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2023 ASPHO Conference Paper and Poster Index

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ABSTRACTS

2023 ASPHO Conference Paper and Poster Index

PLENARY PAPER # 2001 | DIAGNOSES OF ADULT-ONSET HEREDITARY CANCER PREDISPOSITION SYNDROMES IN PEDIATRIC CANCER PATIENTS

Michelle Jacobs, Sarah Austin, Andrea Murad, Erika Koeppe, Dustin Walling, Dan Robinson, Yi-Mi Wu, Arul Chinnaiyan, Rajen Mody
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Background: Adult-onset hereditary cancer predisposition syndromes (HCPSs) are those for which there is no expected increased risk for cancer in children. Rarely, children in families with adult-onset HCPSs present with cancer, but the potential contribution of the HCPS to these pediatric malignancies is unknown. While predictive testing for adult-onset HCPSs is typically deferred for healthy children until adulthood, when HCPS-related screening is initiated, it is increasingly common for children with cancer to have germline testing including adult-onset HCPSs completed.

Objectives: We examined findings from pediatric patients enrolled in one institution's paired tumor-germline sequencing study to inform our knowledge of the potential role these germline pathogenic variants (PVs) may play in childhood cancer development.

Design/Method: Paired tumor-germline sequencing results from pediatric oncology patients up to 25 years old (enrolled 5/2012-12/2022) were analyzed for frequency of germline PVs associated with adult-onset HCPSs. Germline testing included analysis of 181 cancer predisposition genes associated with both pediatric and adult-onset HCPSs. Tumor loss-of-heterozygosity (LOH), immunohistochemistry (IHC) staining, and/or second somatic PV were used to determine possible association with a HCPS.

Results: Of 872 participants, 42 (4.8%) had a total of 43 PVs in genes associated with adult-onset HCPSs, including ATM (3), BARD1 (1), BRCA1 (2), BRCA2 (5), BRIP1 (2), CHEK2 (17), HOXB13 (4), MITF (3), MLH1 (1), MSH6 (2), PALB2 (1), and RAD50 (2). Six (14.3%) had somatic features indicating the adult-onset HCPS likely contributed to their cancer development, rather than the HCPS being an incidental, unrelated finding. These included three patients with Lynch syndrome (two astrocytomas, one glioblastoma) and one each with germline PVs in ATM (glioma), BRIP1 (atypical teratoid rhabdoid tumor), and CHEK2 (mixed germ cell tumor).

Conclusion: These findings suggest most pediatric cancer diagnoses in families with adult-onset HCPSs are unrelated to these syndromes, but rarely these "adult-onset" HCPSs may contribute to cancer diagnoses in children. This work may underestimate the role of these adult-onset HCPSs in pediatric cancer development, as tumors may have other mechanisms of inactivation not identified in this study. None of the adult-onset HCPS-related tumors would have been identified by screening guidelines recommended for adults with these HCPSs. These findings raise the questions of whether cancer risk is truly restricted to adulthood in these syndromes, and how tumors caused by HCPSs may present differently in children than adults. Increased knowledge about potential childhood cancer risks related to these HCPSs could modify predictive genetic testing recommendations for children and enhance existing HCPS screening protocols.

PLENARY PAPER # 2002 | AGGRESSIVE FEVER MANAGEMENT IN PEDIATRIC CHRONIC NEUTROPENIA YET FEW INVASIVE BACTERIAL INFECTIONS

Anna Matthews, Christine Smith, Heather McDaniel, Sara Zarnegar-Lumley, Brianna Smith, Jason Schwartz, Adam Esbenshade, James Connelly
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Background: Pediatric febrile chronic neutropenic (CN) patients are historically treated as high risk for invasive bacterial infection (IBI) despite little supporting data.

Objectives: Identify the frequency and risk factors of IBI in febrile pediatric patients with CN and describe the management and clinical factors associated with medical decision making.

Design/Method: Conducted a retrospective chart review of pediatric (<18 years old) patients with CN (absolute neutrophil count [ANC] <1000 cells/μl for>3 months, excluding Duffy-null and oncology patients) followed in our Pediatric Hematology Clinic between 2016-2022 presenting with fever (> 100.4F). Collected information on neutropenia diagnosis, clinical presentation, labs, imaging, treatment, and outcomes. Separated patients into poor and adequate myeloid reserve (capacity for neutrophil response to infection) categories using neutropenia diagnosis. Separated febrile etiology into invasive bacterial infections (IBI), non-invasive bacterial infection (NIBI) and all other fever etiologies (AOE). Multivariable analysis was done using logistic regression.

Results: We identified 101 CN patients; 67 of whom had 217 febrile events. Events were recorded in patients with poor (45.2%, N = 98) and adequate (54.8%, N = 119) myeloid reserve. ANC was <500 cells/μL at presentation in 34.7% (N = 68) of events. Bacteremia frequency was very low (0.9%) and IBI (5.1%) was comparable to the general pediatric population. Status of myeloid reserve and ANC were not associated with IBI or NIBI independently or when adjusted for each other. Hospital admission was independently associated with several factors in

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multivariable analysis, including poor versus adequate myeloid reserve (46.9% vs. 31.9%, odds ratio [OR] 4.2, 95% confidence interval [CI]1.6-10,7, p = 0.003), an ANC <500 vs ANC≥500 cells/μL (83.8% vs. 18.0%, OR 26.6, CI 9.4-75.6, p <0.001) and empiric antibiotic use (60.8% vs. 5.7%, OR 21.3, 95% CI 7.0-64.9, p <0.001). Fever etiology was not associated with admission, but only 7.1% of initially admitted patients had an IBI. Empiric antibiotics were common for all categories (NIBI:94.9%, IBI:90.9%, and AOE:49.7%). Frequent hospital admission and antibiotic use had consequences; 3.2% developed a nosocomial infection (one each of bacteremia, abscess, cellulitis) and 1.4% an adverse reaction to antibiotics.

Conclusion: Unlike in febrile oncologic neutropenia, CN bacteremia and IBI rates were low. Although ANC and predicted myeloid reserve were associated with clinical decisions, they were not associated with IBI and therefore may not be useful for predicting risk. Despite low rates of IBI, empiric antibiotic and admission rates were high. To address this discrepancy, we plan to analyze additional data to better predict IBI and avoid unnecessary interventions in well appearing CN patients with fever.

YOUNG INVESTIGATOR # 2003 | GUT MICROBIOTA ASSOCIATIONS WITH GD2/GD3 VACCINE RESPONSE IN PATIENTS WITH HIGH-RISK NEUROBLASTOMA

Oriana Miltiadous, Chi Nguyen, Irene Cheung, Brian Kushner, Audrey Mauguen, Nicholas Waters, Anqi Dai, Violetta Kivovich, Eric Littmann, Leana Harford, Sandeep Raj, Jonathan Peled, Kate Markey, Hana Andrlova, Govind Ragupathi, Stephen Roberts, Eric Pamer, Marina Burgos da Silva, Nai-Kong Cheung, Shakeel Modak, Marcel van den Brink

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Background: A GD2/GD3 cancer vaccine that incorporates oral beta-glucan as an adjuvant, tested in phase I and II trials (Clinical Trials.gov NCT00911560) in patients with high-risk neuroblastoma (HR-NB), elicited high anti-GD2 IgG1 titers which correlated with patient survival[1,2]. Interestingly, evidence is beginning to emerge that gut microbiome can modify responses to cancer immunotherapies and immunizations.

Objectives: To evaluate if the gut microbiome composition is associated with responses to the GD2/GD3 vaccine in patients with HR-NB.

Design/Method: 16s rRNA gene sequencing was performed on 345 stool samples from 139 patients with HR-NB receiving the GD2/GD3 vaccine. We used linear discriminant analysis effect size (LefSE) for initial comparisons of microbiome composition between patients with high and low anti-GD2 IgG titers in patients using baseline (+/−15 days) stool samples and then tested the importance of the associations between microbiome and titer response using the microbiome multivariate association tool with linear models (MaAslin2). For correlation with outcomes, LefSE was used initially, and taxa were then tested for associations with progression-free survival (PFS) in a Cox regression model.

Results: High abundance of taxa in the Clostridia class (including *Blautia*, *Lachnospiraceae* and *Intestinibacter*) in baseline stool samples was associated with higher anti-GD2 IgG1 titers. In a multivariate model adjusting for prognostic clinical parameters (including number of prior relapses, antibiotic exposure, history of autologous hematopoietic transplant, microbiome diversity and glucan use during priming), *Intestinibacter* had the strongest correlation with high anti GD2 IgG titers (FDR = 0.14). Several species within this genus are known to produce short-chain fatty acids, which are microbial fermentation products with anti-inflammatory properties that also enhance B/plasma cell responses to vaccines. After adjusting for the number of prior relapses, anti-GD2 IgG titers and glucan timing, high *Clostridia* abundance was associated with better PFS (HR = 0.40; 95%CI 0.18-0.92, p = 0.03). Interestingly, exposure to moderate/high perturbation antibiotics (to which many Clostridia are sensitive) ± 1 month from the start of the vaccine was associated with worse PFS (HR 1.71, 95% CI .93-3.14) though p = 0.08.

Conclusion: Patients with HR-NB with higher fecal abundance of *Clostridia* taxa mounted greater antibody response to GD2/GD3 vaccine and had favorable PFS. The immunobiology behind this association as well as the impact of gut microbiome modulation in improving clinical outcomes deserves further investigation.

1. Cheung, JCO, 2021
2. Cheung, JAMA Oncology, 2022

YOUNG INVESTIGATOR # 2004 | MULTIOMIC ANALYSES REVEAL MOLECULAR LINKS BETWEEN CYSTITIS AND THROMBOTIC MICROANGIOPATHY AFTER HSCT

Anthony Sabulski, Matthew Siefert, Emily Skala, Sheyar Abdullah, Nathan Luebbering, Kasiani Myers, Elizabeth Odegard, Jason Blackard, Alix Sief, Benjamin Laskin, Sonata Jodele, Krishna Roskin, Stella Davies, Assem Ziady

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Background: Most hematopoietic stem cell transplant (HSCT) recipients with BK polyomavirus (BKPyV) viruria do not develop cystitis, therefore, infection alone is not sufficient for pathology. We previously reported an association between BKPyV viremia and thrombotic microangiopathy (TMA) but have not studied the relationship between cystitis and TMA.

Objectives: We hypothesized that TMA is biologically related to BKPyV cystitis. Our objective was to study the connection between cystitis and TMA by performing a multiomic analysis using patient samples and our in vitro BKPyV infection model.

Design/Method: First, we compared the proteome of urine exosomes from three patient cohorts: 1) no BKPyV viruria (n = 10), 2) high BKPyV viruria, no cystitis (≥10^9 copies/mL, n = 10), 3) high BKPyV viruria with

cystitis (n = 10). A parallel study examined the pre-HSCT plasma proteome in patients who developed TMA (n = 7) or did not (n = 14). We then performed single cell RNAseq on primary glomerular endothelial cells cultured with BKPyV and compared the top quartile of infected cells (highest viral transcript/cell) to the bottom quartile (lowest/no viral transcript).

Results: Exosomes from cystitis patients at day 30 had significant PI4K upregulation ($p < 10^{-8}$). NF-κB and FOXP3 pathways were also observed, which cause inflammation and vasculopathy. Exosomes from cystitis patients had an association with kidney disease ($p < 10^{-17}$), complement activation ($p < 10^{-5}$) and blood coagulation ($p < 10^{-4}$) pathways. These pathways align with essential clinical findings in TMA. Samples in the exosome cohort were from patients in a larger published clinical study. Analysis of the entire cohort revealed 81% (22/27) of BKPyV cystitis patients also developed TMA.

In a separate experiment using pre-HSCT plasma samples, proteins related to kidney injury ($p < 10^{-35}$), viral infection ($p < 10^{-32}$), thrombophilia ($p < 10^{-32}$), hypertension ($p < 10^{-22}$) and coagulopathy ($p < 10^{-22}$) were increased in patients who developed TMA compared to those who did not. This confirms pathway overlap exists in the proteome of TMA and cystitis patients in separate patient cohorts. Next, single cell RNAseq using an *in vitro* BKPyV infection model identified changes in complement ($p = 2.4 \times 10^{-5}$), TNFa/NF-κB ($p = 2.4 \times 10^{-5}$), PI3K/AKT/mTOR ($p = 1.6 \times 10^{-5}$) and coagulation ($p = 1.1 \times 10^{-5}$) pathways in cells with the most BKPyV transcripts. This confirms that BKPyV significantly affects TMA and cystitis-related pathways in an isolated system.

Conclusion: This multiomics study of *ex vivo* patient samples and *in vitro* cellular infections shows BKPyV-associated cystitis and TMA are biologically similar and may contribute to one another. Further study is merited to better define the mechanisms of this relationship and explore druggable targets (eg, PI4K) for the treatment of these important HSCT complications.

PAPER # 2005 | CYCLIN-DEPENDENT KINASE 8 AS A NOVEL THERAPEUTIC TARGET IN FUSION-POSITIVE RHABDOMYOSARCOMA

Brian Guedes, Clare Malone, Marissa Just, Kathleen Engel, Seth Zimmerman, Kristianne Oristian, Alexander Kovach, Assil Fahs, Elizabeth Mendes, Ozgun Erdogan, Christian Cerda-Smith, Jack Shern, Kris Wood, Chris Counter, Kimberly Stegmaier, Corinne Linardic

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Background: Rhabdomyosarcoma (RMS) is an aggressive soft tissue sarcoma (STS) and is the most common STS in children and young adults. A subset of RMS is characterized as "fusion-positive" (FP-RMS) based on the presence of a *PAX3-FOXO1* (P3F) fusion oncogene, the product of which is a highly active transcription factor. Patients whose tumors express P3F have especially poor outcomes, with 5-year event-free survival as low as 6% in those with metastatic disease.[1] P3F is thought to be a key driver of disease but is not currently amenable to direct pharmacologic inhibition. In an effort to discover novel therapeutic targets, we identified cyclin-dependent kinase 8 (CDK8) as a unique dependency in FP-RMS. Based on CDK8's function as a member of Mediator complex, we hypothesize that it plays a critical role in the P3F transcriptional network and is thus a targetable vulnerability.

Objectives: To 1) evaluate the effects of CDK8 loss of function (LOF) on FP-RMS oncogenic phenotypes in vitro, 2) understand how the FP-RMS genetic landscape is altered by CDK8 LOF, and 3) investigate the effect of CDK8 pharmacologic inhibition *in vitro* and *in vivo*.

Design/Method: Cancer databases were interrogated to identify selective dependencies in FP-RMS. These *in silico* results were corroborated with an unbiased P3F proximity labelling assay. CDK8 was then genetically inhibited using both shRNA and CRISPR in FP-RMS cell lines and cellular phenotypes were evaluated following CDK8 LOF, including proliferation, apoptosis, and migration. RNAseq and gene set enrichment analysis were performed following CRISPR knockout of CDK8. The effects of several CDK8 small molecule inhibitors on cell viability were assessed using Cell Titer Glo. SEL120-34A was identified as a promising agent and thus selected for evaluation in mouse FP-RMS xenograft studies. Tumors were harvested and samples were evaluated for effects of treatment with SEL120-34A.

Results: CDK8 is a selective dependency in FP-RMS cell lines and is a member of the P3F interactome. Genetic LOF of CDK8 diminished cell growth due to increased apoptosis and down-regulation of P3F super-enhancer genes. Pharmacologic LOF of CDK8 diminished FP-RMS cellular viability in vitro and abrogated xenograft tumor growth in vivo via increased apoptosis.

Conclusion: Together our data identify and validate CDK8 as a novel and translatable therapeutic target in FP-RMS. These data also provide a foundation for further studies investigating the role of CDK8 in PAX3-FOXO1 oncobiology.

[1]Hibbitts et al, *Cancer Med*, 2019.

PAPER # 2006 | TREATMENT OF HIGH-RISK NEUROBLASTOMA USING DINUTUXIMAB CHEMOIMMUNOTHERAPY IN ALL CYCLES OF INDUCTION

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Background: The addition of an anti-GD2 monoclonal antibody (hu14.18K322A) to 6 cycles of Induction chemotherapy for the treatment of patients with high-risk neuroblastoma (HRNBL) led to an end of Induction (EOI) objective response rate (ORR; ≥ partial response [PR]) of 93.8% in a single institution phase 2 clinical trial (NB2012, NCT01857934). Chemoimmunotherapy using dinutuximab (DIN) has been effective in the treatment of patients with relapsed/refractory neuroblastoma and successfully administered to newly diagnosed (HRNBL) patients during Induction cycles 3-5 in a Children's Oncology Group (COG) study (ANBL17P1, NCT03786783). We report the

results of 24 patients with HRNBL treated with DIN in all cycles of Induction therapy.

Objectives: The primary objective was to determine the EOI ORR (≥ PR) of patients diagnosed with HRNBL treated with DIN in all cycles of Induction. The secondary aim was to describe the common toxicities experienced by the patients during Induction chemoimmunotherapy.

Design/Method: This is a single-center retrospective study of patients with HRNBL treated with DIN (17.5 mg/m^2/dose, IV Days 2-5) and GM-CSF (250mcg/m^2/dose, subcutaneous Days 6-count recovery), with or without subcutaneous interleukin 2 (IL-2), with COG Induction chemotherapy. Data was abstracted from the electronic medical record. Toxicities experienced during Induction were graded by CTCAE v.5.0. EOI ORR was evaluated using the Revised International Neuroblastoma Response Criteria (INRC).

Results: Twenty-four patients with HRNBL (21 newly diagnosed, 3 previously treated with intermediate-risk therapy including 2 recurrent and 1 refractory, 15 females, median age 3.1 years; range, 0.35-8.1 years) received Induction chemoimmunotherapy from 1/27/2017 to 12/28/2022. All patients received DIN with all cycles of Induction. The most common DIN-related grade>3 toxicities recorded during Induction included fever (46%), hypoxemia (21%), and hypoalbuminemia (13%). All 24 patients completed EOI evaluations, including 17 with complete response, 7 with PR, 0 with minor response, 0 with stable disease, and 0 with progressive disease. The EOI ORR was 100%.

Conclusion: The administration of DIN and GM-CSF to COG Induction for patients with HRNBL had an encouraging EOI ORR. A randomized phase 3 study of Induction chemoimmunotherapy is warranted.

PAPER # 2007 | FREQUENCY OF PATHOGENIC GERMLINE VARIANTS IN PEDIATRIC MEDULLOBLASTOMA SURVIVORS

Donald Rees, Matthew Gianferante, Jung Kim, Theodora Stavrou, Gregory Reaman, Neal Freedman, W. Ryan Diver, Adriana Lori, Lindsay Morton, Leslie Robison, Gregory Armstrong, Smita Bhatia, Alisa Goldstein, Lisa Mirabello

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Background: Medulloblastoma is the most common malignant brain tumor in children. Most cases are sporadic, but well characterized germline alterations in *APC*, *ELP1*, *GPR161*, *PTCH1*, *PTCH2*, *SUFU*, and *TP53* predispose to medulloblastoma. However, knowledge about pathogenic/likely pathogenic (P/LP) variants in medulloblastoma cases vary based on genes evaluated, patient demographics, and pathogenicity pipelines.

Objectives: To quantify the frequency of germline P/LP variants in cancer susceptibility genes (CSGs) in medulloblastoma patients and available parents compared to controls to better understand germline genetic susceptibility.

Design/Method: Our study included 160 survivors of medulloblastoma diagnosed at <18 years of age with 134 cases from the Childhood Cancer Survivor Study, a cohort of five-year survivors of childhood cancer, and 26 additional cases from Children's National Medical Center (CNMC). Germline exome sequencing was conducted on all cases plus 40 unaffected parents of CNMC cases. Analyses focused on rare variants in 237 known CSGs – 183 autosomal dominant (AD) and 54 autosomal recessive (AR) genes. P/LP variants were identified using ClinVar and InterVar. Variants of unknown significance (VUS) in the seven medulloblastoma predisposing genes were further analyzed as VUS-damaging (and added to P/LP counts) if predicted as loss of function by snpEff or deleterious in three of four in-silico predictors. We compared the frequency of P/LP variants in cases to that in 1657 in-house cancer-free controls using Fisher's exact tests. A Bonferroni correction threshold of p-value <0.002 was considered significant.

Results: Of the 160 cases, 33 (21%) had a germline P/LP variant in one of the 237 CSGs versus 2.6% in controls (p <0.001). Twenty-two individuals (14%) had an AD P/LP variant versus 0.4% in controls (p <0.0001), 11 (7%) had a P/LP variant in a known medulloblastoma predisposition gene (*APC*, *ELP1*, *GPR161*, *PTCH2*, *SUFU*) versus zero in controls (p <0.0001), and 15 (9.4%) had a heterozygous AR P/LP variant versus 2.2% in controls (p <0.001). The CSGs with the most P/LP variants in cases and significantly higher than controls were *ELP1*, *SUFU*, and *PTCH2* (all p <0.0001). *BRIP1* and *CHEK2* (AD), and *AGL* and *MRE11A* (AR) genes had P/LP variants enriched in cases, were nominally significant (all p <0.02), and had not been previously associated with medulloblastoma.

Conclusion: One-fifth of pediatric medulloblastoma survivors had a P/LP CSG variant, some in genes which had not previously been associated with medulloblastoma, and therefore need to be replicated. These findings suggest that routine germline testing for children with medulloblastoma at diagnosis should be considered.

PAPER # 2008 | TARGETING GLIOBLASTOMA & DIFFUSE INTRINSIC PONTINE GLIOMA W/ ANTI-GD2 CAR MODIFIED NK CELLS

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Background: Glioblastoma (GBM) and diffuse intrinsic pontine glioma (DIPG) are universally fatal tumors. Although natural killer (NK) cells infiltrate these tumors, their activity is suppressed. Ex vivo activation of NK cells with cytokines may restore the NK cells' cytolytic activity. The disialoganglioside, GD2, is expressed on GBM and DIPG cells and may be an immunotherapy target. ROR-1 is also expressed in GBM tumors and may serve as an alternative target. NKTR −255 is an IL-15 receptor agonist that activates the IL-15 pathway to expand NK cells and enhance NK cell antibody-dependent cellular cytotoxicity (ADCC).

Objectives: Our hypothesis is that an anti-GD2 CAR NK cell in combination with NKTR-255 and anti-ROR1 antibody can promote NK cell cytotoxicity against GBM and DIPG.

Design/Method: We developed an anti-GD2 CAR NK cell. Anti-GD2 CAR DNA was subcloned into the pcDNA3 vector to generate a CAR. Peripheral blood mononuclear cells were expanded into NK cells using K562-mbIL21-41 BBL feeder cells with IL-2. Anti-GD2 CAR mRNA was synthesized in vitro using the mMESSAGE mMACHINE™ T7 ULTRA Transcription Kit. Anti-GD2 CAR NK cells were generated by non-viral electroporation of anti-GD2 CAR mRNA into ex vivo expanded NK cells. GD2 expression on GBM cell lines and anti-GD2 CAR expression on ex-vivo expanded NK cells were evaluated by flow cytometry. Anti-GD2 CAR NK cells were tested in a cytotoxicity assay against GD2+ GBM cells.

Results: GD2 is expressed in U138 MG GBM cells. Anti-GD2 mRNA was synthesized in vitro andelectroporated into the expanded NK cells and proven by the detection of CAR expression on NK cells via flow cytometry. Additionally, we found that in the tumor:effector cell ratios of 10:1-1:1, the anti-GD2 CAR NK cell had greater cytotoxicity in the GD2+ U-138 MG GBM cell line when compared to the mock NK.

