steroid precautions.
Results
During the one-year intervention period, seven patients were managed and treated per the protocol. Three patients required CGT for refractory acute GVHD, three patients for IPS, and two for chronic GVHD. One patient had to be referred to endocrinology for ongoing AI symptoms despite optimization of maintenance hydrocortisone. Using fasting cortisol levels, three patients have been referred to endocrinology for stimulation testing and have discontinued stress precautions. No patients were admitted in adrenal crisis.
Conclusion
In this single-center QI project, all patients with iatrogenic AI were successfully identified and managed collaboratively by BMT and endocrinology. Given the likelihood HSCT patients on CGT will need management of AI, implementation of this BMT-lead management allows for prompt care and education regarding AI.

Transplantation Biology

1. **Title**: The Effect of SCD-1 Inhibition on Human Hematopoietic Stem Cell Mitochondrial Metabolism, Cell Proliferation, and Differentiation Potential
Authors: Olivia Perrone, Tiziana Coppola, James Bartram, Waseem Nasr, Juying Xu, Marie-Dominique Filippi
Cincinnati Children's Hospital Medical Center

Theme: Transplantation Biology

Background: Due to their inherently high regenerative potential, hematopoietic stem cells (HSCs) are used in a variety of clinical settings, including BMT directly to cure a variety of disorders. During regeneration, HSCs activate and undergo drastic mitochondrial and metabolic remodeling. This remodeling is important for optimal HSC function but is permanently changed after activating stress. It is thus important to identify the metabolic needs of activated HSCs to improve their function for therapeutic purposes. In both murine and human HSC activation, numerous metabolic enzymes get upregulated, including those involved in de novo lipid synthesis however this metabolism is poorly understood in the human system. Stearoyl-co-A-desaturase 1 (SCD-1), an enzyme within the de novo lipid synthesis pathway, is suspected to play a role in metabolic reprogramming after stress.
Objective: We seek to understand the metabolic needs of human HSCs with a focus on SCD-1 both in vitro and in vivo.
Methods: CD34+ mobilized human peripheral blood cells were cultured either in vehicle control conditions or with SCD-1 inhibitor (SCDi). Subsequently, cells were counted and analyzed by flow cytometry on Days 4-5 and 10-15. Both tetramethylrhodamine-ethyl ester dye and MitoSOX reagents

were used to assess mitochondrial membrane potential and mitochondrial reactive oxygen species, respectively.
In vivo Study (Xenotransplant): CD34+ mobilized human peripheral blood cells were cultured for 3 days and transplanted into immunodeficient, sublethally irradiated NSG mice. Peripheral blood of xenotransplanted mice was analyzed monthly for human cell chimerism and mature blood lineage from 1 to 6 months post-transplant. Bone marrow analysis was performed at 6 months as well.
Results: SCDi-treated cultures produce HSCs of similar size and make-up after 5 days. TMRE levels were lower in all HSC populations whereas mitoSOX levels were unchanged by SCD-1 inhibition. In differentiation conditions, SCDi-treated cultures were composed of a smaller proportion of erythroid cells after 10-15 days.
Peripheral blood chimerism in mice transplanted with SCDi was similar to mice transplanted with control-treated cells. SCDi-treated cells gave rise to a T lymphoid-biased graft in the peripheral blood at 5 months post-engraftment. In the bone marrow, SCDi-treated cells generate fewer erythroid cells at 6 months following engraftment.
Conclusion: De novo lipid synthesis is critically important for HSC lineage fate and balanced differentiation in vitro and in vivo but dispensable for proliferation/expansion in vitro. This is clinically relevant as this work may implicate a possible therapeutic target in patients who suffer from persistent cytopenias after BMT and graft failure.

2. Title: Combining Infliximab and Basiliximab is an Effective Treatment for Steroid Refractory Acute Graft-versus-Host Disease after Hematopoietic Stem Cell Transplantation

Authors: Margaret A Boyden MD, Mariah L Wright-Nadkarni MD, Vinita Pai PharmD, Mustafa Mohammed Embaby Ahmed MD, Veronika Polishchuk MD, Hemalatha Rangarajan MD, Margaret Lamb MD, Dean Lee MD PhD, Rolla Abu-Arja MD, Joseph R Stanek MS, Rajinder Bajwa MD