Conclusion: Our data demonstrated successful engineering of anti-GD2 CAR NK cells and increased cytotoxic capacity in the anti-GD2 CAR NK when compared to the mock NK cell. We plan to test the anti-GD2 CAR NK cells on the GD2+ M054K GBM cell line and a GD2+ DIPG cell line. Afterwards, we will test the synergistic effect of the combination of NKTR-255 and anti-ROR1 antibody with the CAR NK cells against the same cell lines.

PAPER # 2009 | RISK FACTORS AND TREATMENT RESPONSE IN KAPOSIFORM HEMANGIOENDOTHELIOMA: A MULTICENTER COHORT STUDY

Alexandra Borst, Whitney Eng, Morgan Griffin, Kiersten Ricci, Elissa Engel, Denise Adams, Jillian Dayneka, Sally Cohen-Cutler, Steven Andreoli, Melinda Wu, Alison Wheeler, Kenneth Heym, Shelley Crary, Taizo Nakano, Rachael Schulte, Bhuvana Setty, Thomas McLean, Kristy Pahl, Stefanos Intzes, Irina Pateva, Max Teitelbaum, Zili Zong, Yimei Li, Michael Jeng

Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, United States

Background: Kaposiform hemangioendothelioma (KHE) and tufted angioma (TA) are vascular tumors primarily affecting young children that may exhibit profound thrombocytopenia, hypofibrinogenemia, and bleeding (known as Kasabach-Merritt phenomenon, KMP). Risk factors for poor outcomes are not well established.

Objectives: Evaluate clinical features for decreased response in KHE/TA.

Design/Method: A multicenter, retrospective cohort study through the ASPHO Vascular Anomalies Special Interest Group compared response to primary intervention incorporating the following endpoints: overall treatment response (OTR), clinical response (ClinR), radiologic response (RadR), and hematologic response (HemR; KMP subjects only). We further analyzed responses to treatment stratifying for KMP, age, and tumor characteristics using Fisher's exact test.

Results: 159 patients with KHE/TA from 17 institutions treated between January 2005-January 2020 were included. Median age at diagnosis was 154 days (IQR 32-510.5). KMP was present in 64 patients (40.3%) Platelet count, hemoglobin, and fibrinogen were lower in the KMP group ($p < 0.001$). KMP was associated with younger age (49.5 vs 293 days, $p < 0.001$), truncal tumor location ($p = 0.029$), tumor size ≥5 cm ($p < 0.001$), more hospitalizations ($p < 0.001$), increased length of stay ($p < 0.001$), and faster treatment initiation ($p < 0.001$). There was no difference in ClinR or RadR at 3 or 6 months in the KMP group. Among all patients, there were no differences in OTR rates for lesions present at birth vs. developing in early infancy vs. later in life. However, patients ≥ 5 years at treatment initiation had significantly lower OTR by 3 months (58.3% vs 88.8%, $p = 0.016$) and 6 months (69.2% vs 90.9%, $p = 0.044$) compared to those ≤ 5 years. For patients <1 year at treatment initiation, ClinR at 3 months was higher (90.2% vs 73.3%, $p = 0.03$), however HemR, RadR, and ClinR at 6 months were no different. There were no differences in OTR at 3 or 6 months comparing tumor site (truncal vs. non-truncal) or size (<5 cm or ≥ 5 cm). Multifocal and extensive tumors (across multiple body sites) had lower rates of HemR at 3 months (75% vs 97.1%, $p = 0.046$), but similar ClinR and RadR. Two patients died, both with KMP and extensive, large lesions ≥ 5 cm.

Conclusion: We confirmed previously reported characteristics of severe KHE/TA with truncal site, large size, young age, and coagulopathy all associated with increased risk for KMP. However, treatment response rates did not vary based on presence of KMP, age <1, tumor size, or location. We identified novel risk factors for decreased treatment response, including age ≥ 5 years at treatment initiation and multifocal/extensive lesions.

PAPER # 2010 | EXAMINING DOUBLE-STRAND BREAK REPAIR IN DIAMOND–BLACKFAN ANEMIA

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Background: Diamond–Blackfan anemia (DBA) is an inherited bone marrow failure syndrome most often due to germline pathogenic variants in ribosomal protein (RP) genes, with *RPS19* and *RPL5* the most frequently mutated. In addition to hypoplastic anemia, patients with DBA are at a moderately increased risk of developing MDS/AML, and solid cancers. Importantly, no causal link between RP deficiency and cancer predisposition has been established.

Objectives: This work aims to elucidate the mechanisms through which RP mutations impact double-strand break (DSB) repair and how this may drive cancer development.

Design/Method: We performed colony survival assays of lymphoblastoid cells, comet assays of CD34+ cells, and DSB repair (DSBR) reporter assays for non-homologous end joining (NHEJ), homologous recombination (HR), single-strand annealing (SSA), and microhomology-mediated end-joining (MMEJ) in U2OS cells to assess

DSBR proficiency. We performed survival assays following PARP-inhibition. We performed western blotting to assess DSBR protein levels. We measured the accumulation of nuclear RPA2 following ionizing radiation (IR) to assess end resction. We generated eGFP-RPS19 and mCherry-RPL5 constructs and monitored their recruitment to sites of DSBs induced by laser micro-irradiation.

Results: DBA patient-derived lymphoblastoid cells were hypersensitive to IR and RPS19-depleted CD34+ cells had delayed resolution of comet tails after IR. We found decreased HR and SSA in RPS19-depleted U2OS cells and unchanged NHEJ and MMEJ. Consistent with a HR defect, RPS19-deficient cells were hypersensitive to PARP inhibition. In constrast to the impact of RPS19 depletion, RPL5-deficient cells had increased NHEJ and MMEJ and unchanged HR and SSA. The levels of key proteins in these DSBR pathways demonstrated only an increase of DNA ligase 4 in both RPS19 and RPL5-deficient cells. Because HR and SSA require extensive resection of the 5′ DNA strand at the DSB, we examined whether RPS19-deficiency impaired this key step and found RPS19 depletion resulted in greater nuclear RPA2. We found that both proteins were rapidly recruited to break sites and the recruitment of RPS19, but not RPL5, was hindered by PARP inhibition.

Conclusion: These results suggest that RPS19- and RPL5- mutated DBA cells have distinct defects in DSBR. As DNA ligase 4 is associated solely with NHEJ, its upregulation does not explain all of the DSBR phenotypes caused by RPS19 and RPL5 deficiency. The reduction in HR and SSA efficiency in RPS19 deficient cells is not due to impaired end resection and may involve a downstream step. These defects may impact DSBR fidelity and contribute to MDS/cancer predisposition in DBA.

PAPER # 2011 | EMICIZUMAB FOR THE TREATMENT OF INFANTS WITH SEVERE HEMOPHILIA A: INTERIM ANALYSIS OF HAVEN 7

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Background: Emicizumab can be started from hemophilia A (HA) diagnosis, reducing bleeding risk in infants with HA (IwHA). This interim analysis (IA) of HAVEN 7 (NCT04431726) evaluates emicizumab prophylaxis in IwHA.

Objectives: To evaluate the efficacy, safety and pharmacokinetics (PK) of emicizumab prophylaxis in IwHA without factor (F)VIII inhibitors.

Design/Method: HAVEN 7 is a Phase 3b, open-label study of emicizumab in IwHA ≤12 months without FVIII inhibitors. IwHA receive emicizumab 3 mg/kg weekly for 4 weeks, then 3 mg/kg every 2 weeks for 52 weeks; participants can then stay on this dose or switch to 1.5 mg/kg weekly or 6 mg/kg every 4 weeks for the 7-year follow-up. Endpoints include: efficacy (treated bleeds; all bleeds; treated spontaneous bleeds; treated joint bleeds); safety; PK; and anti-emicizumab antibodies (ADAs). Annualized bleed rates (ABR) are estimated using a negative binomial regression model.

Results: At the IA cut-off (March 31, 2022), 54 IwHA (55.6% ≥3–≤12 months; 44.4% <3 months; all male) had ≥1 dose of emicizumab; median (range) age: 4.5 (0–11) months at informed consent; 16 (1–26) months at cut-off. Minimally treated (≤5 exposure days with HA-related treatments): 55.6%; previously untreated: 44.4%. Median (range) treatment duration: 42.1 (1–60) weeks.

Overall, 77 bleeds occured in 31 IwHA: 88.3% traumatic; 5.2% procedural; 6.5% spontaneous. One participant had 12 bleeds (all traumatic; none joint/muscle; none treated). Fourteen treated bleeds, all traumatic, were reported in 12 IwHA. No participant had>2 treated bleeds. Mean model-based ABRs (95% confidence interval [CI]) for treated bleeds, all bleeds and treated joint bleeds were 0.4 (0.23–0.65), 1.9 (1.35–2.68) and 0.1 (0.01–0.22), respectively. Overall, 77.8% of IwHA had zero treated bleeds, while 42.6% had no bleeds at all. In total, 92.6% of participants had ≥1 adverse event (AE); 16.7% of AEs were emicizumab-related injection-site reactions. No AEs led to changes in or withdrawal from emicizumab. Eight IwHA reported 12 serious AEs; none were considered emicizumab-related. No deaths/thrombotic events/thrombotic microangiopathies have been reported. None of the 48 IwHA evaluable for immunogenicity tested positive for ADAs. Evaluable PK data in 52 IwHA showed mean emicizumab trough concentrations increased during loading and were maintained thereafter, slightly above 60 μg/mL.

Conclusion: This IA suggests that emicizumab is efficacious and well tolerated in IwHA without FVIII inhibitors.

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PAPER # 2012 | MULTI-LEVEL mHEALTH INTERVENTION BOOSTS HYDROXYUREA ADHERENCE IN PATIENTS WITH SICKLE CELL DISEASE

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Background: Hydroxyurea is an evidence-based sickle cell disease (SCD) disease-modifying treatment; however, adherence is low. We conducted a two-level mobile health (mHealth) intervention targeting the determinants of low hydroxyurea adherence among patients (InCharge Health app) and low prescribing among providers (HU Toolbox).

Objectives: Evaluate effectiveness and implementation of both mHealth interventions in a multi-center study from the NHLBI SCD Implementation Consortium.

Design/Method: Seven academic sites participated in a non-nonrandomized trial. We compared adherence during a 24-week baseline period with adherence during 24 weeks of intervention in patients 15-45 years old with SCD. Adherence was measured by the percentage of days covered (PDC), which is the percentage of days covered by filled hydroxyurea prescriptions during the study period. We hypothesized that the combined intervention would produce an absolute increase of 12% in PDC. Acute care utilization, ASCQ-Me pain impact, pain frequency, pain severity, and PROMIS pain quality patient-reported outcome (PRO) measures were assessed at baseline and 6 months.

Results: The sample comprised 293 patients (51.1% male, median age 27.5 years, 86.8% with HbSS/HbSB0-thalassemia). Change in PDC was evaluable in 235 patients, 199 of whom used InCharge Health at least once (84.7% reach; median usage: 17% of 168 days; IQR: 4.8-45.8%). The mean duration of app usage was 2.3 min/day. Fifty-eight of 89 enrolled providers (76.5% female, 69.7% ages 30-50 years, 49 hematologists, 36 advance care providers, 4 unreported) used the app ≥1 day over 6 months (adoption 65.1%). Only 10 (11.2%) used it ≥6 days over 6 months (maximum: 18 days).

The mean PDC increased from 39.7% to 56.0% ($p < 0.0001$). PDC change was associated with the rate of use of the InCharge Health app (partial correlation adjusted for baseline PDC: 0.23; $p = 0.0004$). The PDC change was accompanied by reductions in rates of emergency department visits 0.6 to 0.33/patient; $p < 0.001$) and hospitalizations (0.72 to 0.45/patient; $p = 0.0002$). Self-reported pain frequency also declined (3.54 to 3.35 events/patient/year, $p = 0.0412$). Only 24% of the patients achieved PDC ≥80%. No changes in pain severity, impact, and quality were observed. Provider use of HU Toolbox was not associated with PDC change.

Conclusion: mHealth tailored to the determinants of low hydroxyurea adherence had high implementation and promoted increased adherence with substantial clinical benefits among patients with SCD. mHealth to support hydroxyurea prescribing among SCD providers had low implementation and did not contribute to the changes. Future studies should focus on pairing mHealth with other synergistic adherence-enhancing interventions for added efficacy and further clinical benefit.

PAPER # 2013 | OVEREXPRESSION OF AMPKγ2 ENHANCES THE METABOLIC CAPACITY AND CYTOTOXICITY OF HUMAN CART CELLS

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Background: Chimeric Antigen Receptor (CAR)T cells have revolutionized the treatment of pediatric relapsed/refractory acute lymphoblastic leukemia (ALL). However, up to 1/3 of patients who receive this therapy experience disease recurrence. Further, CART therapy has seen limited success in solid tumors, where the nutrient-deplete tumor microenvironment poses an even greater challenge to anti-cancer function. With mounting evidence that cellular metabolism controls T cell function, understanding how to modulate T cell metabolism could hold the key to advancing these therapies. AMP-activated protein kinase (AMPK) is a highly conserved metabolic regulator with roles in mitochondrial efficiency, nutrient stress adaptation, and long-term cellular persistence. We have previously demonstrated that increased AMPK signaling through overexpression of the regulatory AMPKγ2 domain in human T cells increases mitochondrial efficiency and inflammatory function in vitro, making this a promising target to improve CART therapy.

Objectives: To investigate whether overexpression of AMPKγ2 in CART cells improves their metabolic efficiency and inflammatory function.

Design/Method: Human T cells were activated and transduced with a lentiviral vector expressing the anti-CD19 CAR along with a BFP tag, followed by either an AMPKγ2 overexpressing vector or an empty vector (EV) control. Co-transduced cells were flow sorted and cultured with IL-2. Metabolism was assessed after 24 hours of activation using the Seahorse metabolic analyzer. Cytotoxicity was measured by co-culturing CART cells with Zs-Green+ NALM6 leukemia targets in physiologic glucose (5.5 mM) RPMI. The Incucyte was used to follow Zs-Green expression to measure NALM6 survival. Interferon(IFN)-γ production was assessed by flow cytometry using intracellular staining after 16 hours of co-culture in the presence of brefeldin A. CARTs were maintained in culture with IL-2 through Day 40, with CAR expression followed by flow cytometry for the BFP tag.

Results: AMPKγ2-CARTs demonstrated a 20% increase in oxidative capacity as well as a 10% increase in glycolytic activity as compared to EV-CARTs upon reactivation in vitro ($p < 0.05$). Further, they exhibited increased killing of NALM6 targets after 72 hours of coculture with a faster loss of green fluorescence measured by the Incucyte ($p < 0.001$), accompanied by a ~15% increase in IFNγ+ CARTs. Finally, AMPKγ2 overexpression improved maintenance of CAR expression over long-term in vitro culture, with AMPK-CARTs demonstrating ~17% higher median fluorescence of the BFP tag ($p < 0.05$).

Conclusion: Increasing AMPK in human CART cells through overexpression of AMPKγ2 mediates enhanced metabolic activity, increased cytotoxicity, and improved long-term persistence in vitro. Work is ongoing to assess these modified CART cells using an in vivo mouse xenograft leukemia model.

PAPER # 2014 | DEFINING THE ROLE OF COHESIN HAPLOINSUFFICIENCY IN THE EVOLUTION FROM TAM TO DS-AMKL

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Background: Transient abnormal myelopoiesis (TAM) is a self-limiting clonal myeloproliferative disorder that occurs in 10-30% of neonates born with Down Syndrome (DS). Approximately 20% of patients who recover from TAM go on to develop acute megakaryoblastic leukemia (DS-AMKL). *GATA1* mutations are universal among patients with TAM and are preserved between TAM and DS-AMKL clones within an individual, suggesting that TAM is a pre-leukemic condition that evolves into AMKL under the influence of an acquired, cooperative mutation(s). Greater than 50% of these cooperative mutations involve genes encoding proteins of the cohesin complex. We hypothesize that cohesin insufficiency disrupts normal tertiary chromatin structure and leads to a rewiring of crucial enhancer-promoter pairs, resulting in aberrant regulation of gene expression and ultimately to DS-AMKL.

Objectives: We aim to establish the impact of impaired cohesin-mediated chromatin structure on hematopoiesis and leukemic transformation in DS-AMKL through creation of a novel murine model.

Design/Method: To establish our murine model we bred Dp16 mice, a validated genetically engineered model which recapitulates many of the features of DS, with mice carrying a constitutive $Gata1^{yeym2}$ truncating mutation to yield mice harboring the universal genetic features of TAM. We then utilized the inducible hematopoietic tissue-specific Mx1-Cre recombinase system to cause heterozygous *Rad21* deletion at 2 weeks of age or prenatally on ED14.5 to recapitulate what we suspect is the natural course of evolution to DS-AMKL.

Results: We generated a cohort of mice in which we induced *Rad21* deletion at 2 weeks of age (N = 25) and a cohort in which *Rad21* deletion was induced prenatally on ED14.5 (N = 35). When we performed serial plating of whole BM cells harvested from mice that underwent *Rad21* deletion at 2 weeks of age in methylcellulose, we found greater colony counts from $Dp16;Gata1^{s};Rad21^{+/\Delta}$ mice compared to wild type control ($p < 0.0001$ on secondary passage). $Dp16;Gata1^{s};Rad21^{+/\Delta}$ mice also exhibited enlarged spleens as well as expansion of the stem cell compartment in the bone marrow compared to wild type controls.

Conclusion: Our results demonstrate that hematopoietic cells from $Dp16;Gata1^{s};Rad21^{+/\Delta}$ mice exhibit increased proliferative and self-renewal capacity in vitro. We also found that $Dp16;Gata1^{s};Rad21^{+/\Delta}$ mice exhibit enlarged spleen and unique expansion of the stem cell compartment in the bone marrow at 18 weeks of age. Our work demonstrates that cohesin insufficiency may impart $Dp16;Gata1^{s}$ mutant cells with enhanced stem cell properties that encourage persistence beyond the newborn period and ultimate malignant transformation.

PAPER # 2015 | THE EFFECT OF METHOTREXATE ON NEUROINFLAMMATION GENE EXPRESSION AND ASSOCIATED NEUROLOGIC SEQUELAE

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Background: Methotrexate treatment in pediatric patients has been associated with long-lasting detrimental neurological and psychological sequela following cancer survival. These sequelae, which persist after methotrexate exposure, may include problems with executive functioning, attention span, and processing speed as well as disorders like ADHD, depression, and anxiety.

Objectives: The goal of our project is to reveal candidate risk genes and pathways contributing to methotrexate-induced neurocognitive and psychiatric late effects.

Design/Method: We are conducting genetic analysis of white matter tissue samples from autopsies of patients previously treated with methotrexate for leukemia or osteosarcoma. Genetic analysis is conducted via RNA extraction from formalin-fixed, paraffin-embedded brain specimens from deceased patients who received methotrexate treatment as well as normal controls. Nanostring, a variation of targeted RNA microarray testing, is used to detect abnormal up- or down-regulation of neuroinflammation-associated genes. Bioinformatics using Ingenuity Pathway Analysis (IPA) is then used to determine affected biological pathways and networks.

A retrospective chart review consisted of the audiological and psychometric testing results of cancer survivors of ages 2-22 enrolled at the Late Effects Clinic at Children's Hospital New Orleans. Specific focus was given to the neurological analysis of living cancer survivors who have completed methotrexate treatment.

Results: Genetic testing of white matter samples has thus far revealed six genes that were three- to eight-fold over- or under-expressed, including a gene associated with myelin sheath damage (CD24). CD24 was found to have an eight-times reduced expression in those treated with methotrexate compared to normal controls. Myelin dysregulation has previously been linked to attention-deficit disorders.

A retrospective chart review of the Behavior Assessment for Children (BASC) demonstrated that patients who received methotrexate were more likely to have their parents report attention problems when compared to patients who had received other cancer treatments (p-value = 0.0339). The data also showed mild evidence that patients who received methotrexate were more likely to have clinically significant scores on the Inattention/Hyperactivity Index (p-value = 0.0798).

Conclusion: Though the cause of methotrexate toxicity remains unclear, disruption of CNS folate metabolism, deregulation of myelination, and direct neuronal damage have all been identified as possible mechanisms. This project seeks to create a better understanding of the genotype-phenotype interactions in cancer survivors who are affected by methotrexate-induced neurological and psychosocial late effects. This understanding may provide better identification of those at-risk for methotrexate toxicities and improve quality of life with access to precision medical interventions, educational materials, and social support.

PAPER # 2016 | RISK OF SEPSIS DURING BLINATUMOMAB ADMINISTRATION: A REPORT FROM THE CHILDREN'S ONCOLOGY GROUP

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Background: Blinatumomab is a bi-specific T-cell engager antibody that improves outcomes for children with relapsed acute lymphoblastic leukemia (ALL) (Brown et al., JAMA, 2021). Administered as a 28-day continuous infusion, blinatumomab is currently dispensed as 24-, 48-, 72-, 96- or 168-hour (7-day) bags. The Food and Drug Administration (FDA) raised theoretical concerns on the risk of bacterial contamination and subsequent bacteremia with 72- or 96-hour bags and halted all trials that permit their use in December 2022.

Objectives: To determine the incidence of sepsis among children receiving blinatumomab on the Children's Oncology Group (COG) trial AALL1731.

Design/Method: AALL1731 includes patients with newly-diagnosed NCI standard risk (SR) ALL; patients with higher risk features are randomized to receive standard chemotherapy vs. an additional 2 cycles of blinatumomab, while patients with Down Syndrome (DS) and high risk (HR) disease nonrandomly receive chemotherapy and 3 cycles of blinatumomab. All episodes of CTCAE v.5-defined sepsis (defined as a positive blood culture in the presence of any other sign or symptom [e.g. fever]) were identified. Simultaneously, a survey administered to participating COG sites determined how often 72- and 96-hour bags were used.

Results: Of 134 COG institutions responding to questions of bag sizes, 9 reported only inpatient use and did not specify bag sizes. Of the remaining 125 COG institutions providing survey responses specifying outpatient bag sizes, 2 (1.6%) reported using 24-hour bags, 5 (4.0%) reported using 48-hour bags, 10 (8.0%) reported using 7-day bags, and 108 (86.4%) reported using a combination of 72- and 96-hour bags. At the time of the most recent data analysis (June 30, 2022), 860 cycles of blinatumomab had been administered to 487 patients (475 non-DS and 12 DS). Sepsis and/or catheter-related blood infections occurred in 17 patients during 18 cycles, yielding an incidence rate of 2.1%. Only one event was assessed as Grade 4; the rest were Grade 3. Two grade 3 events occurred in DS patients. Half (9/18) of infections involved organisms traditionally considered skin-associated, such as Staphylococcus epidermidis or coagulase-negative Staphylococcus.

Conclusion: On AALL1731, with 86.4% of sites administering blinatumomab using 72- or 96-hour bags, we did not observe an unexpected rate of blood infections during blinatumomab administration. The theoretical concern surrounding these bags should be balanced against the increased burden on patients, families and sites, and the risks associated with an increased number of line accesses that would result from switching to 24- and 48-hour bags.

PAPER # 2017 | ANTIMICROBIAL LOCKS FOR CLABSI PREVENTION IN THE INPATIENT SETTING: A COST-EFFECTIVENESS ANALYSIS

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Background: Children with cancer and long-term central venous access are at risk for central line-associated bloodstream infections (CLABSIs). Regular prophylactic administration of an antimicrobial lock solution may reduce the incidence of CLABSIs in the inpatient pediatric oncology setting, but the cost-effectiveness of this strategy for children is unknown.

Objectives: To evaluate the cost-effectiveness of antimicrobial lock prophylaxis among hospitalized children with cancer, from the perspective of the healthcare system.

Design/Method: We constructed a decision-analytic cohort model with a time horizon of 14 days to compare antimicrobial lock prophylaxis with usual care (heparin locks). We estimated the probability of developing a CLABSI for each strategy using incidence rates reported in an aggregate of eight randomized controlled trials in pediatric oncology. We included the probability of line-associated thrombosis as an additional endpoint independent of CLABSI outcome. Costs of medications and administration were estimated by micro-costing institutional data. Costs of managing a CLABSI or thrombotic event were abstracted from the literature. Costs were converted to 2021 US dollars. We analyzed both deterministic and probabilistic models to estimate the incremental cost-effectiveness ratio per CLABSI averted as a primary outcome. We estimated cost-effectiveness first excluding the additive costs of CLABSI management itself, using a predetermined willingness-to-pay threshold equivalent to these additive costs ($83,441, 95% confidence interval: $43,302–$124,606). We also analyzed a second model that included CLABSI management costs to determine potential cost savings. For our probabilistic sensitivity analysis, we modeled uncertainty ranges with beta (for probabilities) or gamma (for costs) distributions.

Results: In the probabilistic analysis (n = 10,000 simulations) excluding the additive costs of CLABSI management, antimicrobial lock prophylaxis was associated with a mean incremental cost of $7,253 per single CLABSI averted. At the predetermined willingness-to-pay threshold, antimicrobial lock prophylaxis was cost-effective in 99.4% (95% confidence interval: 98.1%—99.7%) of simulations. With the additive costs of CLABSI management included, antimicrobial lock prophylaxis strongly dominated usual care (-$76,015 per CLABSI averted). The antimicrobial lock prophylaxis strategy resulted in a single CLABSI averted per 1,568 line-days. Results from the deterministic analyses, including one-way sensitivity analyses, were consistent with these findings. Estimated annual cost savings at our institution (assuming 25,000 patient line-days) of this strategy amounted to $1.2 million.

Conclusion: Antimicrobial lock prophylaxis represents a cost-effective strategy that may generate substantial savings in the pediatric oncology inpatient setting. Further investigation is warranted to estimate

cost-effectiveness in the outpatient setting, as well as among other pediatric patient populations with long-term central venous access.

PAPER # 2018 | DRIVE TIME TO CANCER TREATMENT CENTER AFFECTS PEDIATRIC CANCER SURVIVAL: A POPULATION-BASED ANALYSIS

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Background: Survival disparities have been documented for Hispanic and Black children with cancers. Geographic access to and travel distance to a cancer center has been associated with advanced-stage cancer presentation, less likelihood of chemotherapy delivery, and poorer survival among adults with different types of cancers. However, little is known of the impact of distance to cancer treatment center and risk of death among pediatric cancer populations.

Objectives: To evaluate the association between pediatric cancer mortality and the travel time to the pediatric cancer treatment center closest to patient's residential address at diagnosis. Our hypothesis is that children needing to travel longer to pediatric cancer care experience higher risk of mortality.

Design/Method: The study included 0-19 years old patients diagnosed with a cancer between 1995-2017 per Texas Cancer Registry (TCR). Using geocoded data of each patient's residential address at diagnosis, we performed spatial analysis to create three concentric drive time rings around each patient's address (**short drive time**: 0—15 minutes; **intermediate drive time**: 15 – 60 minutes; and **long drive time**: ≥ 60 minutes). The drive time assigned to a patient was the ring that contained the closest treatment center when driving away from their house. All childhood cancers cases were sub-categorized into three groups: hematologic cancers, central nervous system (CNS) cancers, and solid tumor cancers. Logistic regression models were used to estimate the unadjusted and adjusted odds ratio (OR) for death associated with drive time to treatment center.

Results: A total of 29,555 pediatric cancer cases were available for analysis. In unadjusted models, long drive time to a cancer treatment center (≥ 60 minutes) was associated with higher odds of death across the three cancer subtypes: hematologic (OR: 1.21; 95% CI: 1.05 - 1.40), CNS (OR: 1.19; 95% CI: 1.00 - 1.40), and solid tumor (OR: 1.19; 95% CI: 1.01 - 1.39). After adjusting for sex, age at diagnosis, and socioeconomic factors, long drive time to a cancer treatment center was still associated with higher odds of death across all cancer subtypes: hematologic (OR: 1.29; 95% CI: 1.11 - 1.50), CNS (OR: 1.25; 95% CI: 1.05 - 1.49), and solid tumor (OR: 1.22; 95% CI: 1.03 - 1.44).

Conclusion: Children with cancer needing to drive ≥ 60 minutes to a cancer treatment center experience higher odds of death compared to children whose drive time is short (≤15 minutes). Our findings suggest drive time may represent a significant barrier to healthcare access for children with cancer.

PAPER # 2019 | CAREGIVERS' PERSPECTIVE ON FAMILY LIFE DURING TREATMENT FOR B-ALL FROM THE CHILDREN'S ONCOLOGY GROUP

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Background: Although childhood acute lymphoblastic leukemia (ALL) can be successfully treated by multiagent therapy, the 2-3 years of treatment affect not only the patient, but the entire family. It is important to investigate the impact of ALL treatment on family functioning to help providers deliver family-centered care.

Objectives: To describe positive and negative changes in family life as reported by parents or guardians throughout leukemia therapy on Children's Oncology Group (COG) Protocol AALL0932: 1) overall, 2) across different timepoints, and 3) between therapeutic randomization groups (every 4-week versus 12-week vincristine/dexamethasone pulses).

Design/Method: Parents/guardians of children with standard risk B-ALL (SR-B ALL) who consented to the optional Patient Leukemia Experience Ancillary Study during enrollment on COG AALL0932 answered the free-response question: "How has family life changed since your child's diagnosis of leukemia for the better or for the worse?" Responses were collected at 2, 8, 17, 26, and 38 (boys only) months post-diagnosis; corresponding to the end of consolidation, timepoints throughout maintenance, and end of therapy. Inductive content analysis and iterative readings were used to identify themes and to code free responses. Coding was agreed upon by three independent evaluators.

Results: Nine-hundred and ninety-five responses were collected from a parent/guardian of 468 children who were 45.7% female, 68.6% self-declared White non-Hispanic (9.8% non-White non-Hispanic, 16.2% Hispanic, remainder unknown), and a mean age of 6.0 ± 1.6 years at enrollment. Among the 995 responses across all timepoints, the most frequently mentioned stressors were limitation of family activities outside the home (20%), strain on siblings (19%), financial strain (19%), work challenges (18%), and concern about patient symptoms (e.g., fatigue, hair loss, behavioral changes; 18%). Positive changes included family bonding (25%), community support (13%), re-evaluation of priorities (7%), gifts because of cancer diagnosis (5%), and enhanced spirituality (4%). A lower proportion of respondents reported stressors at 26 months than at 2 months, except for concern about patient symptoms (18% at 2 months; 21% at 26 months). A higher proportion of respondents reported positive changes at 26 months, except for community support (16% at 2 months; 11% at 26 months). Responses did not differ between randomization groups.

Conclusion: Treatment for SR-B ALL impacts family life in both positive and negative ways. While many stressors diminish over time, concern about patient symptoms persist. Families acknowledge increasing positive changes later in treatment but lose some early community support.

Together, these results inform the need for improved supportive care strategies throughout leukemia therapy.

PAPER # 2020 | CORE COMPONENTS OF THERAPEUTIC ALLIANCE FOR ADOLESCENT AND YOUNG ADULTS WITH ADVANCED CANCER

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Background: Cancer is the leading disease-related cause of death for adolescents and young adults (AYA). AYAs are at risk for inferior quality cancer care due to their unique needs at this transitional stage of life. Therapeutic alliance, defined as the collaborative bond between clinicians and patients, is an important aspect of quality care. Prior studies have demonstrated that a strong therapeutic alliance is associated with improved outcomes for patient care, caregiver well-being and bereavement. We lack data on important aspects that contribute to building this relationship from the patient and family caregiver perspective for AYA advanced cancer patients.

Objectives: Define components of the therapeutic alliance between AYAs with advanced cancer, their families and their clinicians and identify barriers to building therapeutic alliance in this population.

Design/Method: This study was a multi-center qualitative study of AYAs (ages 12-39) with advanced cancer, caregivers and clinicians, who participated in semi-structured recorded interviews to discuss their experiences surrounding end-of-life (EOL) care to identify patient-centered priority domains of high quality EOL care. We performed secondary content analysis to identify participants' perspectives on what constitutes the therapeutic alliance for AYAs and their families.

Results: This study included 80 participants: 23 patients, 28 caregivers, and 29 clinicians including physicians, advanced care practitioners, nurses, and psychosocial clinicians. The mean patient age was 29 years ($\pm$ 7.3). Caregivers included 22 parents, 5 spouses/partners, and 1 sibling; Most were bereaved (82%). We identified six components of therapeutic alliance in this sample: compassion; sense of connection; clinician presence; information sharing; shared goals; and individualization of care. We also identified important barriers to building a strong therapeutic alliance: conflict between managing patient and caregiver needs; fragmentation of medical care; and clinician-identified communication challenges with the AYA population. These challenges included discomfort discussing EOL care with young patients, lack of training, concern for loss of hope, fear of ruining the therapeutic bond, and emotional avoidance of difficult conversations.

Conclusion: Therapeutic alliance for AYAs with advanced cancer has multiple components including aspects of personal connection and communication. The need for individualized, patient-centered care was apparent across all domains as a critical aspect of therapeutic alliance for this population. This study included the perspectives of patients and caregivers as key stakeholders on defining the components of therapeutic alliance, which was previously lacking in the literature. Clinicians can draw on these elements to better support and address barriers to high quality EOL care for AYAs.

PAPER # 2021 | BLOOD? PLEASE! LIMITING THE USE OF PRBCS IN ASYMPTOMATIC IRON DEFICIENCY ANEMIA

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Background: The use of packed red blood cells (PRBCs) for the treatment of asymptomatic iron deficiency anemia (IDA) is a targeted area of improvement in Pediatric Hematology, as supported by the American Society of Hematology/American Society of Pediatric Hematology/Oncology (ASH/ASPHO) choosing wisely campaign. PRBCs are a finite resource, and carry greater treatment associated risks for IDA as compared to iron therapies. The use of oral and intravenous iron is an effective, well tolerated therapy modality for IDA which can be overlooked based on a patient's degree of anemia.

Objectives: Decrease the percentage of PRBC transfusions in all admitted iron deficiency anemia patients from a baseline of 69% to a target of 50% by December 2022 and sustain for 12 months.

Design/Method: PDSA methodology was used for this quality improvement (QI) initiative. The population of interest was identified as hospital admitted patients with the primary diagnosis of iron deficiency anemia. Data were collected from March 2019 through November 2022. In February of 2022, clinical practice guideline (CPG) development was initiated, outlining the treatment for symptomatic and asymptomatic patients with IDA. In parallel with CPG development, education about IDA management was shared with the adolescent medicine, emergency medicine, gastroenterology, hematology, and hospital pediatrics services to improve the management of IDA. The pre-education/baseline group is defined as patients admitted from March of 2019 through February 2022, and the post-education/post-intervention group defined as patients admitted from March 2022 through November 2022. The CPG for IDA was effectively launched on October 11, 2022. Chi-square tests were used for statistical comparisons.

Results: In the pre-education/baseline group 69% (n = 55/79) of patients received PRBC transfusion for treatment of IDA, compared to the post-education/intervention group where 32% (n = 18/55) of patients received PRBC transfusion for treatment of IDA (p-value <0.0001). In the pre-education/baseline group, 16.3% (n = 9/55) of patients received PRBC transfusions which were not indicated based on the developed CPG, compared to 11% (n = 2/18) in the post-education/intervention group (p-value = 0.72).

Conclusion: Education of multidisciplinary teams, and their engagement in the IDA-CPG development led to a clinically significant overall reduction in PRBC transfusion for IDA. The new aim of our QI initiative will be defined as decreasing the percentage of inappropriate PRBC

transfusions as defined by the CPG from a baseline of 11% to 5% by July of 2023 and sustain for 12 months.

PAPER # 2022 | SICKLE CELL DISEASE AND SARS-COV-2 PATIENT OUTCOMES: RESULTS FROM THE PEDIATRIC COVID-19 REGISTRY

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Background: Children and adolescents with sickle cell disease (SCD) are at risk of severe presentation for certain infections relative to otherwise healthy children. The differential impact of the COVID-19 pandemic has been reported for various patient populations but there are limited data documenting outcomes of SARS-CoV-2 in pediatric SCD.

Objectives: To describe clinical outcomes of pediatric patients with SCD and SARS-CoV-2 infection relative to infection outcomes in general pediatric (GP) and other immunocompromised patients (IC: malignancy, stem cell and solid organ transplant, and primary immunodeficiency) between March 25, 2020, and April 30, 2021.

Design/Method: Retrospective cohort study leveraging a convenience sample of patients <21 years old testing positive for SARS-CoV-2 at institutions contributing data to the Pediatric COVID-19 US Registry. Data were entered into a REDCap™ database. Baseline data included demographics, underlying comorbidities, and symptoms. Follow-up assessments at seven and 28 days after index testing captured symptom progression, medical management, and outcomes.

Results: The analyzed sample included 210 (SCD), 331 (IC), and 10,367 (GP) patients. Age and sex distributions were similar across groups. Seventy-six (36%) patients with SCD were hospitalized for COVID-19 compared to 1,483 (14.3%) GP patients and 114 (34.4%) IC patients. Of 76 hospitalized SCD patients, 38 (50%) had a moderate oxygen requirement compared to 427/1,483 (29%) and 37/114 (32.5%) of GP and IC patients, respectively. Of hospitalized patients, 18.4% of SCD patients required ICU care compared to 35% of GP and 32% of IC patients.

Four patients with SCD developed MIS-C, all requiring ICU care. One MIS-C patient had a pulmonary embolism; this was the only thrombotic event reported in the SCD cohort. There were no deaths in the SCD population; deaths were rare for GP (0.05%) and IC (1.2%) patients.

Conclusion: In the first 13 months of the COVID-19 pandemic, children and adolescents with SCD and SARS-CoV-2 frequently required hospitalization and supplemental oxygen. These rates were higher for patients with SCD compared to IC and GP patient populations. Interestingly, fewer hospitalized SCD patients required ICU care relative to other groups. Further research into this paradox is needed, but possible explanations include a lower threshold for admission of patients with SCD or simultaneous co-morbidities including acute chest syndrome, severe anemia, or pain. MIS-C was diagnosed in four SCD patients, all requiring ICU care. No SCD deaths were reported. Increased hospitalizations and oxygen requirements in patients with SCD highlight the importance of vaccination and early diagnosis in this patient group.

PAPER # 2023 | PREDICTORS OF SUSTAINED HBF RESPONSE TO HYDROXYUREA IN PATIENTS WITH HBSS

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Background: High fetal hemoglobin (HbF) during hydroxyurea therapy is associated with lower morbidity and mortality in sickle cell anemia (SCA). HbF levels are not consistently sustained long-term in all patients with SCA, despite adequate hydroxyurea adherence. Better characterization of the decline of HbF over time is needed.

Objectives: To compare pre-treatment laboratory variables, treatment characteristics, pre- and post-treatment acute care utilization (ACU) of individuals with HbSS on hydroxyurea who had sustained HbF response (HbF>20% for>80% of treatment time post-maximum dose versus those with non-sustained HbF response (HbF>20% for <80% of treatment time post-maximum dose).

Design/Method: We conducted a retrospective review of participants with HbSS enrolled in the Sickle Cell Clinical Research and Intervention Program, an ongoing lifetime SCA cohort study. Participants received hydroxyurea for>1 year and had $\geq$ 3 HbF/CBC values after the maximum hydroxyurea dose was achieved. Adherence was not directly measured, but non-adherence was estimated by an average decline in MCV>10% from their peak value.

Results: Of the 310 eligible participants, 109 (35%) were considered non-adherent and removed. Of the remaining 201, the mean treatment duration post-maximum dose was 13.4 (standard deviation [SD]: 7.6) years. The mean averaged HbF values post-maximum-dose for sustained response to hydroxyurea was 30.7% (SD: 6.8) verse 17.0% (SD: 4.4) for non-sustained. Sustained response was associated with higher mean baseline hemoglobin (10.0 vs. 9.3 g/dL), younger age when maximum dose was achieved (5.5 vs. 8.0 years), shorter duration of treatment since post-maximum dose achieved (10.8 vs. 16.3 years), lower maximum dose (26.9 vs. 28.5 mg/kg/day), and lower ACU rate post-maximum dose (1.24 vs. 1.99 events/person-year). In multivariable logistic regression analysis controlled for total treatment duration, lower maximum dose (OR [Odds Ratio] 1.1, 95%CI 1.0-1.2), earlier age of hydroxyurea initiation (OR 1.1, 95%CI 1.0-1.2), and higher baseline hemoglobin concentration (OR 0.8, 95%CI 0.6-1.0) were independently associated with sustained response. In multivariable Quasi-Poisson regression analysis controlled for total treatment duration, non-sustained response was associated with three times more frequent ACU events post-maximum dose (est 1.1, standard error = 0.3). Other baseline demographic and laboratory characteristics did not predict HbF response or ACU.

Conclusion: Early age at initiation of hydroxyurea and higher baseline Hb may contribute to sustained HbF response, even with lower maximum dose values during treatment. The sustained response corresponds to lower ACUs post-treatment. Pharmacokinetic and genetic studies are needed to identify additional predictors of non-sustained HbF response to hydroxyurea to guide modifications to therapy.

PAPER # 2024 | OUTCOMES OF PARTIAL T CELL-DEPLETED STEM CELL TRANSPLANTATION FOR PATIENTS WITH HEMOGLOBINOPATHIES

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Background: Matched related donor stem cell transplantation (MRD-SCT) is an established curative therapy for patients with sickle cell disease (SCD) and beta thalassemia major (BTM); however, most lack available donors. Unrelated donor (URD)-SCT for SCD and BTM using T cell-replete grafts is complicated by high rates of GvHD, whereas haploidentical related SCT and unrelated cord blood SCT are associated with high graft failure rates. We have previously shown that *ex vivo* partial T-cell depletion (pTCD) of URD peripheral stem cell (PSC) grafts for other transplant indications effectively facilitates engraftment while preventing GvHD. We hypothesize pTCD would similarly improve outcomes for patients with SCD and BTM undergoing URD-SCT. We present outcomes of 14 patients with SCD or BTM who received URD-PSCT with pTCD.

Objectives: Determine whether pTCD and URD-PSCT in patients with SCD/BTM results in durable donor engraftment without severe GvHD.

Design/Method: Fourteen patients with SCD (9) or BTM (5) lacking matched related donors underwent URD-SCT using 10/10 (5) or 9/10 (9) HLA-matched donors. Conditioning included a hydroxyurea prophase followed by thymoglobulin, fludarabine, thiotepa, and busulfan. Donor PSCs underwent pTCD using CliniMACS (Miltenyi). The initial 4 patients underwent pTCD via CD3+/CD19+ depletion with $1x10^5$ CD3+ cell/kg addback per expanded access protocol NCT0235665. For the remaining patients, TCR$\alpha\beta$+ T cell/CD19+ depletion was performed via a separate expanded access study (NCT03145545, n = 4) or a prospective clinical trial (NCT04523376, n = 6). Patients received a median of $12.9x10^6$ CD34+ cells/kg ($5.5x10^6$-$16.6x10^6$).

Results: Median follow-up is 20 months (3-36). 1- and 3-year overall survival is 92.8%. Median time to neutrophil engraftment was 13.5 (11-18) days. Time to platelet engraftment was notably rapid at 15.5 (10-17) days. All surviving patients are transfusion-independent. No patients developed Grade II-IV acute GVHD or chronic extensive GVHD. Five patients had CMV reactivation, but none developed end-organ disease. Two patients with SCD and 9/10 matched donors experienced graft failure. One developed donor-type aplasia at 8 months post-SCT and received a successful second SCT using the same donor. The second had a history of Moya-Moya and exhibited early secondary graft failure. He engrafted with a second SCT, but subsequently developed multiple infections and thrombotic microangiopathy and ultimately died of intracranial hemorrhage. Notably, both patients had a history of RBC and HLA alloimmunization due to extensive pre-SCT transfusion histories.

Conclusion: URD-PSCT with pTCD via CD3+/CD19+ depletion with T-cell addback or TCR$\alpha\beta$+ T cell/CD19 depletion is associated with excellent engraftment, overall survival, and minimal GvHD in patients with SCD and BTM.

POSTER # 001 | CREATION OF A PRECISION MEDICINE TEAM & REGISTRY: PROVIDING TREATMENT PLANS AND TRACKING BIOMARKERS

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Background: Recent advances in biotechnology have allowed identification of features unique to formation of malignant tumors. This has consequently led to formation of a niche branch described as Precision Medicine designed to optimize efficiency or therapeutic benefit for particular groups of patients. Historically, children have received lesser focus than their adult counterparts with regard to precision medicine initiatives. Through the formation of a dedicated interdisciplinary team, we have been able to focus on the development of first, second, and further lines of treatment utilizing molecular test results performed as standard of care for children with newly diagnosed and relapsed malignancies.

A plethora of clinical trials have been conducted demonstrating that matched therapy is associated with both superior outcome and fewer toxicities. Yet, adoption of such practices in pediatrics are not universal. With this in mind, we decided to extensively expand next generation sequencing (NGS) of patients at our hospital and simultaneously establish a database to store this information, track trends in molecular testing as well as treatment regimens used.

Objectives: To create an in-house registry of patients that have molecular testing to track changes in their tumor bio-markers and follow treatment decisions that have been made based on commercial NGS results.

Design/Method: The study team created a secure RedCap database to store patients' diagnosis, test results, and treatment. The Precision Medicine Group, constituted of oncologist, molecular pathologist, pharmacist, research team, team nurse and solid tumor coordinator continues to meet bi-weekly to review all NGS results for available therapeutic options. This information can be acted upon as needed when a patient is determined to have relapsed or refractory disease. The interdisciplinary nature of this program allows for real time review of research protocols, potential investigational agents, and commercially available options.

Results: Results show that since 2019 when NGS testing became more prevalent, our team has evaluated 151 patients' results and treated 24 of them using either an investigational targeted therapy or with commercial agents based on NGS test results. The formation of the precision medicine clinic and a related database have highlighted the importance to track all treatment decisions and the role played by NGS test results in influencing those decisions.

Conclusion: The development of a precision medicine team and registry will allow providers to organize data and develop individualized treatment plans. In the future these endeavors are likely to help identify trends in pediatric oncology bio-marker changes.

POSTER # 002 | CHARACTERISTICS OF EXTRA-ENDOCRINE FEATURES IN A CHOHORT OF PATIENTS WITH MEN2B SEEN AT THE NIH

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Background: Multiple endocrine neoplasia type 2B **(**MEN2B) is a rare autosomal dominant cancer predisposition syndrome caused by an activating germline mutation of the rearranged during transfection (*RET*) proto-oncogene (typically p.M918T). MEN2B is associated with 100% risk of medullary thyroid carcinoma (MTC), and approximately 50% lifetime risk of pheochromocytoma (PHEO). Mucosal ganglioneuromas, marfanoid habitus, gastrointestinal and musculoskeletal manifestations are common non-tumor manifestations of MEN2B syndrome.