Theme: Transplantation Biology

Background: Outcomes for patients with steroid refractory acute graft-versus-host disease (SRaGvHD) are poor, and until recently, not many options for treatment were available.
Objective: To evaluate the safety and efficacy of combination therapy with infliximab and basiliximab for SRaGvHD. Methods: This is a single center, retrospective study of pediatric patients treated with infliximab and basiliximab for SRaGvHD after allogeneic hematopoietic stem cell transplantation. The diagnosis of acute graft-versus-host disease (GvHD) was made clinically, with histopathologic confirmation done when possible. SRaGvHD was defined as no response to treatment with systemic steroids (2mg/kg/day prednisolone equivalent) for at least 5 days. Basiliximab 10mg (patients weighing <35 kg) or 20mg (patients weighing >35 kg) followed by infliximab 10 mg/kg/dose were given IV on days 1, 8, 15, and 22 after the diagnosis of SRaGVHD, continued weekly until response was achieved, and then weaned off. Descriptive statistics were used to analyze outcomes.
Results: Between January 2009 and June 2023, 340 allogeneic transplants were performed at Nationwide Children's Hospital, in Columbus, Ohio, United States of America. 129 patients (37.9%) developed acute GvHD. After five days of systemic steroids, 21/129 (16.3%) were diagnosed with SRaGvHD and started on infliximab and basiliximab. One week after starting the monoclonal antibodies, steroids were weaned to 1 mg/kg/day, followed by a 10% wean every 57 days. After four weeks of treatment, 20/21 (95.2%) patients were alive: 5 (23.8%), 11 (52.4%), 1 (4.8%) and 3 (14.2%) had complete, partial, mixed, and no responses (CR, PR, MR, and PR) respectively. Over a six-month period, complete response was observed in 12 patients (57.1%). Median numbers of basiliximab and infliximab doses administered were 5 (range 1-54) and 4 (range 1-13) respectively. Overall, 15/21 patients (71.4%)

developed one or more infections, with 10 (47.6%), 8 (38.1%), and 2 (9.5%) having viral, bacterial, or fungal infections, respectively. Overall survival at day 100 from SRaGvHD diagnosis was 76.2% for all patients treated with infliximab and basiliximab. The primary cause of death was relapse/recurrence of underlying disease and infections, with 12/21 patients (57.1%) alive at last follow up (median 2.8 years (range 0.90-10.6 years)), with 8/21 (38.1%) having chronic GvHD.
Conclusions: Combination therapy with infliximab and basiliximab is a safe and effective therapy for patients with SRaGvHD. Infectious complications and relapse/recurrent disease remain a significant problem, as expected in this heavily immunosuppressed population. Further prospective studies may help determine optimal duration of therapy.

3. **Title:** Human Hematopoietic Stem Cells Have Altered Mitochondrial Activity after Stem Cell Transplantation

Tiziana Coppola, MD, Olivia Perrone, MD, James Batram, PhD, Waseem Nasr, PhD, Sydney Treichel, Juying Xu, Kasiani Myers, MD, and Marie-Dominique Filippi, PhD

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Theme: Transplantation Biology

Background: Hematopoietic stem cells (HSCs) give rise to the entire blood system and can be the only curative option for many malignancies. HSCT success depends on the quantity of HSCs and their ability to produce life-long blood. However, transplanted HSCs sustain injury that alters their subsequent ability to generate blood cells. This leads to ineffective hematopoiesis and can ultimately lead to graft failure. Our goal is to elucidate mechanisms behind post-transplant HSC decline.
Objective: Mitochondria are critically important for HSC function. During regeneration of bone marrow, HSCs become activated and undergo mitochondrial reprogramming, including reorganization of the mitochondrial network and enhanced mitochondrial activity. After transplantation, HSCs accumulate mitochondria abnormal in organization and activity, leading to HSC functional decline and ineffective hematopoiesis. While replicated in murine models, this has not been studied within humans. Our hypothesis is that after transplantation, human HSCs have altered mitochondria leading to ineffective hematopoiesis.
Design/Methods: We examined HSC functional changes using post-transplant samples from patient bone marrow and a xenotransplant system (human CD34+ peripheral blood stem cells transplanted into sublethally-irradiated immunodeficient NOD/SCID/IL-2 receptor-γ null mice). We measured mitochondrial membrane potential (MMP) using tetramethyl rhodamine ethyl ester (TMRE) dye and analyzed via flow cytometry.
Results: In the xenotransplant model, the MMP of transplanted huCD34+CD38-CD90+ HSCs was similar to the non-transplanted HSCs. However, transplanted huCD34+CD38+ progenitors showed increased MMP compared to non-transplanted, huCD34+CD38+ progenitor cells. The MMP of CD34+CD38+ progenitors from transplanted bone marrow patient samples also differed from non-transplanted CD34+CD38+ bone marrow control cells. To understand if alterations in mitochondrial activity affect HSC differentiation, we assessed xenotransplanted HSCs in vitro. Post-transplanted huCD34+ cells failed to expand within 6 days of in vitro culture and primarily differentiated into myeloid cells. Non-transplanted huCD34+ cells differentiated into myeloid, erythroid, and megakaryocytic cells. If the post-transplanted HSCs were placed in culture for 4 days, the cultured cells generated myeloid, erythroid, and megakaryocytic cells similar to non-transplanted HSCs. This suggests that transplanted HSCs have decreased differentiation ability and respond differently to cytokines in vitro.

Conclusions: In conclusion, this study shows that both mitochondrial activity and in vitro cell growth changes in HSCs after transplantation. This reveals that human HSCs and progenitor cells incur injury after transplantation. The changes in mitochondrial activity in transplanted HSCs may play a role in post-transplant HSC decline. Future single cell RNA sequencing analyses will provide mechanistic information regarding post-transplant changes in metabolism and potential targets for improving HSC function in transplant patients.