Objectives: To characterize the tumor and non-tumor features of MEN2B patients followed at the National Institutes of Health (NIH).

Design/Method: We analyzed the clinical data including physical exams, laboratory examinations, and imaging findings collected up to January 2023 for 52 patients with MEN2B followed at the NIH. Patients were enrolled in either the natural history study of children and adults with MEN2 (NCT01660984) or the natural history and biospecimen acquisition study for children and adults with rare solid tumors (NCT03739827). Data were obtained from medical records and evaluations performed during study visits at the NIH Clinical Center in Bethesda, Maryland, USA. Occurrence of non-tumor manifestations, PHEO, and MTC were assessed.

Results: All 52 patients had a germline *RET* p.M918T mutation. Age at diagnosis of MEN2B ranged from <1 year to 30 years old (median of 10 years), and 27 (52%) were female while 25 (48%) were male patients. Neurological, skeletal, gastrointestinal, and genitourinary manifestations were common in our population with 35 patients (67.3%) having neurological manifestations including hypotonia and breath holding spells in infancy. Thirty-four patients (65.4%) had skeletal features of MEN2B including scoliosis, pectus excavatum, and pes cavus. Thirty-four patients (65.4%) had gastrointestinal symptoms such as constipation and diarrhea, and 25 patients (48.1%) had genitourinary findings including kidney stones, orchiopexy, and urinary frequency/incontinence. All 52 patients (100%) had a history of MTC, and 13/52 patients (25%) had a confirmed diagnosis of PHEO by the data cut-off of January 2023. The median age of diagnosis of MTC and PHEO were 10 and 17 years respectively. Most common presenting symptoms leading to diagnosis of MEN2B/MTC included neck swelling (due to thyroid tumor formation or adenopathy), ganglioneuromas identified during routine medical care, and gastrointestinal issues that manifested early in life.

Conclusion: In addition to well-characterized extra-endocrine manifestations of MEN2B, patients with this syndrome may also have neurological, gastrointestinal, and genitourinary issues. Recognition of these features of MEN2B may facilitate earlier diagnosis of patients with this rare syndrome.

POSTER # 003 | PSYCHOSOCIAL SCREENING IN A MULTIDISCIPLINARY PEDIATRIC AND YOUNG ADULT CANCER PREDISPOSITION CLINIC

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Background: Screening guidelines for inherited cancer syndromes require a lifetime of medical tests and procedures. However, little is known about barriers to attendance at cancer predisposition clinics (CPC).

Objectives: Using quality improvement (QI) methodology, we aimed to develop a psychosocial screening tool to identify barriers and to perform screening in at least 75% of patients to increase adherence to CPC appointments.

Design/Method: Our QI project consisted of three components: qualitative assessment of barriers and development of screening tool; implementation of screening; interventions to address barriers. Health beliefs, sources of distress and barriers to care were evaluated using the Impact of Events Scale-Revised (IES-R) and Illness Attitudes Scale (IAS) by a psychologist. Qualitative analysis of the interviews was used to develop a driver diagram, a Pareto chart, and a SMART Aim. A **psychosocial screening tool** was designed by adapting the existing Cancer Worry Scale (CWS). Retrospective review of clinic notes provided baseline data. In the first Plan-Do-Study-Act (PDSA) cycle, a social worker contacted family members via telephone using the screening tool. Subsequently, a **standard resource sheet** was developed to share with patients. In the second PDSA cycle, the social worker performed the telephone screen, provided resources and documented barriers and outcomes on a tracking spreadsheet. At the end of the second PDSA cycle, the results were examined for trends among common diagnoses, age and years from diagnosis. The **primary measure** was completion of psychosocial screen prior to the clinic visit. The **secondary measure** was attendance at the clinic visit.

Results: Sixteen patients with cancer predisposition were interviewed for the initial qualitative assessment of barriers. The driver diagram

and Pareto analysis identified psychological factors, time, distance and insurance concerns as the main barriers. Retrospective chart review indicated 2/22 (7%) of patients had a documented psychosocial evaluation prior to CPC visit. In the first PDSA cycle, 16/18 patients (89%) completed screening prior to clinic visit. In the second PDSA cycle, 16/20 patients (80%) completed screening prior to the clinic visit. All patients who underwent screening attended their subsequent CPC appointment. Those who did not complete screening missed their CPC visit. High CWS scores were found across entire cohort.

Conclusion: We developed a feasible psychosocial screening tool and implemented it prior to CPC visit in>80% patients presenting for surveillance. Previously unmet needs for community, mental health and school support were addressed. Future efforts to address distress in cancer predisposition patients are warranted. Supported by CPRIT RP220137

POSTER # 004 | FAMILY RESPONSE TO DETECTION OF A GERMLINE PATHOGENIC VARIANT ON PAIRED TUMOR-GERMLINE SEQUENCING

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Background: Precision oncology via tumor sequencing is increasingly used in pediatric oncology. Paired tumor-germline sequencing specifically allows for the identification of somatic variants for targeted therapy and detection of germline pathogenic variants (GPVs) causative of hereditary cancer predisposition syndromes. Identification of GPVs allows for tailored screening with the goal of cancer early detection or prevention. However, it is crucial that GPVs be incorporated into medical care and shared with family members to realize this potential.

Objectives: We sought follow up with families whose child had a GPV identified via this study to assess recall of results and actions taken based on this finding.

Design/Method: Seven hundred and forty patients aged 0-25 were enrolled in a paired tumor-germline sequencing study at an academic medical center between 5/2012-8/2021. Sequencing results, including GPV findings, were disclosed to patients/parents/guardians by their oncology providers. Ninety-seven participants (13.1%) had one or more GPVs consistent with cancer predisposition. Contact information was available for 88/97 (90.7%) individuals, and phone surveys to assess actions taken after receipt of results were completed for 53/88 (60.2%) participants between 10/2021-2/2022. Thirty-five (39.7%) could not be reached or declined to participate. Surveys were completed with a parent (n = 49, 92.5%) or with participants over age 18 (n = 4, 7.5%).

Results: Forty-three (81.1%) individuals responded "Yes" to the question "Did DNA sequencing identify a genetic change associated with an increased risk for cancer?" while seven (13.2%) responded "No" and three (5.7%) were unsure. The 43 participants who remembered receiving information about a GPV associated with cancer predisposition reported changes occurred to the children's cancer screening or other medical care in 16 (37.2%) cases based on the PGV. Twenty-three (53.5%) individuals reported at least one family member pursued their own germline genetic testing based on the GPV finding, most commonly one or both parents (n = 21, 91.3%). Sixteen (34.9%) participants adopted healthier habits after participation in this study. Many reported feeling overwhelmed with the sequencing results and information about the GPV and/or being unable to follow-up with a genetics provider due to a focus on the cancer treatment.

Conclusion: While most patients/parents recalled having a GPV identified on paired tumor-germline testing, fewer patients endorsed using these results for cancer screening and cascade testing. Further work is needed to determine what factors affect recall of GPV results and to determine patient and family preferences for timing and method of result return to optimize their use in care.

POSTER # 005 | GENETIC TESTING IN A PEDIATRIC SOLID TUMOR POPULATION AT PHOENIX CHILDREN'S HOSPITAL

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Background: Germline variants associated with cancer predisposition genes (CPG) have been discovered in 8-10% of all pediatric cancers. Cancer predisposition genetics is an area of rapid growth and innovation as testing becomes more readily available. Solid tumors comprise approximately one-third of all childhood cancers and numerous are known to be associated with cancer predisposition. The frequency of germline genetic testing for the solid tumor population at our institution was previously not known.

Objectives: The primary objective of this project is to define the frequency of germline genetic testing in the solid tumor population at our hospital from 2011-2021. Secondarily, we aim to approach "high risk" solid tumor patients who were not previously tested for genetic counseling and testing to define the incidence of CPG in this population.

Design/Method: A comprehensive list of pediatric solid tumor patients diagnosed at Phoenix Children's between 2011-2021 was compiled. Patients diagnosed with osteosarcoma, rhabdomyosarcoma, and hepatoblastoma underwent thorough chart review for mention of genetic counseling or testing as well as testing results if performed. Charts were also reviewed for "high risk" features, defined as the following: personal history of prior cancer, positive family history for cancer, and somatic mutations or tumor histology suggestive of possible CPG. For certain diagnoses, patient age was also considered.

Results: From 2011-2021, 72 were diagnosed with osteosarcoma. Five (6.9%) underwent genetic testing, and 1/5 (20%) had a positive result for CPG. Twenty-eight patients were diagnosed with hepatoblastoma. Nine (32%) underwent genetic testing, and 5 (55.6%) had a positive

result. Fifty-five patients were diagnosed with rhabdomyosarcoma, of which none underwent germline genetic testing.

Conclusion: We have identified a low rate of germline genetic testing in the solid tumor population at our institution. We are in the process of identifying "high risk" factors that would suggest a role for genetic counseling and testing. At the time of presentation, we will have more data on testing of "high risk" patients with solid tumors at our center.

POSTER # 006 | IMPLEMENTATION OF SEQUENCING-BASED DIAGNOSTICS FOR PEDIATRIC CANCER IN RESOURCE-LIMITED SETTINGS

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Background: Overall survival for pediatric cancer in low- and middle-income countries (LMICs) remains at 30% compared to 80% in high-income countries. One contribution to limited survival is access to appropriate cancer diagnostics. Genome sequencing-based diagnostics can provide classification for pediatric cancer, leading to more effective treatment selection with the goal of improved survival for children.

Objectives: Our aim is to understand barriers and opportunities for implementation of genomic sequencing for pediatric cancer classification in LMICs to contribute to improved survival for children with cancer.

Design/Method: A mixed methods research design was used. Across World Bank income classification and regions, twelve site champions contributed to a survey identifying available resources for implementation of genomic sequencing-based diagnostics. Semi-structured interviews with key implementation partners at six sites are underway. Twelve interviews, informed by the Consolidated Framework for Implementation Research, across two sites have been completed. Rapid qualitative analysis is being performed to identify key themes regarding implementation barriers and facilitators.

Results: Survey findings revealed that the mean annual case volume per site was 266 diagnoses for leukemia/lymphoma, 219 for non-CNS solid tumor cases, and 105 for CNS tumors (n = 11). All sites had access to morphologic analysis, 92% to immunohistochemistry, 83% to flow cytometry, 58% to cytogenetics, and 75% to PCR, microarray, or DNA mutation panels. Partner sites that had experienced development of a tumor repository were equal to 58%. Based on a Likert Scale (1- No Research Availability / Capacity to 4- Always Available With Capacity), on average, partner sites had moderate-to-extensive research personnel (3.6), moderate-to-extensive laboratory equipment available (3.45), and limited-to-moderate experience with genomic sequencing (2.89) (n = 12). Three sites had no experience with genomic sequencing.

Rapid qualitative analysis of interviews (n = 7) from the first partner site identified several implementation barriers and facilitators for sequencing technology. Initial barriers were thematically represented by money, manpower, and machine. Specifically, the largest needs were human resource training and site-level implementation costs. Facilitators were that sequencing technology for pediatric cancer would be innovative, stable, and supported at the partner site. Interviewees expressed optimistic support for the relative advantage of sequencing-based diagnostics compared with locally-available standard of care. Collection of quantitative and qualitative data and analysis is ongoing.

Conclusion: Findings at the initial partner site demonstrate that diagnostic technology for pediatric cancer is desired and seems appropriate. Future work should focus on developing and testing strategies to support the infrastructure, education, training, and financial needs to implement sequencing-based diagnostics in resource-limited settings.

POSTER # 007 | DEVELOPMENT OF A COMPREHENSIVE PROGRAM FOR EVALUATION OF PREDISPOSITION TO HEMATOLOGIC MALIGNANCIES

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Background: Germline pathogenic variants underlie or contribute to an estimated 20% of leukemia and 50% of aplastic anemia. Early diagnosis of inherited predisposition to hematologic malignancy (IPHM) and bone marrow failure is critical for treatment planning, allowing for avoidance of excessive chemo-radiation toxicity and appropriate Stem Cell Transplant (SCT) donor selection. Additionally, non-hematological surveillance may be initiated for other associated manifestations. Identification also may lead to cascade genetic testing for at-risk family members.

Objectives: Describe a framework and outcomes for a comprehensive program for evaluation of inherited predispositions to hematologic malignancy.

Design/Method: We established a multicenter collaborative program between three hospitals [Huntsman Cancer Institute at University of Utah, LDS Hospital at Intermountain Healthcare, and Primary Children's Hospital (all in Salt Lake City, UT)] with specific criteria for genetic evaluation defined prospectively. All patients identified for evaluation were assessed by a certified genetic counselor. Germline genetic testing was performed using DNA from culture fibroblast derived from skin biopsies. Laboratory selection for germline genetic testing was based on insurance coverage, admission status, personal history, family history, turnaround time, time to SCT, and comprehensiveness of panel.

Results: Between October 2021 and April 2022, 61 patients were identified prospectively who met evaluation criteria for referral to genetic counseling. Median age was 35 years (range newborn to 77 years), and 26% (16/61) were under age 18. The most common reasons for evaluation were cytopenia (n = 14), myelodysplastic syndrome (n = 10), and acute myeloid leukemia (n = 16). Fifty-two patients underwent

germline genetic testing, eleven were found to have pathogenic/likely pathogenic variants and eight were identified with suspicious variants of uncertain significance. In the pediatric setting, this included one patient with Shwachman-Diamond syndrome, one patient with a balanced translocation resulting in a whole gene deletion of *TUBB1*, and one patient with a *TINF2* pathogenic variant associated with Dyskeratosis Congenita.

Conclusion: The results of this study show the feasibility of developing a comprehensive, collaborative program for evaluation of IPHM. Essential to the success is a readily available genetic counselor with expertise in IPHM, active communication with pediatric and adult clinicians who treat patients with hematologic malignancies and bone marrow failure, and laboratory support for obtaining skin biopsies, culturing fibroblasts, and extracting and preserving DNA. Our program can serve as a blueprint for establishing a service line for comprehensive germline testing for IPHM at other medical centers.

POSTER # 008 | BENEFITS AND HARMS OF ONLINE PATIENT PORTAL USE IN PEDIATRIC AND ADOLESCENT ONCOLOGY

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Background: The 21st Century Cures Act has resulted in many adolescents with cancer and parents having access to electronic health information through online patient portals. This new transparency could benefit or hinder communication between families and clinicians, depending on how this technology is used.

Objectives: To interview oncology physicians and advanced practice providers (APPs) to discern their perceptions on benefits and problems created by portal use, as well as accommodations they have made to integrate portals into their practice.

Design/Method: We performed semistructured interviews with 52 pediatric and adolescent oncology clinicians (29 physicians and 23 APPs). We recruited clinicians from a national cohort supplemented by snowball sampling. We performed thematic analysis of transcripts to identify overarching themes.

Results: Participants represented 25 different pediatric cancer centers. Mean age of physicians was 44 years and APPs was 45 years. All clinicians had a nursing pool that screened and triaged portal messages. Clinicians described benefits of portal use that centered around 5 themes: (1) improving efficiency and accuracy of communication, (2) bolstering family/clinician relationships, (3) promoting open and adaptive communication, (4) supporting parents in managing child's care, and (5) decreasing communication workload. Specific to adolescents, clinicians described portals empowering adolescents to become involved in care. Clinicians described problems created by parental portal use that centered around 5 themes: (1) creating emotional distress and confusion, (2) diminishing quality of documentation, (3) increasing workload and changing workflows, (4) diminishing trusting relationships, and (5) parents misusing portal messaging. Specific to adolescent care, clinicians described problems related to 3 themes: (1) creating familial discord, (2) threatening confidentiality, and (3) creating emotional distress from reviewing results without context or support. Clinicians described 4 types of accommodations they had made to adapt to portal use: (1) modifying note writing, (2) increasing collaborations within the medical team, (3) providing guidance and advice to families about portal use, and (4) adapting workflows to be timelier. Clinicians often described how the benefits were in tension with the problems, which they described as "double-edged swords".

Conclusion: Online patient portals offer benefits and challenges to communication in pediatric and adolescent oncology. Clinicians might leverage portals to improve communication by providing guidance to families before results are released, and by developing new workflows to ensure accurate, adaptive, and timely communication with families. In another arm of this project, we will explore the perspectives of adolescents with cancer and their parents.

POSTER # 009 | A COMPARATIVE ANALYSIS OF THE CLINICAL TESTING AND REPORTING OF METHOTREXATE LEVELS

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Background: Methotrexate is an antineoplastic anti-metabolite commonly used at high doses in pediatric oncology for the treatment of certain malignancies such as osteosarcoma, CNS malignancies and lymphomas. Toxicity from methotrexate is widespread involving multiple systems notably including the gastrointestinal, hematologic, renal, mucocutaneous and neural systems. Glucarpidase reduces the methotrexate concentration by cleaving it into non-toxic metabolites, 4-deoxy-4-amino-N10-methylpteroic acid (DAMPA) and glutamate which are eliminated by the liver. High performance liquid chromatography (HPLC) or liquid chromatography with tandem mass spectrometry (LC-MS/MS) are the gold standard tests for evaluating methotrexate levels as DAMPA cross-reacts with the more commonly used enzyme immunoassay measurements.

Objectives: To review existing literature to compare the methotrexate levels reported via the enzyme immunoassay, HPLC and LC-MS/MS methods.

Design/Method: A review of existing literature limited between the years 2000 and 2022 was conducted utilizing the PubMed database using the search terms "methotrexate" linked with the Boolean operator AND to the terms "high performance liquid chromatography (HPLC)" OR "liquid chromatography with tandem mass spectrometry (LC-MS/MS)" OR "immunoassay". Results were then analyzed for trends between HPLC and immunoassay measurements which recurred consistently throughout the literature.

Results: The initial search resulted in 26 articles. The prominent trends from these articles were discordance between the commonly used methotrexate immunoassays which overestimated the overall methotrexate concentrations compared to HPLC and LC-MS/MS

even when glucarpidase was not administered to patients. Notably, these studies demonstrated a more pronounced overestimation for methotrexate concentrations below 0.2 micromoles/L with a higher coefficient of variance noted at the lower end of the analytical measuring range for the immunoassay levels compared to those obtained by HPLC and LC-MS/MS.

Conclusion: In our pediatric patients the methotrexate threshold for discharge is set to reduce the risk of toxicity. However, from literature HPLC and LC-MS/MS are superior to the more commonly used immunoassay methods which may grossly overestimate methotrexate levels especially at lower concentrations. This is of critical importance as in our pediatric population we run the risk of unnecessarily prolonging hospital admissions thus further disrupting quality of life and so must be accurately balanced with the risk of toxicity to our patients.

POSTER # 010 | THE SAFETY NURSE ROLE: REDUCING ERROR, PROMOTING PATIENT SAFETY DURING CHEMOTHERAPY ADMINISTRATION

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Background: Chemotherapy has the potential for immediate patient harm if not given correctly, therefore reduction in administration errors is a vital element of pediatric oncology nursing. The Safety Nurse role at St. Jude Children's Research Hospital (SJCRH) has been implemented since the mid-1980s. A nurse is assigned this role each shift to review all chemotherapy orders, appointments, and medications prior to a patient being assigned to a bedside nurse. These are the nurse's sole responsibilities for the shift and he or she does not take a patient load. These nurses receive special training in the role, including three shifts of orientation to the roles and responsibilities of verifying chemotherapy orders, confirming protocol compliance, and ensuring correct dosage. This role is unique to SJCRH and is not a universal standard of care per the Association of Pediatric Hematology and Oncology Nursing.

Objectives: This quality improvement (QI) project examined whether the established Safety Nurse role at SJCRH assists in lowering chemotherapy administration errors in pediatric oncology patients receiving chemotherapy in the Outpatient Infusion Center.

Design/Method: Fourteen Safety Nurses participated in the completion of daily assessments that tracked corrections needed to chemotherapy orders and appointments. The tasks of the Safety Nurse are all completed before the administering nurse receives the chemotherapy to give to the patient. For this project, the Safety Nurses tracked the following data points: Electronic Event Reporting System safety reports completed, incorrect orders corrected, additional orders needed, no "okay to give" documented, no order for chemo, no appointment for chemo, and order clarification needed.

Results: Over the course of forty-eight days the Safety Nurses reported 122 total incidents of the surveyed data points occurring. In these same forty-eight days 3,360 patient appointments took place. 3.3% of appointments included orders that required error-correction. These potential errors were caught prior to chemotherapy administration and therefore before any harm could reach the patient. The SJCRH Outpatient Infusion Center has a chemotherapy administration error rate below 1%, compared to the national average of 3%–5%.

Conclusion: Given that during forty-eight days the Safety Nurses caught 122 incidents of potential errors requiring intervention and correction and given SJCRH's lower-than-average administration error rate, it is recommended that a Safety Nurse be utilized in pediatric oncology care to reduce chemotherapy administration error rates. This project confirms the efficacy and benefit of the Safety Nurse role.

Keywords: pediatric oncology, chemotherapy, medication errors, chemotherapy error, safety nurse, outpatient infusion center

POSTER # 011 | PAPER-BASED CHEMOTHERAPY ORDERS TO COMPUTERIZED PROVIDER ORDER ENTRY– A SINGLE INSTITUTE EXPERIENCE

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Background: Electronic health record (EHR) use has significantly increased in the last two decades, reaching 88% in the U.S. by 2021. However, there might be a lag in transitioning chemotherapy orders electronically due to the complexity of chemotherapy treatment. Computerized provider order entry (CPOE) is known to reduce medical errors. Currently, there is no standard approach for transitioning from a paper-based system to CPOE due to various commercialized EHR use, product and software functionality variations even with the same EHR vendor, the complex nature of multi-agent chemotherapy use, and challenges from the constant evolution of chemotherapy treatment protocols.

Objectives: To share the institutional experience of converting paper-based chemotherapy orders to electronic orders within the EHR (Cerner-based).

Design/Method: We describe our multidisciplinary approach to building, validating, and implementing numerous electronic chemotherapy regimens along with laboratory orders and supportive therapy, known as Day-of-Treatment (DOT) Powerplan, which is organized by disease types in the inpatient and ambulatory settings at our children's hospital. We also present our approach to using DOT to standardize the administration of asparaginase products through multiple changes in drug availability and supportive care recommendations.

Results: In 2016, Intermountain Health adopted the commercial EHR product Cerner. In 2019, a multidisciplinary team consisting of clinical expertise (pediatric oncologists, advanced practitioners, pharmacists, nurses, and nursing administrators) and technological expertise (informatics analysts, project managers) was assembled to develop and implement CPOE chemotherapy orders. The go-live occurred two

years later, in 2021. Currently, we have 71 disease protocols with 887 powerplans built and implemented (~84% completed). Safety events related to chemotherapy orders decreased from 26 a year pre-DOT to 16 post-DOT. To standardize the administration of asparaginase products, a vital component of the pediatric acute lymphoblastic leukemia backbone, we were able to update our DOT Powerplans to incorporate newly FDA-approved medications, Calaspargase and Rylaze, as well as standardize supportive care recommendations for the administration of asparaginase products.

Conclusion: Transitioning pediatric chemotherapy orders from a paper-based system to electronic order entry is a highly complex process requiring a multidisciplinary effort. Ultimately, the goal is to eliminate transcription errors and illegibility associated with paper-based chemotherapy orders, standardize electronic chemotherapy orders in inpatient and ambulatory settings, and improve patient safety and provider workflow efficiency. Our institution has nearly transitioned all pediatric chemotherapy orders to CPOE in our Cerner-based EHR. We hope to share our experience with other pediatric hospitals that desire to achieve a similar goal.

POSTER # 012 | ABSTRACTION OF PEDIATRIC CANCER REGIMENS IN HEMONC.ORG FOR THE NATIONAL CHILDHOOD CANCER REGISTRY

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Background: The National Childhood Cancer Registry (NCCR), as part of the Childhood Cancer Data Initiative (CCDI), seeks to connect childhood cancer data from heterogenous sources, including Real World Data (RWD) from central cancer registries and electronic health records (EHRs), to enhance pediatric cancer surveillance and research. However, a major challenge is inferring which treatment regimen patients received outside of clinical trials using RWD. HemOnc.org is the largest freely available resource for chemotherapy regimens, and the HemOnc Ontology serves as a data standard that is useful for automated regimen classification. In collaboration with the NCCR, HemOnc.org is expanding its pediatric regimen content to improve the resource's usefulness for NCCR, CCDI, and the wider cancer data science community.

Objectives: Our objective is to describe pediatric cancer regimen abstraction for HemOnc.org in support of the NCCR.

Design/Method: The HemOnc.org Pediatric Oncology Team consists of 3 board certified pediatric oncologist/informaticists, 1 pediatric oncologist/informaticist in training, and 1 cancer pharmacist/informaticist. The team prioritized regimen abstraction based on current and historical clinical relevance, real world analytics from EHRs and cancer registries, recency, availability of published regimen details, and other factors. Actively enrolling research protocols were excluded. Treatment details abstracted include chemotherapies, radiotherapies, and supportive care if applicable. After regimens are published to the HemOnc.org website, a parser then extracts regimen content into an openly available computable OMOP ontology, allowing reuse by other data systems. HemOnc.org development is funded by NCI ClinCORE consultancies through Westat Inc. and NIH Grant U24 CA265879.

Results: As of January 2023, HemOnc.org contains over 900 content pages, over 250 disease pages, and over 4,000 adult and pediatric cancer regimens. Since 2021, we have abstracted over 70 pediatric regimens, arms and variants, including 27 leukemia/lymphoma regimens, 19 sarcoma regimens, and 15 neuro-oncology regimens, amongst others.

Conclusion: Effective reuse of real-world treatment data from cancer registries and EHRs requires a computable chemotherapy regimen resource. Our work in building pediatric cancer regimen content within HemOnc.org is vital for the future of data-driven pediatric cancer surveillance and research. Challenges include the limited availability of subject matter experts with both pediatric oncology and informatics expertise, publication lag associated with clinical trials data, and incomplete regimen details within publications. Work is ongoing to improve the depth and quality of this community resource, and engagement and participation by the wider childhood cancer community is welcome.

POSTER # 013 | FEASIBILITY OF A PEDIATRIC PHYSICAL ACTIVITY PROGRAM FOR CHILDREN UNDERGOING CANCER TREATMENT

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Background: It is critical for pediatric patients diagnosed with cancer to engage in physical activity (PA) as it may improve physical function and the development of motor skills in early childhood. However, PA opportunities are often limited.

Objectives: To test the feasibility and adherence to a virtual PA program for pediatric cancer patients.

Design/Method: Pediatric patients undergoing cancer treatment were referred to the Pediatric Physical Activity program (PePA) by the Children's Hospital's oncology team using rolling recruitment. The target sample size was 20-25 patients. Eligibility included being 5-18 years old, a referral from the oncology team, ineligibility for physical therapy as determined by the pediatric therapy team, having English literacy and internet accessibility and undergoing active cancer treatment. Patients enrolled in an online 12-week PA intervention with similar-aged peers over 2 rounds (2x/week, 60 min/session) of the intervention. Patients completed surveys where they shared their hobbies and interests and were provided a Zoom link to join. They were given PA equipment (i.e., yoga ball, mat). Trained undergraduate Kinesiology students designed and delivered the PA lessons which included yoga, dancing, calisthenics, and Tai Chi. PA duration (visual inspection of recorded sessions) and intensity (wrist-based heart rate monitors) were measured.

Results: Ten patients enrolled in the study (5, 5-7 years-olds; 5, 13-16-year-olds). One patient from each group completed 95% and 79% of the 24 sessions, respectively. These 2 patients reported improved balance and enjoyment of the program. The teen also reported improved posture. One 6-year-old completed 100% of sessions during the 2nd round and reported improved strength. PA leaders led the 5-7-year-old and 13-16-year-old groups through 29 ± 4 and 33 ± 9 minutes of PA, respectively. Average PA intensity was 25 ± 5% heart rate reserve (HRR) and varied based upon activity. Teens rated their perceived exertion (RPE) of the PA as 2-7 on a scale of 1-10. Three-fourths through the first round, the duration for the 5-7-year-olds was reduced to 45 minutes to match energy levels. Reasons why children did not complete the intervention included: fatigue (n = 1), lack of energy (n = 1), lack of interest (n = 2), no time due to appointments/school (n = 2), already engaged in PA (physical education in school, n = 1), no reason given (n = 1).

Conclusion: PA intensity fell at the lower end of the recommended 30-45% HRR range for adult patients undergoing cancer treatment. Low intensity PA improved balance and strength. Program adherence was difficult to achieve, but those who completed the program reported physical benefit.

POSTER # 014 | PLATINUM COMPOUND ASSOCIATED OTOTOXICITY

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Background: Platinum compounds have been used since the 1970s to treat pediatric cancers. Unfortunately, these effective cancer fighting drugs can cause sensorineural hearing loss. Recently, sodium thiosulfate (STS) has shown promise as an effective otoprotectant. This has led to Food and Drug Administration approval of STS for children ages one month and older who are receiving cisplatin for treatment of non-metastatic solid tumors including brain tumors. Therefore, by understanding the scope of platinum compound associated hearing loss at Dayton Children's Hospital (DCH), it will be possible to assess the need and benefit of adopting the standard use of otoprotectant.

Objectives: The primary objective is to quantify the prevalence of hearing loss within pediatric cancer patients who received platinum compounds, determine the significance of hearing loss following platinum compound chemotherapy, and determine the contribution of additional ototoxic factors such as radiation therapy and other ototoxic drugs.

Design/Method: This study is a retrospective case study of pediatric patients who received platinum compounds between 2010 and 2021. This data was stratified by cancer diagnosis, age at diagnosis of cancer, age at chemotherapy and radiation therapy, platinum compound type received and cumulative dose given, radiation therapy received, additional ototoxic drugs given, hearing aids prescribed, baseline hearing threshold prior to chemotherapy, hearing threshold following platinum compound chemotherapy and change in hearing threshold for the following frequencies: 500, 1000, 2000, 4000, and 8000 hertz (Hz).

Results: Ninety-eight cases met the inclusion criteria; however, sixty-eight had incomplete audiology reports. Of the remaining thirty cases, cisplatin was the most common chemotherapy given and furosemide was the most common ototoxic drug received. Fourteen patients (47%) received radiation therapy. The average cumulative chemotherapy doses were 258 mg/m^2 for cisplatin, 3041 mg/m^2 for carboplatin, and 218 mg/m^2 for oxaliplatin. Nine patients (30%) required hearing aids and a significant change in hearing threshold was noted at 8000 Hz (14.4 ± 20 decibels (dB); p = 0.009). Those requiring hearing aids received higher cumulative cisplatin dosages (273 mg/m^2 vs 249 mg/m^2) and had greater changes in hearing thresholds for all measured frequencies (1.7 vs −0.6 dB 500 Hz, 0.6 vs −0.6 dB 1000 Hz, 2.5 vs 0.0 dB 2000 Hz, 13.1 vs 3.3 dB 4000 Hz, 23.1 vs 10.7 dB 8000 Hz) when compared to those without hearing aids.

Conclusion: Our patient population would benefit from the addition of sodium thiosulfate to the formulary. Incorporation of therapy is anticipated to reduce the incidence of hearing loss by 50%.

POSTER # 015 | FACTORS INFLUENCING DELAYED CLEARANCE OF HIGH DOSE METHOTREXATE IN PEDIATRIC ONCOLOGY PATIENTS

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Background: High dose methotrexate (HDMTX), is frequently utilized in pediatric malignancies. Methotrexate toxicity correlates with its serum concentration, and its area underneath the curve can be mediated by achieving targeted serum methotrexate (MTX) levels at specified times. Despite established administration protocols and supportive care, failure to achieve targeted MTX clearance leads to prolonged intravenous (IV) fluid and leucovorin administration, extended lengths of stay in the hospital, and potential toxicity.

Objectives: To determine the incidence of delayed clearance associated with HDMTX administration in pediatric oncology patients, and to identify modifiable risk factors that could be used to optimize MTX clearance and achieve targeted intravenous fluid duration and hospitalization.

Design/Method: We performed a retrospective chart review between 2010-2017 of oncology patients treated at St. Louis Children's Hospital receiving HDMTX as part of their treatment plans. This population consisted of patients with one of two diagnoses: 1) leukemia, receiving 5 g/m2, and 2) osteosarcoma, receiving 12 g/m2. Data was extracted from both the electronic medical record and paper chemotherapy roadmaps. Relevant data including diagnosis, sex, age, race, concurrent IV medications, IV fluid administration details, urine output over the course of hospitalization were collected. The primary outcome measure was delayed clearance, defined as the failure to achieve the

targeted clearance time (> 48 hours and>72 hours for leukemia and osteosarcoma patients, respectively).

Results: Data from 447 HDMTX administrations (206 leukemia, 241 osteosarcoma) was included and analyzed. Delayed clearance of HDMTX was observed in 52% of leukemia administrations and in 48% of osteosarcoma administrations. Univariate analysis revealed that delayed clearance was associated with the diagnosis of leukemia, using multiple bags of MTX, a higher 24-hour serum MTX level, less IV fluids within the 24—48-hour time interval, and less urine output in the first 24 hours. Multivariate analysis revealed delayed clearance was associated with the diagnosis of leukemia OR = 8.72 (3.13-24.32, p <.0001), the administration of lorazepam within the first 24 hours which suggests more anti-emetic medication demands OR = 3.03 (1.56-5.89, p = 0.001), and increasing number of IV medications from hour 72-96 OR = 2.47 (1.85-3.29, p <.0001). Delayed clearance was negatively associated with increasing number of IV medications from hour 24-48 OR = 0.53 (0.43-0.67 p <0.0001).

Conclusion: Achieving targeted clearance times for HDMTX administrations continues to be a challenge. Understanding the relationship of supportive care medication administration and delayed clearance will provide potential interventions that could be tested to optimize MTX clearance.

POSTER # 016 | DRONABINOL AS AN ANTIEMETIC FOR PATIENTS WITH PEDIATRIC CANCER: A MULTICENTER, RETROSPECTIVE STUDY

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Background: Advances in chemotherapy have allowed pediatric cancer survival rates to increase to more than 80%.[1] However, chemotherapy takes an exceptional toll on quality of life due to adverse effects, of which chemotherapy-induced nausea and vomiting (CINV) is particularly distressing. Dronabinol is a Δ^9-tetrahydrocannabinol with antiemetic properties. However, there are no large-scale studies investigating the safety and efficacy of dronabinol among pediatric oncology patients.

Objectives: This study aims to describe the efficacy and safety of dronabinol when given to pediatric patients to control chemotherapy-induced vomiting (CIV).

Design/Method: We initiated a retrospective, multicenter (6 centers) chart review of pediatric patients with cancer who received dronabinol for CIV management during an inpatient admission between January 1, 2014, and April 15, 2021. Data collected included: dronabinol dosage, dronabinol indication, cancer diagnosis, chemotherapy received, other antiemetics received, adverse effects, and vomiting events. Eligible patients (n = 76) were divided into two groups: 1) dronabinol prescribed for CIV prophylaxis and 2) dronabinol prescribed as needed for breakthrough CIV treatment. Data was collected for the acute and delayed CINV phases for the prophylaxis group and for 6-12 hours post dronabinol dose for breakthrough group. The primary study endpoint, vomiting control, was evaluated for the prophylaxis and breakthrough groups, respectively. Complete control was defined as no vomits or retches.

Results: Most patients (70%) receiving dronabinol for CIV prophylaxis (n = 37; median age 13.5 years (range 3.7-21.1 years), 62% male) did not vomit during the entire acute phase. Similarly, most patients (87%) in the breakthrough group (n = 39; median age 12.7 years (range 0.9-17.8 years), 79% male) did not vomit during the 6-12 hour period after the first dronabinol dose. Two patients (3%) experienced failure to control CIV. Adverse events of minor clinical significance (somnolence, dizziness, euphoria, dry mouth, rash, transient transaminitis) were identified in eight patients. No serious adverse events were identified.

Conclusion: Dronabinol completely controlled CIV in a majority of pediatric patients with few adverse effects of minor clinical significance reported. Dronabinol warrants further investigation in a large, multicenter, prospective, randomized clinical trial to determine its optimal usage for CIV control in pediatric patients.

1. Saletta, Translational Pediatrics, 2014

POSTER # 017 | ASSESSING DEMOGRAPHIC DATA FOR PARTICIPANTS ENROLLED ON NCI PEDIATRIC ONCOLOGY BRANCH PROTOCOLS

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Background: Patients from marginalized racial and ethnic groups are underrepresented in adult oncology clinical trials, but less is known about the patterns of clinical trial enrollment in pediatric oncology. The National Cancer Institute (NCI) Pediatric Oncology Branch (POB) develops novel therapies for children and young adults with refractory cancers. In 2020, the POB Diversity Working Group (DWG) formed to identify and address issues related to diversity. This group identified a need to synthesize centralized POB demographic data to better understand the diversity and needs of our patient population.

Objectives: To describe demographic characteristics of the patients enrolled on NCI POB interventional trials and natural history studies.

Design/Method: An initial dataset was obtained from NIH Central Registration for all POB research participants from 2010-2020, including medical record number, race, ethnicity, primary language, sex assigned at birth, research protocol, and age at enrollment. Home address and diagnosis were not available from Central Registration; therefore, a different database, the Biomedical Translational Research Information System, was used to obtain additional data. This analysis was approved as a Quality Assurance initiative, so was exempt from further institutional review.

Results: Out of 2376 participants aged 1 month to 81 years, the racial distribution was as follows: 64.3% white, 16.1% Black, 4.6% Asian, 0.5%

American Indian/Alaska Native, 0.1% Native Hawaiian, 5.5% multiple races, 9.0% unknown. There was no option for NIH research participants to select "other race". The ethnic distribution was 13.2% Hispanic or Latino, 81.7% not Hispanic or Latino, 5.1% unknown. For reference, 2020 US Census data reported the following distributions for the general population: 61.6% white, 12.4% Black, 6% Asian, 10.2% multiple races, 1.1% American Indian/Alaska Native, 0.2% Native Hawaiian, and 6.2% some other race; 18.7% Hispanic/Latino. Primary language was 91.7% English, 4.6% Spanish, 1.9% other languages, and 1.9% missing. 89.8% of patients lived in the United States and 10.2% were international patients.

Conclusion: Comparing POB research participants to the US general population, Black individuals were slightly overrepresented, while Hispanic/Latino individuals were relatively underrepresented. Reducing the frequency of missing/unknown data is identified as an area for improvement. Furthermore, while self-report for race/ethnicity data is widely considered best practice, it was not possible to determine how demographic data were collected for each POB protocol. The accurate and consistent collection of self-reported race/ethnicity data should be a priority for the field of pediatric oncology. Future analyses will compare racial/ethnic representation by disease and study type to help guide future DWG initiatives.

POSTER # 018 | FITNESS TRACKER USE TO ASSESS PHYSICAL ACTIVITY AND ITS EFFECTS IN PEDIATRIC PATIENTS WITH CANCER

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Background: Though long-term outcomes for pediatric cancer continue to improve, survivors frequently develop treatment related chronic health conditions. Physical activity may improve quality of life (QoL) and decrease chronic health conditions. Research describing physical activity and acceptable interventions to increase it in pediatric patients undergoing chemotherapy is lacking.

Objectives: To describe the physical activity of children and adolescents currently undergoing therapy and evaluate the effects of fitness tracker use (Garmin ® watches). To examine patient reported outcomes including fatigue, pain, and overall QoL.

Design/Method: Participants aged 7-21 years undergoing chemotherapy were invited to participate in a 6 week, single-arm trial. Fitness trackers were worn for 6 weeks. Fitness tracker interfaces were masked (i.e., no visual or auditory feedback) during weeks 1-2 and unmasked during weeks 3-6. During weeks 5-6, participants also received motivational text messages. Number of steps, hours of sleep, and minutes of moderate-vigorous activity were collected from the Garmin ® app for each day the fitness tracker was worn. Pre and post the intervention period participants completed PROMIS ® surveys to assess fatigue, pain, and QoL.

Results: Seventeen participants (35% female, mean age 11.2 years) with 9 different childhood cancers were enrolled. Fitness trackers were worn 76% of study days. Participants had 26.2 active minutes when masked to the interface and 36.7 active minutes when unmasked. They had 3160 steps per day when masked to the interface vs. 3760 when unmasked.

Participant reported and parent perceived reports of fatigue, pain, and life satisfaction ranged from 40-58 on PROMIS® scales (national averages are 40-60). The correlation between parental perception and participant reported fatigue, pain and QoL were 0.75, 0.53, and 0.51 respectively. Lastly, participants slept a median of 8.6 hours each night with an average bedtime of 11:26pm.

Conclusion: Though participants in this small pilot study did not meet the daily recommendations for physical activity, there was a non-statistically significant increase in measures of physical activity when participants could interact with the tracker's interface. Surprisingly, fatigue, pain, and life satisfaction outcomes were within the normal for the general population. There were differences between parental perception and participant reported fatigue and QoL. Participants also slept less than the daily recommendation for age. Overall, results show that fitness tracker use during chemotherapy is feasible and may improve pediatric cancer patient's activity level though larger, adequately powered studies are necessary.

POSTER # 019 | IMPROVING GUIDELINE-CONCORDANT CARE FOR TUMOR LYSIS SYNDROME IN PEDIATRIC ONCOLOGY PATIENTS

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Background: Tumor lysis syndrome (TLS) is an oncologic emergency caused by rapid destruction of cancer cells and release of intracellular contents into the bloodstream. Early intervention and a prophylactic strategy can prevent serious morbidity and mortality. Despite recognition of TLS for decades, there remains significant variation in management such as use of alkalinizing fluids, which is not consistent with current guidelines.

Objectives: We developed a clinical pathway and corresponding order set to identify patients at risk for TLS and provide a data-concordant treatment approach. We aimed to improve adherence to these standards to $\geq$60% and discontinuation of alkalinized fluid use within 1 year of implementation.

Design/Method: A multidisciplinary team was assembled to create a publicly accessible clinical pathway to identify patients at highest risk of developing TLS and its complications. It provides a tiered approach starting with baseline risk assessment associated with a new diagnosis or relapse of a hematologic malignancy or bulky solid tumor, the presence of additional risk factors, and the use of novel agents.

Initial recommendations for laboratory and imaging studies are outlined. Patients without emergent TLS signs/symptoms are assigned to low-, intermediate-, or high-risk groups based on laboratory findings and tumor burden. Patients with emergent TLS signs/symptoms are assigned to the severe-risk group and are recommended for ICU admission with consultation to Nephrology for consideration of renal replacement therapy. Guidelines for IV hydration, laboratory, vital sign and urine output monitoring frequency, and medication prophylaxis are adjusted based on risk category. The pathway also provides guidance on reassessing treatment response and escalation/de-escalation of care.

We provided education to physicians, advanced practice providers, nurses, and pharmacists on use of the pathway and created an order set in the electronic order entry system that directly corresponded to the pathway.

Results: The clinical pathway was published online (https://www.chop.edu/clinical-pathway/clinical-pathway-evaluation-and-treatment-oncology-patients-risk-tumor-lysis-clinical-pathway) on June 11, 2021, and the order set was released on November 1, 2021. In the first 12 months following order set release, pathway utilization was 60% (68 of 114 total patients meeting pathway inclusion criteria), meeting our goal of ≥60% adherence. Isotonic IV fluids were utilized in patients treated per the pathway. Analyses of laboratory monitoring frequency and rates of electrolyte derangements, and ICU transfers are ongoing.

Conclusion: Through a multidisciplinary, multi-pronged approach in a single pediatric center, we standardized TLS management to reflect evidence-based guidelines. Despite challenges including reluctance to change practices, we demonstrate early success in promoting data-concordant care for an at-risk patient population.

POSTER # 020 | STANDARDIZING SDOH SCREENINGS TO IMPROVE COMMUNICATION OF UNMET PATIENT NEEDS ACROSS CARE TEAMS

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Background: Overall survival outcomes for childhood cancers have improved, but disparities persist and may continue to widen. Social determinants of health (SDOH) can contribute to these disparities and significantly impact patients' abilities to obtain a timely diagnosis, receive appropriate treatment, and adhere to therapy. Early identification of unmet needs is critical to support patients and families.

Objectives: This quality improvement project aims to identify patients' unmet needs through a standardized SDOH screening process and to increase medical team awareness of important social and environmental factors that are known to disproportionately impact health care outcomes. Measured goals include increasing the percentage of newly diagnosed oncology or admitted bone marrow transplant patients with an SDOH screen completed within 30 days to 80%, increasing the percentage of screening results reviewed with the medical team to 80%, and increasing the percentage of SDOH notes attested by a provider to 80%.

Design/Method: A multidisciplinary quality improvement team utilized the Model for Improvement with rapid PDSA cycles to test change ideas. An aim statement, key driver diagram, and process flow chart were completed. The team developed an SDOH tool relevant to this patient population, electronic health record note template, and crosswalk document with best practice interventions. Time is reserved at team meetings to discuss screening results and interventions. Annotated run charts are used to evaluate improvements.

Results: Data collection began in February 2022. A nonrandom signal of change indicates improvement in the percentage of patients who received an SDOH screen within 30 days of diagnosis or BMT admission: the current median is 100%. Measures for the percentage of patients' screening results reviewed with the medical team and patients with an SDOH note attested by a provider are also meeting goal. Additional data is collected on the percentage of patients who screen positive, frequency of positive screens for the 11 categories assessed, and percentage of patients who screened positive that received an intervention. Currently, the median percentage of patients with a positive screen that received an intervention is 100%.

Conclusion: Overall, this work has increased awareness of patients' unmet needs and promoted partnership between the medical and social work teams. The ability to quickly identify needs and provide relevant interventions reduces barriers to treatment. Future efforts will focus on integration with the EMR, determining a process for rescreening patients, and spread to additional patient populations.

POSTER # 021 | PEDIATRIC PATIENTS REPORT THE BENEFITS OF VIRTUAL PHYSICAL ACTIVITY DURING CANCER TREATMENT

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Background: Pediatric patients diagnosed with cancer report more barriers to physical activity (PA) and have less opportunities to be physically active than healthy peers. PA supports the development of motor skills, fosters physical and mental growth of the child and may attenuate the side effects of cancer treatment (i.e., cachexia). While PA has been shown to be an important aspect in survivorship care, pragmatic implementation of PA programs is sparse.

Objectives: To create the most beneficial program, we sought to gather information about the experience of participants of the program. In

order to do this, we conducted focus groups with participants and parents following each round of the intervention.

Design/Method: Three focus groups were conducted as part of a pilot study of online physical activity for pediatric cancer patients. The parent study was a virtual group-based (by age) physical activity intervention led by college student leaders. The current analysis includes two participants (plus one parent), with one participant (5-7 year age group) and his parent included at two time points (post 24 sessions and post 48 sessions) and one participant (13-16 year old age group) at one time point (post 24 sessions). Focus groups were conducted for approximately one hour each and were coded by 3 investigators after the first round of the intervention and by two investigators after the second round. Coders met to discuss codes and determine themes.

Results: The following four themes were identified: 1) *physical impacts* (eg., "his balance seemed better and his strength seemed better"), 2) *psychosocial impacts* (eg., "he was a lot more involved in the session, a lot more happy and energetic [when his sister joined the session]"), 3) *delivery feedback* (eg., "knowing how to set-up [for a given session]...that was good. I like that you [program administrator] did that."), and 4) *extrinsic/intrinsic rationale for joining/staying* (eg., "he's getting that set exercise time").

Conclusion: Overall, the participants who finished reported many benefits, with benefits continuing through the second round. Some of the benefits took longer to develop (eg., muscular strength, self-regulation to continue exercising throughout the session). Participants reported being able to do more than they anticipated and also learned when to modify the session and rest. A commonality among completing participants was a high level of social support from household members that was necessary for commitment, engagement and benefit.

POSTER # 022 | PREVENTING INFECTION IN PATIENTS RECEIVING CHEMOTHERAPY: A SURVEY OF PROVIDER RECOMMENDATIONS

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Background: Sepsis is the leading cause of mortality in patients with childhood cancer receiving cytotoxic chemotherapy. To maintain patient health, healthcare providers often recommend following guidelines about hand and dental hygiene and screening visitors for illness, though infectious risk mitigation measures are not universally defined. We hypothesized that variability of infection control recommendations amongst pediatric hematology/oncology/transplant (PHOT) providers leads to delivery of conservative instructions that may impact patient quality of life.

Objectives: To define infection exposure precautions recommended to pediatric patients receiving chemotherapy by PHOT providers, including nurses, advanced practice providers (APPs), fellows and attendings.

Design/Method: An electronic anonymous survey was developed and piloted by a group of PHOT providers to assess providers' methods for educating patients and families on limiting infectious exposures. Five clinical vignettes were utilized to analyze how providers balance the competing priorities of safety and quality of life. The survey was IRB approved and disseminated via email to PHOT providers across the United States. Descriptive analyses were performed.

Results: A total of 535 providers completed the survey, with a response rate of 14.4% (523/3700). The majority of respondents were attending physicians (385, 72%), followed by fellows (60, 11%), APPs (38, 7%), and nurses (36, 7%). Eighty-seven percent of respondents reported standard institutional guidelines for preventing infection in chemotherapy patients with ample resources provided to patients. Eighty-three percent of participants reported that nurses are responsible for relaying discharge instructions to patients, including recommendations for preventing infection. Answers to clinical vignettes varied based on the responder's role, years of experience, and areas of clinical focus. On average, nurses made more conservative recommendations for avoiding infectious exposures compared to the recommendations of attendings. For example, nurses were more likely to recommend virtual school options for patients on chemotherapy while attendings were more flexible in allowing in-person learning. On average, providers with more years of clinical experience expressed more liberal recommendations, while those with less experience provided more conservative recommendations for avoiding infectious exposures.

Conclusion: The high degree of incongruency in responses to clinical vignettes is likely representative of large variations in recommendations given to real patients. This survey demonstrates the importance of collaboration between all members of the care team in defining priorities for balancing safety risk and quality of life in order to provide consistent messaging to patients. Survey response variations highlight the need for universal guidelines to standardize provider recommendations for limiting infectious exposures in pediatric patients receiving chemotherapy.

POSTER # 023 | DEVELOPMENT OF A LOW-RISK FEBRILE NEUTROPENIA CLINICAL PATHWAY USING QUALITY IMPROVEMENT METHODOLOGY

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Background: Febrile neutropenia (FN) is a common side effect of chemotherapy and a major reason for unplanned hospitalizations in children with cancer. Currently patients with FN at our institution are admitted for broad spectrum antibiotics until fever resolves and neutrophils recover, which may take multiple days. Growing evidence supports outpatient management of patients with low-risk FN, and many hospitals across the US have implemented a low-risk FN clinical pathway.

Objectives: Our Global Aim was to develop a low-risk FN clinical pathway for early discharge to decrease complications associated with long

hospitalizations, decrease hospital costs, and improve quality of life. Our SMART Aim was to increase the percentage of children with cancer admitted with low-risk FN who are discharged within 2 days from admission from 0% to 50% over 12 months using Quality Improvement (QI) methodology.

Design/Method: QI tools used included process maps and key driver and Ishikawa diagrams. We previously developed a risk stratification algorithm which was implemented over the prior year. We reviewed the data from the past year and modified the low-risk criteria based on baseline data as well as provider feedback. Interventions included creation of an algorithm for early discharge for patients with low-risk FN, addition of an EPIC smart block for easy documentation, dissemination of the algorithm at several meetings, email reminders and expansion to include all oncology patients. Interventions were evaluated using PDSA cycles.

Results: The low-risk clinical pathway was rolled out in February 2022. From February 2022 to November 2022, there were a total of 117 FN admissions. Seventeen patients met low risk criteria and were eligible for early discharge, and 76% (13/17) of these patients were discharged within 2 days. There were no serious infectious complications in the patients who met low-risk FN criteria and there were no readmissions for fevers or other infectious concerns within 72 hours of discharge in those who were discharged within 2 days.

Conclusion: We were successful in achieving our SMART aim and in developing and implementing a low-risk FN clinical pathway at Rady Children's Hospital San Diego using QI methodology. Future steps include the development of a QI project for outpatient management of patients with low-risk FN.

POSTER # 024 | INFECTIOUS DISEASE RISK FACTORS AND INCIDENCE OF BACTEREMIA AND FEBRILE NEUTROPENIA DURING COVID-19

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Background: Children receiving chemotherapy for cancer will endure periods of significant neutropenia. A subset of these patients develop bacteremia and sepsis, which is the leading cause of mortality in patients with childhood cancer. A child's risk for developing bacteremia is influenced by the presence of an indwelling central line or catheter, depth and duration of neutropenia, and mucosal integrity. Environmental infectious disease risk factors (IDRFs), such as visiting crowded public places, may lead to febrile illnesses, though the relationship between environmental IDRFs and bacteremia has been difficult to study. The mandatory "stay at home" order implemented during the initial response to the COVID-19 pandemic offers a unique period of reduced outside exposures to study this question.

Objectives: We aimed to investigate the incidence of febrile neutropenia and bacteremia among pediatric patients during a period of high exposure to environmental IDRFs compared to a period of low exposure to environmental IDRFs. Given the lockdowns and school closures observed in response to the start of the COVID-19 pandemic, we anticipated the period between March 2020 and March 2021 to have overall decreased exposure to environmental IDRFs compared to previous years.

Design/Method: Using the new clinical and health data platform, ATLAS, developed at Montefiore Einstein, we performed retrospective chart review to compare the incidence of fever, neutropenia, and bacteremia during the pre-COVID-19 isolation period (3/15/2019 – 3/14/2020) and during the COVID-19 isolation period (3/15/2020 – 3/14/2021). Statistical significance was calculated using the two proportion z-test.

Results: The incidence of hospital visits by pediatric patients with cancer decreased by 23% during the initial COVID-19 isolation period (n = 2454) compared to the prior year (n = 3194), although patients presenting with neutropenia accounted for roughly one-third of visits both years. There was a significant decrease in the proportion of patients with febrile neutropenia during the first year of the COVID-19 pandemic (9%) compared to the year prior (12%, $p = 0.03$), although the incidence of patients with bacteremia and febrile neutropenia were comparable (1.7% during vs. 1.4% pre-COVID-19, $p = 0.60$).

Conclusion: These findings show that the incidence of bacteremia did not decrease with lower exposure to environmental IDRFs, suggesting exposure to environmental IDRFs plays a minor role in the development of bacteremia in patients with febrile neutropenia. This has implications for recommendations on activities patients undergoing cancer treatment can safely engage in while neutropenic, and development of consensus guidelines may significantly improve these children's quality of life.

POSTER # 025 | THE IMPACT OF RESPIRATORY VIRAL INFECTIONS IN PEDIATRIC CANCER PATIENTS WITH FEBRILE NEUTROPENIA

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Background: Respiratory viral testing is frequently used in the evaluation of pediatric cancer patients with febrile neutropenia (FN). The clinical significance of a positive respiratory viral panel (RVP) and potential association with adverse clinical outcomes are not well characterized.

Objectives: To determine the prevalence of respiratory viral infections and evaluate their association with adverse clinical outcomes in pediatric cancer patients with FN.

Design/Method: A retrospective convenience sample of pediatric cancer patients with FN from 2009-2022 at a single institution was identified, and 685 episodes of severe FN met inclusion criteria including fever (≥38.0°C), a central line, not already on intravenous antibiotics, and a presenting absolute neutrophil count (ANC) of <500 cells/μl. RVP results, COVID-19 PCR, and rapid influenza antigen results were captured as well as clinical outcomes. Pearson's Chi-square test/Fisher's exact test were used to test the association between RVP and adverse clinical outcomes.

Results: An RVP was performed in 47.9% (N = 328) of episodes and was positive in 41.2% (N = 135). The most common viruses detected were rhinovirus/enterovirus (60%), non-COVID-19 coronavirus (17.8%), parainfluenza (12.5%), metapneumovirus (5.2%), and respiratory syncytial virus (5.2%). COVID-19 was detected in 5% (8/161). Influenza was detected by RVP or rapid antigen test in 2.3% (9/320), however the positivity rate was higher (6.1%) in tests conducted January through March. The RVP was positive for multiple viruses in 4.0% (N = 13), and coinfection with bacteria and virus occurred in 5.2% (N = 18) of patients. A major complication, defined as ICU admission, new oxygen requirement, need for pressor support, or death during the febrile episode, occurred in 7.6% (N = 25). There were no significant differences in complications based on RVP positivity (ICU admission 3.0% with positive RVP vs. 5.2% negative, oxygen requirement [6.7% vs. 5.7%], vasopressor support [1.5% vs. 2.6%], or death during the febrile episode [1.5% vs 0.5%]). Upper respiratory symptoms were significantly more common in those with parainfluenza (88.2%. p = 0.013), rhinovirus/enterovirus (81.5%, p <0.001), non-COVID-19 coronavirus (83.3%, p = 0.013), and multi-viral positivity (100%, p = 0.002) as compared to 59.5% in all episodes with RVP testing. Lower respiratory symptoms were significantly more common in those with parainfluenza (29.4%, p = 0.013), multi-viral (30.8%, p = 0.023), and COVID-19 (37.5%, p = 0.033) vs. 9.1% in all who underwent RVP testing.

Conclusion: RVP positivity is common in pediatric febrile neutropenia but rarely leads to severe complications. COVID-19, parainfluenza, and multi-viral positivity were associated with lower respiratory symptoms in this cohort. A planned larger future study will allow for more virus specific analysis.

POSTER # 027 | NON-NEUTROPENIC FEVER IN CHILDREN WITH CANCER IN A MIDDLE-INCOME COUNTRY

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Background: Infection is one of the significant causes of mortality in children with cancer worldwide. Fever in an immunocompromised patient remains a common complication that requires urgent evaluation and management in outpatient settings during treatment. Prior studies mainly focused on febrile neutropenia. However, limited studies on clinical characteristics, outcomes, and consensus management guidelines in non-neutropenic fever (NNF) patients contribute to variability in practice among limited resource settings.

Objectives: To describe the clinical characteristics, management, and outcomes of pediatric cancer patients presenting with NNF episodes in a single urban academic outpatient in a developing country.

Design/Method: Retrospective chart review of patients $\leq$18 years of age receiving chemotherapy treatment from January 2016 to July 2020. Clinical characteristics, management and outcomes of patients with NNF episodes (body temperature>38°C for 1 hour or>38.3°C once, and absolute neutrophil count (ANC)>500 cells/mm^3) were collected. Descriptive statistics were analyzed.

Results: A total of 41 NNF episodes in 51 patients presenting to the outpatient were documented (M: F = 27: 24). Nearly all participants had no central venous catheter (50/51). The primary cancer was acute lymphoblastic leukemia (51%), solid tumor (17.6%), and medulloblastoma (9.8%). Clinical sepsis occurred in 17.1% of presentations. The common clinically documented infections were respiratory tract infection (56.1%), urinary tract infection (14.6%), gastrointestinal infection (12.2%), and fever of unknown origin (12.2%). The causative pathogens could be demonstrated in only 39% of NNF episodes without any positive hemoculture. The common identified pathogens were virus (21.9%), gram-positive bacteria (9.8%), gram-negative bacteria (7.3%), and atypical pathogen (2.4%). Empiric treatment with antibiotics was administered in 92.7%. Ceftriaxone monotherapy was the most common antibiotic of choice. Using current local practice recommendations, we found that 80% of outpatients with NNF episodes were admitted with a median length of stay of 6 days. Among hospitalized patients, 6% of NNF episodes (2/33) required intensive care, and there was one NNF-related death with Human Boca virus pneumonia with multi-organ failure. The mortality rate was 2.4%.

Conclusion: Within a limited resource setting in Thailand, we found that a majority of outpatient pediatric cancer patients with NNF are hospitalized. The causative pathogen can be identified in 39% of NNF episodes, and the most common identified pathogen was the virus. However, many patients receive intravenous antibiotics and are probably unnecessarily admitted. This study reveals information that can be implemented for future cohorts to improve clinical management and outcomes in NNF patients in similar resourced environments.

POSTER # 028 | INFORMATICS METHODS TO EVALUATE LOW RISK FEBRILE NEUTROPENIA RISK STRATIFICATION MODELS IN LEUKEMIA

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Background: Febrile neutropenia (FN) is a common complication requiring prompt evaluation and treatment. Several prediction models have been developed to identify patients with low-risk FN (LRFN) who may be treated less conservatively, but these models are from single institutions with limited patient numbers, lack geographical diversity and may not be applicable to broader populations. No single prediction rule has been widely adopted. De-identified Electronic Health Record (EHR) data warehouses, such as Oracle Cerner's Health Facts (HF) provide large-scale, geographically diverse populations rich in detail (68 million patients from 100 health systems). Challenges in working with big data exist and detailed research methods for handling data warehouses are limited.

Objectives: Develop reproducible methods for defining a large, geographically diverse virtual data cohort of pediatric patients with acute lymphoblastic leukemia (ALL) and acute myeloid leukemia (AML) with FN and evaluate availability of variables potentially predictive of LRFN.
Design/Method: We conducted a retrospective analysis of HF to identify pediatric patients with ED encounters and ALL or AML using ICD-9 and ICD-10 diagnosis codes from 2009-2017. Clinical and laboratory information for each visit was captured.
Results: Excluding for age <18 years and diagnosis codes, we found 15,244 pediatric patients with ALL or AML, with 1470 patients having 3214 ED encounters after diagnosis. Utilizing a combination of diagnosis codes for FN and clinical events (absolute neutrophil count (ANC) <500 or documented fever), we identified 146 ED patients with 210 encounters having ANC <500 and either documented fever or coded as fever. The majority [190/210 (90.5%)] of encounters meeting strict FN criteria had cultures, with 16 positive cultures (7.6%). For FN encounters with a positive culture, 81% had an ANC <100 and 56% had an absolute phagocyte count <100. The discharge disposition field was inconsistently utilized by the top 10 facilities, with 0 admissions in 3 facilities based on coded disposition, requiring the addition of subsequent clinical events to determine true disposition.
Conclusion: We describe a reproducible method of combining discrete data with diagnosis codes to ensure accurate clinical diagnosis and initial assessment of risk variables. Our methods to validate data included a manual review by informaticians to ensure that discharge disposition was accurately reflected, followed by confirmation using additional clinical events in the 24-hour period after ED visits. Challenges in working with big data were encountered, including variations in implementation of the EHR leading to difficulties in lab naming, units conversion, interpreting discharge disposition field and verifying accurate bacteriology results.

POSTER # 029 | IMPACT OF REPORTED FEVER ON OUTCOMES OF FEBRILE NEUTROPENIA IN CHILDREN WITH CANCER

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Background: Pediatric oncology patients who develop fever at home are frequently evaluated in the emergency department (ED). Many chemotherapeutic agents cause bone marrow suppression resulting in a low absolute neutrophil count (ANC), limiting the patient's ability to respond to infections. These patients are subsequently susceptible to bacterial infection, which may lead to sepsis and death if not promptly treated. Initial manifestation of bacterial infection is often fever. Emergency protocols often require laboratory evaluation, intravenous antibiotics and monitoring for sepsis. ANC is typically used as a marker of immune function and impacts Length of Stay (LOS). There is a subset of oncology patients who present to the ED with a reported fever at home, yet without fever when arriving in the ED. It is important that risk criteria are established to categorize these patients upon ED presentation.
Objectives: To compare ED and hospital LOS in pediatric oncology patients admitted for febrile neutropenia between those with fever only at home and those with both fever at home and on arrival to the ED.
Design/Method: Data was collected from the Quality Assurance Database from the Fever in Oncology Patient Pathway from Connecticut Children's for a cohort of children with ages from birth to 24 years admitted between 2018 to 2021 for febrile neutropenia. Data collected included age, race/ethnicity, temperature, ANC, oncologic diagnosis, ED LOS (minutes) and hospital LOS (hours).
Results: One hundred and ninety-one children presented to the ED with fever at home during the study period, 39% female, 59% male, 11.0% Black, 45.0% White, 6.28% Asian, and 38.2% Hispanic, mean age 8.8 years (+/−6.2). All children were admitted. Children with fever in ED had 262 min ED LOS and those without fever 227 min, $p < 0.05$; fever in ED had 179 hours hospital LOS and those without fever 37.4 hours, $p < 0.01$. Age, sex, and cancer type were not significantly associated with LOS. ANC levels and antibiotic administration times were similar in both groups.
Conclusion: Children with oncologic diseases with fever at home and presented to ED with a fever had longer ED and hospital LOS than children who presented to the ED without a fever. The absence of documented fever in ED could be a low-risk predictor among pediatric cancer patients with febrile neutropenia who present to the ED. Future studies can look at additional outcome variables to establish a greater depth of risk criteria.

POSTER # 030 | EFFICACY OF PALLIATIVE ORAL ETOPOSIDE AND IMPACT ON QUALITY OF LIFE IN PEDIATRIC MALIGNANCIES

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Background: Oral etoposide has been given as palliative treatment for pediatric patients with recurrent/refractory malignancies. There is, however, limited research regarding efficacy of oral etoposide and quality of life (QoL) measures for patients receiving oral etoposide. Existing studies suggest variability in dosing and outcome based on the type of malignancy, as well as the number of lines of treatment received previously. There are no definitive data demonstrating clear benefit of such therapy for overall survival.
Objectives: To assess the efficacy of single-agent oral etoposide given as palliative chemotherapy at Ann & Robert H. Lurie Children's Hospital of Chicago (LCH) and its impact on QoL measures.
Design/Method: We conducted a retrospective chart review evaluating all patients with recurrent/refractory malignancy treated with

single-agent oral etoposide at LCH from May 2010 to September 2021. Efficacy (disease response, duration of survival) and QoL (number of transfusions, clinic visits, outpatient visits, hospitalizations, and length of stay) measures were collected while on oral etoposide. Survival analysis was performed using LIFETEST. QoL measures were compared to the most recent prior treatment using paired two tailed t-tests.

Results: 76 patients received at least one dose of single-agent oral etoposide – 43 had CNS tumors, 29 had extra-cranial solid tumors, and 4 had leukemia or lymphoma. Median survival was 101 days, with a mean survival of 150 days. 48 patients had imaging performed on oral etoposide; 4 (8.3%) had reduction of disease burden, 15 (31.2%) had stable disease, and 29 (60.4%) had disease progression as their best response. There was a reduction in the number of clinic visits ($p = 0.007$), outpatient visits ($p = 0.002$), hospitalizations ($p = 0.02$) and hospital length of stay ($p = 0.01$) compared to the most recent prior treatment.

Conclusion: Our single institution experience suggests that palliative oral etoposide may benefit pediatric patients with recurrent/refractory malignancies based on imaging documenting stable disease or better in a significant proportion of patients and less time spent at the hospital compared to the prior treatment. We recognize that we cannot definitively ascertain survival benefit without a randomized study and that changing from curative to palliative intent of therapy may contribute to the reduction in time spent at the hospital.

POSTER # 031 | PERIPROCEDURAL INTEGRATIVE MODALITIES TO DECREASE ANXIETY AND PAIN IN PEDIATRIC ONCOLOGY PATIENTS

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Background: Pediatric oncology patients have increased rates of anxiety and pain due in part to the number of painful procedures integral to their treatment. Randomized controlled trials have shown guided imagery can decrease anxiety and pain when used in the perioperative period both in same-day and minor surgical procedures. Music and other integrative modalities have similar positive effects.

Objectives: This quality improvement project aims to decrease pain and anxiety in patients undergoing outpatient procedures in the pediatric hematology oncology clinic. Specific goals measured include decreasing weekly percentage of patients requiring OTC pain medications or other pain-relieving measures for postoperative pain by 25% from a baseline of 32% to 24%, decreasing anxiety measured by modified Yale Preoperative Anxiety Scale (mYPAS-SF) score by 25% from a baseline of 30.3 to 23, and providing integrative modalities including Reiki, music therapy, guided imagery, or art therapy pre-procedure to 90% of need-stratified patients.

Design/Method: The Model for Improvement QI framework was used by a multidisciplinary team including physicians, reiki masters, nurses, child life specialists, and nurse anesthetists. An aim statement, Key Driver Diagram, and multiple rapid-cycle PDSAs were utilized. Annotated run charts and Shewhart charts evaluated improvement. COVID complicated the project, causing significant turnover, shifting priorities, and necessitating alternative communication methods to facilitate thorough data collection. Among the numerous change ideas tried, creating a data collection tool for improvement analysis, creating a process to identify need-based patients via the mYPAS-SF tool, and prioritizing patients for treatment on subsequent visits were most impactful. Didactics were offered for teammates, anesthesiologists, and oncology providers.

Results: Data collection began November 2020 and continues through December 2022. Shewhart charts show special cause variation indicating improvement in percentage of patients requiring OTC pain medications or other pain-relieving measures for postoperative pain and anxiety as measured by the average mYPAS-SF scores to 9% and 24 respectively. The goal to reduce OTC pain medication needs or other pain-relieving measures for postoperative pain is being met. There has been a reduction in anxiety observed in patients via the mYPAS-SF score, but goal has not been met. The percentage of need-stratified patients receiving integrative modality treatments also improved to a median of 100% meeting goal.

Conclusion: A systematic approach to enhancing patient care by providing integrative modalities to patients most in need is beneficial in improving pain and anxiety in an outpatient procedure setting.

POSTER # 032 | PALLIATIVE CARE CONSULTATION PRACTICES IN PEDIATRIC ONCOLOGY PATIENTS IN A SINGLE INSTITUTION

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Background: Palliative care consultations in pediatric oncology patients are relatively underused compared to adult oncology patients. However, the importance of early intervention palliative care has been shown to improve quality of life in the adult population and may have the same results in the pediatric population.

Objectives: The aim of this study is to characterize palliative care consultation patterns in pediatric oncology patients at a single institution.

Design/Method: This is an IRB-approved single institution retrospective study from November 2017 to November 2021. Demographics such as age, race, sex, relevant medical diagnoses were collected. Other information collected included the number of days from palliative care consultation to death, duration of palliative care, amount of unplanned time spent in intensive and inpatient care, and amount of medication used for symptom control.

Results: Of the 342 subjects identified, 46 patients received palliative care consults. The average time from diagnosis to consult and unplanned inpatient days for those who received a consult was 450 and 47 days, respectively. Average days number of days from palliative

care consult to death in patients receiving consultation was 47. Of the patients receiving consults, 28% of those patients had relapsed disease.
Conclusion: We anticipate palliative care consultations will be comparable to that of other institutions with palliative care consultations primarily reserved for relapsed or progressive disease and used towards the end of life.

POSTER # 033 | EXPLORING FAMILY PLANNING AND CONTRACEPTION NEEDS OF ADOLESCENT AND YOUNG ADULT WOMEN WITH CANCER

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Background: Adolescent and young adult (AYA) women undergoing cancer therapy have unique sexual and reproductive health (SRH) needs. Sexually active cancer survivors have a threefold increased risk of unintended pregnancy compared to the general US population. Despite this, a small minority of AYA women with cancer use contraception during and after treatment.
Objectives: Our study explores the attitudes and perspectives of AYA women with cancer and their parents related to family planning, contraception needs, and SRH care provision during and after chemotherapy treatment.
Design/Method: We recruited women ages 15-39 years with cancer and/or their parents to participate in individual semi-structured, telephone-based interviews exploring their perceptions of fertility during and after chemotherapy treatment, choice of contraceptive method during and after treatment, and experiences with SRH care provision during cancer therapy. We transcribed interviews verbatim and conducted content and thematic analysis using an inductive approach.
Results: Twenty participants (13 AYA patients and 7 parents; patient age range 16-23 years old) completed interviews. Four major themes were identified: 1) Cancer patients engage in sexual relationships similar to healthy peers yet feel unique relationship stressors related to their cancer. In particular, patients have difficulty navigating disclosure of the impact of cancer and chemotherapy on future fertility to new partners. 2) A cancer diagnosis influences patient's decision-making and preferences regarding contraception, including prioritization of factors such as bodily autonomy and minimizing impact on daily life. 3) The regularity of oncology appointments and the habit of taking scheduled cancer-directed medications at home facilitate adherence to pharmacologic contraceptive regimens; and 4) Patients and parents rely on their oncologist to initiate contraception counseling.
Conclusion: AYA women with cancer voice unique stressors and priorities surrounding sexual and reproductive healthcare during chemotherapy treatment. Both patients and their parents view contraception and SRH counseling as a core responsibility of the oncologist. These data highlight the importance of creating innovative systems of care which support and compel oncologists to address SRH care in AYA women with cancer throughout therapy.

POSTER # 034 | ATTITUDES AND PRACTICES TOWARDS FERTILITY PRESERVATION AMONG HEMATOLOGIST/ONCOLOGISTS IN SAUDI ARABIA: A CALL FOR ESTABLISHING NATIONAL FERTILITY PRESERVATION UNITS

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Background: Fertility Preservation practices have evolved dramatically over the last decade. Incorporating fertility preservation practices are recommended by national and international oncology guidelines. Despite these guidelines, Fertility counseling is either not offered or preservation services and resources are not available.
Objectives: To evaluate the availability of fertility preservation services along with awareness and practices among oncologists in regard to fertility preservation.
Design/Method: The study was a questionnaire-based-quantitative cross-sectional. The study population included oncologists who treated cancer patients of reproductive and childhood age. The questionnaire covered background, the scope of practice, oncologists-patients counseling about infertility risk, and options for fertility preservation. Data were analyzed and compassion of variables was done using a chi-square test.
Results: There was a total of 89 Participants with the majority being Pediatric Hematology/ Oncology physicians (68) in comparison to (21) Adult Oncologists and Hematologists.
96% of Participants had thought and worried about Infertility in their Patients. Only 30% of participants had access to local fertility experts compared to 70% who did not have access. Most referral patterns happen post-therapy (88%) and only (12%) refer prior to treatment. There was a consensus agreement of 100% of the participants that establishing an Oncofertility unit is essential for patients with Cancer.
Conclusion: Establishing a new service such as a fertility preservation unit within the Oncology center is essential. Identifying barriers to opening such units is crucial. Identifying resources in each center and designing initiative that help patients get appropriate counselling is needed.

POSTER # 035 | ESTABLISHMENT OF ROUTINE DEPRESSION AND ANXIETY SCREENING FOR AYAs IN PEDIATRIC ONCOLOGY CLINIC

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Background: Adolescents and young adults (AYAs) with chronic illness are at increased risk for mental illness compared to their healthy peers, with pediatric oncology patients estimated to have a depression rate of up to 33%. Further, subclinical symptoms are also associated with psychosocial impairment and future mental health concerns. Reports of mental health screening in pediatric hematology/oncology clinics are scarce, despite the known impacts of childhood cancer on long-term mental health. We aim to address this gap in care through a quality improvement project in which we pilot the implementation of routine mental health screening in our pediatric hematology/oncology clinic.

Objectives: 1) Evaluate the percentage of eligible patients who complete screening

2) Investigate the rate of positive screens in our patient population

3) Investigate the rate of subclinical symptoms in our patient population

Design/Method: Mental health screening questionnaires were administered to eligible patients during clinic visits at the C.S. Mott pediatric hematology/oncology outpatient clinic over a period of 6 months. The screening tools used were PHQ-A and GAD-7, which have been previously validated and recommended for use in patients 12 years or older to screen for depression and anxiety, respectively. Providers were alerted to positive screens by a member of the clinical team, and surveys were subsequently de-identified for data collection.

Results: Over the first 3-month period, there was a 77% completion rate. Among these, 46% of patients endorsed some symptoms of depression or anxiety as indicated by a score of mild or greater on either survey. For those with a positive screening, 47% scored in the moderate to severe range, reflecting a 22% occurrence of clinically significant scores among those who were screened.

Conclusion: About 22% of our patient population reported moderate to severe symptoms of depression and/or anxiety, indicating clinically significant symptoms. This supports prior knowledge that pediatric oncology patients are at higher risk for anxiety and depression than age-matched peers. An additional 24% reported mild, or subclinical symptoms. Given prior knowledge that even subclinical symptoms can affect wellbeing, these mildly positive screenings also warrant attention. While the surveys are not diagnostic tools and do not reflect the true rates of depression and/or anxiety in our patient population, The prevalence of symptomatic patients supports the need for awareness of mental health needs in AYAs being treated for cancer.

POSTER # 036 | ADDRESSING AGE-APPROPRIATE CANCER CARE FOR ADOLESCENTS AND YOUNG ADULTS

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Background: Adolescents and young adults (AYAs), normally defined as patients between 15 and 39 years of age, are often lost in the healthcare system that concentrates primarily on pediatric and adult cancers[1]. AYA cancer presentation can differ, and treatments are less established compared to pediatric and adult cancers[2]. Many AYA patients are treated in pediatric facilities, which can lead to age-appropriate needs not being met.

Objectives: The goal of this project is to examine the AYA patient experience and assess if AYAs receive age-appropriate care at Cook Children's Hospital in Fort Worth, Texas.

Design/Method: Patient reported outcomes surveys were administered to AYA patients diagnosed between 1/1/2016 and 1/1/2020 with at least one of the following cancers: acute lymphoblastic leukemia, acute myeloblastic leukemia, Hodgkin lymphoma, non-Hodgkin lymphoma, testicular germ cell tumor, ovarian germ cell tumor, or sarcoma. Eighty-five patients were eligible to participate in the study. The survey and chart review included information pertaining to demographics, socioeconomic factors, treatment, and diagnosis-related questions.

Results: Seventeen patients have completed the survey. Patients rated age-appropriateness and quality of care on a five-point Likert scale. On average, patients rated the following aspects of their care as highly satisfactory for age-appropriateness: communication with medical staff ($M = 4.80$, $SD = 0.40$), staff recognition of life events ($M = 4.71$, $SD = 0.46$), provider attitude ($M = 4.86$, $SD = 0.37$), and support provided to their families ($M = 4.82$, $SD = 0.40$). Although still highly rated, the physical environment ($M = 4.38$, $SD = 0.91$) and recreational activities ($M = 4.35$, $SD = 0.87$) were reported to be slightly lower than the other categories for age-appropriateness.

Conclusion: AYA patients face unique challenges related to their cancer presentation and psychosocial needs. Interactions between patients, their physicians, and their environment all contribute to the patients' treatment experience and providing comprehensive, age-appropriate care is important. Overall, patients reported receiving age-appropriate care at Cook Children's Hospital but reported slightly less satisfaction with the facilities and age-related activities. Based on these findings, continuing to establish age-appropriate resources and physical spaces for AYA patients can greatly enhance their quality of care and treatment experience. Beginning in 2016, Cook Children's AYA clinic had already initiated changes to establish supportive resources for AYAs, including creating a designated AYA lounge and implementing more programmatic psychosocial care through psychological interventions and AYA-specific support groups.

1. Alvarez, The Lancet Oncology, 2022
2. Smith, Pediatric Blood & Cancer, 2019

POSTER # 037 | VIEWS OF NON-PHYSICIAN STAKEHOLDERS ON BARRIERS & FACILITATORS TO AYA CANCER CARE IN LATIN AMERICA

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Background: Cancer is the fourth leading cause of death in adolescents and young adults (AYA) worldwide. Although the burden of cancer in AYA has decreased in most of the world in recent years, this is not true for many low- and middle-income countries (LMIC) where over 90% of AYAs with cancer live.

Objectives: This study investigates the needs of AYAs with cancer in Latin America through the perspectives of non-physician health care providers and stakeholders.

Design/Method: Semi-structured interviews were conducted with 30 non-physician stakeholders, including oncology nurses, social workers, nutritionists, psychologists, and non-governmental organization (NGO) personnel, from Mexico, Peru, Central America, and the Caribbean over Zoom. Participants were recruited through previously identified physician liaisons in each country. Interviews were conducted in Spanish and then transcripts were de-identified, translated to English, and transcribed. Using thematic analysis, transcripts were coded and key themes identified until thematic saturation was reached using Atlas.ti.

Results: Thirty participants representing eight countries were interviewed, providing 1202 minutes of transcript data. Participants reported barriers, facilitators, and strategies to improve the delivery of health care for AYAs with cancer in Latin America at the patient, parent, and hospital level. Barriers to care included the following: patient level (e.g. financial barriers, language barriers), hospital level (e.g. costs of providing psychological support, costs of hiring staff), and parent level (e.g. difficulty working with providers and parents, limited health literacy).

Facilitators of care included the following: patient level (e.g. educating patients about their illness, existing support groups), parent level (e.g. educating families), and hospital level (e.g. multidisciplinary services, an initial comprehensive assessment). Finally, strategies included patient level (e.g. more AYA specific treatment sites, providing education for patients), parent level (e.g. more advocacy, social support), and hospital level (e.g. increasing funding and volunteers, more resources within the hospital for providers) factors.

Conclusion: We assessed barriers and facilitators to care for AYAs with cancer in LMIC from the perspectives of non-physician stakeholders in Latin America. Similar to high-income countries, AYAs with cancer in Latin America face challenges due to their age, difficulty with access to care, and lack of an exclusive space for AYA care. Further, AYA patients could benefit from multidisciplinary teamwork. As LMIC build their cancer control programs, it is essential to consider these items when building AYA programs.

POSTER # 038 | PRACTICES OF PEDIATRIC AND AYA FEMALE FERTILITY PRESERVATION CARE IN THE UNITED STATES AND CANADA

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Background: One in four pediatric female oncology patients is impacted by the devastating late effect of infertility. Families should be informed about available options early, such as embryo and oocyte cryopreservation in post-pubertal females. For pre-pubertal females, ovarian cryopreservation is the only available option at this time.

Objectives: To explore the current practices, attitudes, and institutional resources regarding offering fertility preservation to female cancer patients by pediatric oncologists across United States and Canada.

Design/Method: A survey was sent to all Children's Oncology Group Treating Physician Members in the United States and Canada (2190 members). Survey was emailed weekly for 3-weeks via SurveyMonkey.

Results: 296 responses were received (13.5%). Most of the providers do not work at a practice with a dedicated AYA program (61.8%); however, most have a fertility preservation team (63.2%). Approximately half of practices have a gynecologist (53.5%), but only 30.9% staff an endocrinologist.

82.4 % of physicians discuss the possibility of infertility with all patients receiving chemotherapy, but only 12.7% offer fertility preservation to all patients receiving chemotherapy. Approximately half of respondents stated they start offering fertility preservation in post-pubertal patients (56.5%) only, while 7.7% also offer fertility preservation to pre-pubertal patients. 11.8% base the decision to offer fertility preservation on tanner staging with the majority beginning at tanner stage III (85%). However, the majority of respondents feel cancer diagnosis (63.3%) and BMT candidate status (43.4%) are more influential factors to offer fertility preservation conversation than age (26.5%) or tanner staging (17.7%). 43.2% offer fertility preservation irrespective of age. Most fertility preservation discussions occur as part of the overall discussion of treatment side effects (70%), rather than a separate, dedicated meeting (30%). Ewing sarcoma (74.6%), osteosarcoma (69.7%) and transplant candidate status (70%) are the most common cancer diagnoses offered fertility preservation. 72.9% of respondents noted that insufficient time before starting chemotherapy is a barrier to offering fertility preservation. Cryopreservation of eggs is the most offered form of fertility preservation (85.5%) followed by ovarian suppression (77.9%).

Conclusion: The American Society of Clinical Oncology guidelines regarding fertility preservation recommends discussing fertility preservation with all patients of reproductive age and with parents/guardians of children and adolescents if infertility is a potential risk, however, less than 15% of female patients undergoing cancer

treatment are offered fertility preservation. More resources, physician support, and education are needed to overcome barriers, including insufficient time before starting chemotherapy, for female fertility preservation to become universally available to all cancer patients.

POSTER # 039 | AYA NEEDS ASSESSMENT: IDENTIFYING UNMET CAREER/SCHOOL CHALLENGES DURING TREATMENT AND SURVIVORSHIP

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Background: Data from the AYA Hope study shows a cancer diagnosis has a negative impact on work and school for adolescents and young adults (AYAs). However, more descriptive information is needed on specific needs that may not be currently met by hospital care teams. Most research focuses on non-US populations, whose educational/vocational systems can vary, so research is needed with US samples. To address these gaps, the current study uses the recently developed Needs Assessment and Services Bridge (NA-SB) to examine the psychosocial and vocational needs of AYAs using a person-centered approach.

Objectives: The purpose of this study was to expand upon the NA-SB to capture unmet school and career needs of AYA participants in a career-based mentorship program.

Design/Method: The NA-SB was shortened to fit the program and statements were added to assess unmet school and career needs. This adaptation has 9 demographic items and 38 items assessing social support, emotional health, and work and educational needs.

Results: Data collection is ongoing, but 45 participants have completed the assessment from 11 different US hospital systems (59% female, 78% White, 63% in survivorship, M = 19.8 years old, SD = 3.31). Participants reported an average of 18 needs with which they want more help. The most commonly reported were: getting experience in a career field I am interested in (83%), opportunities to network (78%), and figuring out how to plan for my desired career (64%). The least commonly reported were: help with transitioning back to school (22%), engaging me in decision-making about my treatment (23%), and deciding if I should go to a trade school or college (24%).

Conclusion: This adapted assessment provides a more comprehensive representation of the unmet needs of AYA patients and survivors. The highest-rated needs were items added to the adaptation related to school and career preparedness, some of which have not previously been noted in research. Several of the added statements were reported as unmet needs by three times as many respondents as the original statements, which address the care team, emotional health, and peer support. Future research with this data will examine how needs change or differ between participants in active treatment vs. survivorship at varying stages, and how these needs can be addressed. This study contributes to growing literature on vocational needs of AYAs in the US, and how hospital care teams and support organizations can collaborate to mitigate these needs.

POSTER # 040 | IMPLEMENTING EATING DISORDER SCREENING IN ADOLESCENT AND YOUNG ADULT PATIENTS WITH CANCER

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Background: Eating disorders are common in the general adolescent and young adult (AYA) population. The American Academy of Pediatrics recommends yearly screening for eating disorders in AYA patients (15-39 years). Risk factors for the development of an eating disorder include underlying psychiatric conditions, stressful life events, family history, and underlying chronic illnesses.

AYAs with cancer possess several of these risk factors and may be exposed to weight-altering therapies, experience nausea and taste alterations, and have their weight and nutrition emphasized during routine clinical encounters. Collectively, these factors may alter the ability to maintain healthy eating behaviors and impact body image. Cancer treatment interrupts many aspects of their lives, including reducing independence and disrupting their academic, professional, and social activities, which may be additional stressors that increase eating disorder risk. Currently, there is no data regarding the prevalence of eating disorders in AYA patients with cancer. Since cancer therapy disrupts patients' abilities to routinely follow with their primary care physicians, eating disorders may go undetected if screening does not occur in oncology clinics.

Objectives: This is a quality improvement project designed to implement eating disorder screening in AYA oncology patients.

Design/Method: Inclusion Criteria: Patients with an oncologic diagnosis aged 13 years and older were included. Patients needed to be either off therapy or in maintenance therapy.

Exclusion Criteria: Patients with known eating disorders were excluded. Patients receiving maintenance therapy that included steroids were excluded.

Method: During regularly scheduled oncology visits, eligible patients were given the SCOFF questionnaire, a validated eating disorder screening method utilized by general pediatric offices. The questionnaires were scored by a study team member. In the event of a positive screening (score of 2 or greater), the primary oncology team was notified, and the patient was referred to adolescent medicine for further management.

Results: 103 patients completed the SCOFF questionnaire at their routine oncology appointments over a 4-month period. 6 of the 103 patients (5.8%) had a positive screening. All 6 of these patients were referred to adolescent medicine for further resources and work up.

Conclusion: Screening was feasible and acceptable in our pediatric oncology clinic, and results were comparable to the prevalence of eating disorders in the general AYA population. Since AYAs with a history

of cancer are at risk for developing eating disorders, oncology clinics should implement screening in off therapy patients. Further studies are needed to develop appropriate screening methods for on therapy patients.

POSTER # 041 | TOWARDS A STANDARD OF CARE IN ONCOFERTILITY DOCUMENTATION: A QI INITIATIVE AT NYU LANGONE HEALTH

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Background: Advances in pediatric cancer therapy have led to an increased number of patients achieving disease-free long-term survival. In this context, mitigating late effects, such as infertility has become a high priority as successful fertility preservation may be possible. The Pediatric Initiative Network redefined historical risk stratifications and provided a model to help estimate infertility risk and to guide management of fertility preservation. At our local institution, there was no standardized documentation of oncofertility discussion in patient charts.

Objectives: To standardize the documentation of treatment related fertility risk and fertility preservation discussions at cancer diagnosis, utilizing the risk assessment classification of The Pediatric Initiative Network.

Design/Method: We performed one plan-do-study-act (PDSA) cycle introducing a two-section smart phrase in the electronic health record (EHR) program Epic® to standardize documentation. The first section defines fertility risk and the second documents the individualized discussion and fertility preservation plan. An outside expert on fertility preservation, the division oncofertility work group and faculty independently reviewed the smart phrase prior to its utilization. Continued education on fertility risk assessment was given to medical providers to increase compliance.

Results: A cohort including 25 patients with newly diagnosed leukemia in 2021 served as baseline. Eighteen (72%) patients had minimally increased risk (MIR) of infertility and 7 (28%) had a high level of increased risk (HLIR) due to needing a stem cell transplant. Fertility discussion was reported in 10 patients with only 4 (16%) having detailed documentation entered in the EHR at disease progression. The PDSA cycle encompassed 35 new oncologic diagnoses from February to November 2022. In this cohort, twenty-six (74.3%) patients had MIR of infertility, two (5.7%) had significantly increased risk and seven (20%) had HLIR. Oncofertility notes were documented in 14 patients (40%). The subset with HLIR was uniformly offered fertility counseling and preservation options/referral, which were documented at diagnosis, increasing earlier appropriate, detailed documentation from 16% to 40%. Incomplete compliance with smart phrase was related to high prevalence of MIR of infertility in both cohorts, no definitive risk at diagnosis, and lack of fertility preservation options for females and prepubertal patients.

Conclusion: Standardizing oncofertility practice documentation helped identify gaps in patient care while raising institutional awareness. Further PDSA cycles incorporating surveys, educational materials and referral pathways are needed to increase success of cancer-related fertility preservation. QI interventions can provide a framework for intra- and inter-institutional health policies needed to improve practice.

POSTER # 042 | FOUNDATIONS FOR IMPROVING ONCOFERTILITY EXPERIENCE AMONG CHILDREN WITH CANCER AND THEIR FAMILIES

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Background: Infertility is a well-described, potential long-term effect of cancer therapy that may result from a variety of treatment modalities including alkylating agents, heavy metals, and irradiation of the gonads or brain. At Riley Hospital for Children, a dedicated team of Oncofertility providers was initiated to provide consultations over 3 years ago. During this time consult frequency was tracked, but we lack an understanding of what the Oncofertility experience has been for our population and where perceived shortcomings in the consult process may lie.

Objectives: We seek to understand the experience and perceptions of the Oncofertility consult process by interviewing children with cancer and their caregivers. Specific topics to explore included family-centered experience, provider-focused fertility conversation structure, and areas for improvements.

Design/Method: In this qualitative study we utilized a semi-structured interview guide to explore the Oncofertility consult process. Specific areas addressed included planning for and perceptions of the fertility preservation procedure (if applicable), overall perceptions and experience related to fertility preservation discussions, and clinical care. Using the semi-structured interview guide, we interviewed parents/guardians of children with cancer. Interviews were conducted over the phone and audio recorded. Interview transcriptions were analyzed to identify common themes related to both positive and negative experiences and perceptions.

Results: Themes were categorized into perceived usefulness of the consult and perceived improvements to the process. Participants identified perceived usefulness themes such as (1) feeling well-informed regarding the risk of infertility and available options for intervention, and (2) valuing team-based support for navigating decisions about fertility. Perceived improvement themes included (1) desire for a more guided approach to the fertility preservation process, and (2) more opportunity for continued consultation to aid in processing information.

Conclusion: Through this qualitative evaluation, we gained valuable insight into the strengths and areas for improvement. Team-based care was highly valued by participants, and as such supports continued involvement from all members of the multidisciplinary Oncofertil-

ity team. Moving forward, this study highlights the importance of team-based consultations and establishes the need for a new guided approach to working through fertility preservation interventions. Next steps will include design and implementation of a staged consultation process, with specific steps for patients choosing to pursue fertility preservation.

POSTER # 043 | IF YOU DIDN'T DOCUMENT, IT DIDN'T HAPPEN: FERTILITY DISCUSSION AT TIME OF PEDIATRIC CANCER DIAGNOSIS

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Background: Over 80% of pediatric patients with cancer become long-term survivors. After enduring intensive chemotherapy, surgery, and/or radiation, survivors are at risk for long-term and frequently devastating late effects including premature ovarian insufficiency and infertility. Per American Society of Clinical Oncology guidelines, health care providers (HCPs) caring for patients with cancer, regardless of age, should address the possibility of infertility as soon as possible and refer patients interested in fertility preservation to reproductive specialists. Low rates of oncofertility risk discussion and documentation at our institution led us to implement a quality improvement initiative.

Objectives: SMART aim: To Improve infertility risk discussion and documentation in the electronical medical record (EMR) to>70% among all eligible newly diagnosed oncology patients at Children's Health in Dallas/Plano, TX by September 2022.

Design/Method: Plan-Do-Study-Act (PDSA) Cycle 1: EMR and newly diagnosed patients tracking methods (personal communication with inpatient and outpatient teams, data from cancer registry) were utilized to collect information on infertility risk documentation. 9/2018-8/2019 We implemented the "fertility discussion tab" in the oncology history, developed a process map, and assessed available community resources. 9/2020-9/2021 Ishikawa results and sustainability were analyzed. Barriers identified via existing literature and communication with HCPs included discomfort discussing infertility risk at time of diagnosis, knowledge gap in addressing infertility risk and available community resources, and difficulty remembering to include details of this discussion in EMR. PDSA Cycle 2: We created a smart phrase to enable efficient documentation, shared community resources to HCPs, and conducted educational sessions among all providers. Smart phrase was implemented; team reviewed data monthly during implementation phase 09/2021-08/2022. All newly diagnosed oncology patients anticipated to receive therapy were included.

Results: PDSA Cycle 1: N = 206 patients. 170 (82%) had fertility discussion documented in the EMR at the time of diagnosis. Sustainability usage of fertility tab 9/2019-9/2021 was low (<50%). PDSA Cycle 2: N = 161 (68 hematologic, 93 solid; 94 males, 67 females; median age 8yo). 140 (86%) had infertility discussion documented utilizing smart phrase in the EMR. Patients with hematologic malignancies were less likely to have infertility risk discussions documented compared to patients with solid tumors (11% vs 16%).

Conclusion: We exceeded our aim for documenting infertility risk discussion in the EMR for newly diagnosed pediatric oncology patients via implementing smart phrase to ease documentation and collaborating among hematology/oncology, reproductive endocrinology, and information technology. Next cycles will address sustainability and will focus on improving referral pathways to reproductive endocrinology.

POSTER # 044 | HEMOLYTIC UREMIC SYNDROME AS A RARE COMPLICATION IN A CASE OF CASTLEMAN DISEASE

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Background: Castleman disease (CD) is characterized by abnormal reactive proliferation of lymphocytes. It typically occurs in adults in their third decade of life but can also occur in children. Presentation depends on disease phenotype with localized lymphadenopathy in Unicentric CD and a plethora of systemic symptoms in Multicentric CD. Therapy is tailored to the type and presentation with resection being curative in Unicentric CD and immunomodulatory therapy in Multicentric CD. Atypical HUS is a rare but life-threatening complication of Castleman disease.

Objectives: To report a unique case of atypical HUS in the setting of new diagnosis multicentric Castleman disease

Design/Method: This study is a case report to highlight a rare complication of Castleman Disease seen in a pediatric patient

Results: A previously healthy 17 year-old male presented with symptoms that were originally attributed to HUS for 4 weeks prior to diagnosis. He was admitted to the pediatric intensive care unit for persistent fevers, anasarca, pericardial effusion, pulmonary edema, anemia, thrombocytopenia and AKI. Full infectious work up including HHV8 (RT-PCR) and Karius test was negative with exception of EBV (IgG positive and less than 1000 copies on PCR). He was treated for AKI with Eculizumab empirically, several rounds of CRRT and HD with some improvement on renal function but minimal improvement overall. Lymph node biopsy confirmed Castleman Disease, and thrombotic microangiopathy was noted on renal biopsy. He completed Eculizumab course for the atypical HUS. Tocilizumab and methylprednisolone were then initiated with good symptomatic response.

Conclusion: The patient's symptoms were consistent with idiopathic type MCD (iMCD-TAFRO) complicated with aHUS. During his hospital stay, this patient's renal status would momentarily respond to hemodialysis but his overall condition did not improve without consistent daily treatment. After lymph node biopsy confirmed Castleman disease, the patient was started on a combination of high-dose steroids and Tocilizumab with clinical response. Thus while treating patients with renal failure with signs of HUS, it is important to consider the

possibility of Castleman disease. The working hypothesis for this association between these two entities involves VEGF dysregulation in CD as a driver for microangiopathy, but research is ongoing to elucidate this connection.

POSTER # 045 | USE OF NEXT GENERATION SEQUENCING TO ACCURATELY DIAGNOSE HISTOLOGICALLY AMBIGUOUS PEDIATRIC TUMORS

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Background: Bone and soft-tissue sarcomas represent a heterogeneous group of mesenchymal tumors with more than 70 subtypes. Diagnostic challenges may exist due to overlapping clinical and histologic characteristics among certain subtypes. Next Generation Sequencing (NGS) can help establish a precise diagnosis when histologic and immunohistochemistry profiles are ambiguous.

Objectives: This case series describes the use of NGS to diagnose two pediatric patients with histologically and immuno-biologically ambiguous soft tissue mass.

Design/Method: Case Series

Results: Patient 1: A 16-year-old male presented with a six-month history of right lower extremity pain and swelling. MRI revealed a large lobulated mass within the proximal right tibia measuring 10.7 x 10.0 x 7.2 cm. PET scan demonstrated extensive metastasis to the adjacent musculature and distant lymph nodes in the pelvis. Biopsy showed a poorly differentiated small round cell sarcoma that was positive for BCL-6 corepressor (BCOR), CD99, Friend Leukemia Virus Integration Site 1 (FLI1), and Transducin-like enhancer of split 1 (TLE1). Cells were negative for NKX2.2. The immunoprofile suggested a diagnosis of BCOR-sarcoma. NGS results revealed the presence of a characteristic fusion between EWS RNA-binding protein 1 (EWSR1) and FLI1, confirming the diagnosis of Ewing Sarcoma, despite the unusual immunohistochemistry profile. The patient was treated per COG protocol AEWS1221 and is currently in remission.

Patient 2: An 8-year-old male presented with a mass of the anterior chest wall. CT chest demonstrated a lobulated, enhancing nodule within the subcutaneous of the right upper chest measuring 2.3 x 1.9 cm. Histology from surgical resection revealed a well-circumscribed hypercellular tumor composed of groups of large spindle and epithelioid cells with high mitotic activity. Cells were positive for Smooth Muscle Actin (SMA) and negative for FOS and FOSB. A potential diagnosis of proliferative fasciitis was suggested, but sarcoma was considered given the hypercellularity and high mitotic activity. Initial NGS showed chromosomal changes (+2, 7p-, 11q+, and 19p-). Repeat NGS analyses performed at another laboratory revealed zero tumor mutational burden and no chromosomal structural changes, which was more suggestive of a benign soft tissue tumor. The patient is free of disease and continues to receive close surveillance post-tumor resection.

Conclusion: Establishing a precise diagnosis has important prognostic and therapeutic implications. This case series highlights the role of NGS in accurately diagnosing histologically and immunohistochemically ambiguous soft tissue mass.

POSTER # 046 | TAFRO SYNDROME: AN UNCOMMON PRESENTATION IN A PEDIATRIC PATIENT

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Background: TAFRO syndrome, which involves a constellation of symptoms including thrombocytopenia, anasarca, fever, reticulin fibrosis, and organomegaly, was first described in 2010 as a subtype of idiopathic Multicentric Castleman's Disease (iMCD). It typically presents at 50-59 years, and extremely few reports exist in children. As the dysregulation of cytokines and IL-6 drive the disease process, treatment revolves around the use of IL-6 inhibitors, Siltuximbab or Tocilizumab, with or without steroids.

Objectives: Describe a case of TAFRO syndrome in a child.

Design/Method: Case Report

Results: A 12-year-old obese male presented with intermittent fevers to 102F, umbilical pain, vomiting, and diarrhea for 1 month. Labs revealed hemoglobin of 6.3 g/dl with MCV of 85.4fL, reticulocyte count of 2.6, DAT IgG positive, complement negative, low platelets of 112,000/mcL, and normal WBC count. Stool studies were positive for H Pylori but negative for other infectious etiologies and occult blood. Abnormal abdominal ultrasound findings were further evaluated by CT showing diffuse thoracic and abdominopelvic lymphadenopathy with mildly enlarged, nonspecific appearing lymph nodes, hepatomegaly, bilateral nephromegaly, and splenomegaly. Suspicion for leukemia was ruled out with negative bone marrow biopsy and aspiration only resulting nonspecific histiocytic clusters. Further work-up revealed a mild coagulopathy (PT 16.7, PTT 38.5, and INR 1.5), elevated LDH (352 unit/L), elevated uric acid (8 mg/dL), elevated PTH (410.8pg/mL) with hypocalcemia (6.1 ml/dL), and elevated sedimentation rate (106 mm/hr). Autoimmune work-up revealed positive ANA (> = 1:1280), positive Rheumatoid factor (40), high SS-A (> 8), negative DS-DNA, and normal C3 and C4. IL-2 and IL-6 receptors were markedly elevated at 5,953 (normal <838) and (23.70pg/mL (normal <5), respectively. HLH and ALPS genetic panels were also negative. HHV8 IgG titer was negative (<1:20) and VEGF was not elevated (<31). Infectious work-up was negative. While lymph node biopsy was pending, his clinical condition deteriorated developing anasarca, respiratory distress, and fluid overload requiring intubation. Due to suspicion of Castleman's disease and possible autoimmune process, he was started on Tocilizumab 8 mg/kilogram, high-dose steroids, and hydroxychloroquine. He remained admitted for more than 2 weeks until the biopsy resulted. He improved after the first dose of Tocilizumab

and thus steroids were weaned gradually. He was discharged on Tocilizumab and hydroxychloroquine and remains clinically well on this regimen.

Conclusion: Due to overlapping characteristics with other autoimmune processes and paucity of literature, TAFRO could present as a diagnostic dilemma in pediatrics. Early recognition and timely treatment can help prevent significant morbidity as noted in our patient.

POSTER # 047 | RENAL CYSTS IN BLOOM SYNDROME PATIENTS

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Background: Bloom syndrome (BSyn) is a rare autosomal recessive disorder caused by germline variants in *BLM*, which encodes for the DNA helicase RECQL3, leading to chromosomal instability with an increase in sister chromatid exchange. Clinically, BSyn is characterized by small stature, often presenting as infants born small for gestational age, facial anomalies, sun-sensitivity leading to telangiectatic skin lesions, typically on the face, hypo- and hyper-pigmented skin lesions, immunodeficiency leading to recurrent gut and respiratory infections, facial anomalies, and an increased rate of malignancy. The BSyn Registry recently reported that about 53% of participants in the Registry had developed cancer, with hematologic malignancies being the most common. The most common solid tumors were colorectal, breast, and oropharyngeal carcinoma. Wilms tumor was reported in 9 participants or 3.6% of total cancer cases, with patients one to eleven years old at diagnosis. Although the prevalence of Wilms tumor is less than the standard 5% threshold for warranting surveillance, because it is still a significantly higher risk than the general population, experts have continued to recommend abdominal ultrasound at diagnosis and every 3 months through age 8. Interestingly, there is only one published report documenting a renal cyst found as part of a larger workup for a BSyn patient.

Objectives: We describe a case series of four BSyn patients found to have renal cysts in childhood.

Design/Method:

Results: We identified four BSyn patients with renal cysts. Two patients have isolated right renal cysts found at 22 months and 3 years, while the other two patients have multiple bilateral cysts found at 8 months and 21 years. None of the patients have any known renal disease or routinely follow with a nephrologist. The patient with a right renal cyst diagnosed at three years of age also requires a gastrostomy tube for nutritional support and has an ADHD diagnosis, and the patient with multiple bilateral renal cysts found at 21 years of age also has a diagnosis of Crohn's disease and a history of diffuse large B-cell lymphoma. Planned surveillance includes continued abdominal ultrasounds to monitor for changes in number and size.

Conclusion: Renal cysts were found in four BSyn patients, a novel finding warranting further follow up. If more prevalent than previously known, renal cysts could prompt assessment for BSyn in appropriate patients. Additionally, the known association of polycystic kidney patients and increased risk for renal disease, including malignancy, could warrant closer renal follow up for BSyn patients.

POSTER # 048 | HIGH RISK LEUKEMIA FOLLOWING SURVEILLANCE FOR CONGENITAL NEUROBLASTOMA

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Background: Neuroblastomas are the third most common solid tumors in children and the most common abdominal tumor. Congenital neuroblastomas are defined as those detected before 4 months of age. Depending on the findings at diagnosis, many patients can simply be observed and not be treated with systemic chemotherapy. Some children that receive systemic chemotherapy for treatment of a neuroblastoma will subsequently develop a secondary malignancy. In this case, the patient continued to be observed without treatment and then subsequently developed a malignancy.

Objectives: Exploration of subsequent leukemia in a patient with congenital neuroblastoma that had not been treated with systemic chemotherapy.

Design/Method: Patient was born 40 w 1 d, NSVD with an uncomplicated birth and pregnancy. On day 3 of life, a sacral dimple was evaluated by ultrasound, which revealed a left posterior mediastinal mass (25.6 mm x 27.2 mm). MRI validated these findings and found no evidence of metastasis. Urine catecholamines were negative. MIBG was positive only at the mass. Resection was unwarranted. MYC-N status was not determined.

He was defined as INGR stage L1 based on MIBG positivity only at the site of the mass and being under 12 months. The initial mass size was 6.48 cm3. As he was asymptomatic, he was monitored. An MRI at 6 weeks showed an increase of 52% to 13.28m3, it was difficult to determine if it was a growth of the mass. Subsequent MRIs showed no significant growth.

At 1.4 years of age, routine blood work showed white blood cell count 84.0, hemoglogbin 7.8, and platelets 44 with a blast count of 63% with bone marrow aspirate confirming a diagnosis of B-cell lymphoblastic leukemia. He was treated PER AALL1732.

Mother (39), father (?), and brother (15) with no past medical history. Cytogenetics showed trisomy 4, 7, 10, 12, 17, 21, and 22. Initial genetics workup showed 46 chromosomes, XY with a negative Klinefelter workup. Genetics workup is ongoing. He has tolerated his treatment well.

Results: Patient is currently 3 years old and in maintenance and has tolerated his treatment well. Subsequent scans have shown no significant change to his mass. His most recent MRI showed the mass was 2.81

cm3. His further genetic work up will hopefully elucidate an unknown etiology.

Conclusion: This patient highlights the importance of thorough evaluation and monitoring for oncologic process. Of particular interest is that most subsequent malignancies following neuroblastomas occur after receiving systemic chemotherapy and do not occur spontaneously.

POSTER # 049 | NTRK-ASSOCIATED TUMORS, CHALLENGES AND OPPORTUNITIES

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Background: Identifying NTRK fusions in different types of pediatric cancers leads to new opportunities for utilizing targeted therapy. NTRK targeted therapy has shown tremendous advances for neoadjuvant and adjuvant therapy and has shown excellent and durable outcomes.

Objectives: To discuss challenges with diagnosis and access to medication in NTRK-associated tumors.

Design/Method: Three cases of pediatric NTRK-associated tumors are presented. Clinical presentation, immunohistochemistry, molecular testing, treatment modality, and outcome were collected and described.

Results: Case 1- A 10-year-old girl presented with acute lower back pain. MRI showed a mixed solid and cystic spinal mass suggestive of a low-grade tumor. Molecular testing was positive for AGAP1-NTRK2 fusion. She was started on larotrectinib post-symptomatic disease progression. Interruption of therapy due to drug unavailability led to further tumor progression. Symptoms were controlled with the reintroduction of larotrectinib.

Case 2 - A 2-month-old boy presented with left thigh swelling science birth. MRI of leg showed a posterior compartment solid/ cystic mass invading the sciatic nerve. Microscopically the tumor was suggestive of infantile fibrosarcoma. TRK Immunohistochemistry, molecular testing was not available. Local control with wide excision of the tumor with the sciatic nerve. Residual deficits with functional impairments were observed.

Case 3 -A 20-month-old girl presented with right thigh swelling. MRI of the leg showed a solid posterior compartment thigh mass compressing on the neurovascular bundle with anterior displacement of the sciatic nerve. Microscopically the tumor showed a spindle cell tumor with densely cellular neoplasm composed of intersecting fascicles of spindle cells. Molecular testing came positive for LMNA-NTRK1. The patient was started on oral entrectinib for two consecutive months. Disease assessment post-two cycles showed a significant reduction in mass size with less displacement of the sciatic nerve. Local control was successfully done post-two cycles with no neurological sequelae.

Conclusion: The discovery of NTRK inhibitors as targeted agents spared patients from mutilating surgeries such as seen in case two and avoid toxicities with traditional chemotherapies such as seen in cases one and three. Future directions on screening measures, testing and access to medication are essential for the care of these patients.

POSTER # 050 | ADDRESSING CHILDHOOD CANCER DISPARITIES BETWEEN COUNTRIES: A PRE-EXISTING PROBLEM

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Background: Cancer treatment is standardized around the world, however there are still differences in survival and access to treatments. The COVID-19 pandemic made these differences even more evident. According to the World Health Organization (WHO), there are profound inequalities in outcomes in pediatric cancer between countries, showing that only 20-30% of children living in low-and middle-income countries (LMICs) have probabilities of surviving, while more than 80% of children with cancer who are treated with modern multidisciplinary treatments in developed countries are cured.

Objectives: Report cases of pediatric patients diagnosed with cancer in Latin America who then came seeking further medical treatment in the US.

Design/Method: This was a hospital-based, retrospective case-series that identified pediatric patients with any type of malignancy diagnosed and treated outside the US, who in 2021 came seeking further medical treatment in the US.

Results: In 2021, 12 new patients left their countries seeking further opportunities for treatment in our hospital. They were between the ages of 2-15 years old. Five of them had metastatic disease on arrival. They all started treatment around two weeks after being restratified and evaluated by the Hematology/Oncology department. Some examples are described below.

Case 1: Patient diagnosed with recurrent rhabdomyosarcoma of the nasopharynx in Honduras. Told there was no other options to be offered. Brought to the US after recurrence of disease and is now receiving treatment.

Case 2: Patient diagnosed with Burkitt's Lymphoma in January, 2021. Brought to the US from Venezuela given the lack of resources and treatments available in their home country.

Case 3: Patient with Leukemia, brought from Nicaragua after relapsing. Found out once in the US and after relapsing, she was Ph Chromosome positive, and had been undertreated back home.

Conclusion: We should aim for medicine to be collaborative, global, and interconnected. These cases highlight how patients from Latin American countries are facing suboptimal care, and the pandemic further exacerbated a pre-existent issue. Patients in LMICs experienced more frequent unavailability of chemotherapy agents and interruptions in radiotherapy compared to high-income countries. They suffered cancellation of surgeries, radiotherapy, and shortages of essential medicines. Moreover, diagnosis was delayed due to overwhelmed hospital inpatient services and cancellation of essential outpatient services. Increased collaboration is needed to ensure access to state of art medicine for pediatric cancer patients around the world. Strategies

involving global partnerships, multidisciplinary care and research have the potential to create a positive impact.

POSTER # 051 | LATE EFFECTS OF SYSTEMIC DOXORUBICIN ON DETRUSOR CONTRACTILITY IN MURINE MODEL

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Background: Doxorubicin (DOX) based chemotherapy is a common therapy for childhood cancers which is well known to cause various side effects such as cardiotoxicity and cardiomyopathy. However, DOX exposure effects on bladder function have not been fully studied. Our recent clinical study have indicated that childhood cancer survivors with a history of DOX and/or vincristine exposure report increased lower urinary tract (LUT) dysfunction. This dysfunction was more prominent among female patients; however, the mechanism is yet to be understood.

Objectives: The current translational study aimed to investigate the late effects of systemic DOX on LUT function in childhood cancer survivors receiving chemotherapy by studying a murine model of DOX exposure.

Design/Method: After IACUC approval, 3 mg/kg of DOX was administered intravenously to eight female CD-1 mice (starting at 3.5 weeks) for six consecutive weeks (18 mg/kg cumulative dose). Control mice were treated with saline similarly. Five weeks after the final injections, in vitro physiological recording of bladder strips for detrusor muscle (DSM) contractility was performed.

Results: The nerve-mediated DSM contractile responses in DOX exposed mice declined by 56.2% compared to the control group. However, the contractility via cholinergic receptor activation was not significantly different, suggesting neural-specific activity changes. Subanalysis of DSM contractility via nerve stimulation showed significant changes in purinergic and cholinergic pathway contributions. The DOX group exhibited a 51.3% increase in purinergic ($p < 0.05$) and a 52.9% decrease in cholinergic ($p < 0.005$) pathway contributions. Direct activation of DSM by KCl in the DOX group showed a 31.8% reduction in peak force, although the change was not statistically significant. There were no significant changes in bladder weight, DSM baseline activity, and 24-hour urine volume between DOX and the control groups.

Conclusion: DOX exposure in juvenile mice yielded changes in LUT physiology with an increase in purinergic and a decrease in cholinergic contribution to DSM contractility. The final DOX injection and DSM contractility studies were equivalent to the early youth (15-17 years-old) and late youth age groups in humans (20-22 years-old), respectively. Our previous investigations on the early effects of DOX exposure indicate notable impact on detrusor smooth muscle. The present study suggests that bladder neurotoxicity can be seen as part of the later effects of DOX exposure. These findings further support consideration of urological follow-up for LUT function in childhood cancer survivors exposed to DOX.

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POSTER # 052 | SEXUAL DYSFUNCTION IN SURVIVORS OF PEDIATRIC CANCER

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Background: Cancer treatments, delays in psychosexual development, and treatment-related comorbidities can have lasting adverse effects on sexual health in adult survivors of pediatric cancer. Despite this, prevalence of sexual dysfunction has been minimally studied relative to other late effects.

Objectives: To determine patient-reported prevalence of sexual dysfunction in adult survivors of pediatric cancer and examine frequency of patient responses to sexual health questions.

Design/Method: Survivors of pediatric cancer seen in the Vanderbilt REACH for survivorship clinic between 2007-2017 were enrolled on a study that included prospective surveys completed prior to/during their annual visits. Patient demographic, cancer diagnosis, and sexual health data were collected for analysis. To meet inclusion criteria, patients were diagnosed with pediatric cancer before age 26 and were at least age 18 at time of survey completion.

Results: Our dataset included 133 survivors with 57.1% female respondents (N = 76) and 42.9% male respondents (N = 57). Median age was 24 years (interquartile range [IQR] 20-27 years) and a median of 10 years (IQR 7-15 years) post cancer therapy. Cancer diagnoses included hematologic malignancy (47.4%, N = 63), non-central nervous system (CNS) solid tumor (42.9%, N = 57), and CNS tumor (9.8%, N = 13). The response rates for individual sexual health questions varied from 15.1%–89.1% and were lowest (15.1%–30.7%) when patients were asked whether they stopped sexual activity due to symptoms. Of female survivors, 23.1% (N = 12/52) endorsed vaginal dryness, 22.4% (N = 11/49) endorsed lack of sexual desire, and 14% (N = 7/50) endorsed painful intercourse. Symptoms were severe enough to stop sexual activity for 15.8% (N = 3/19) of women experiencing vaginal dryness, 27.3% (N = 6/22) experiencing lack of desire, and 11.1% (N = 2/18) experiencing pain with intercourse. Of male survivors, 4.9% (N = 2/41) endorsed lack of sexual desire, 9.8% (N = 4/41) endorsed difficulty with getting or keeping an erection, and 7.3% (N = 3/41) endorsed delayed ejaculation. Symptoms were severe enough to stop sexual activity for 20% (N = 2/10) of men experiencing erectile dysfunction and 10% (N = 1/10) experiencing delayed ejaculation.

Conclusion: In our patient population, both male and female survivors of pediatric cancer reported sexual dysfunction. High non-response rates for certain sexual history questions could suggest patient sensitivity towards the topic and indicate need for improved screening methods in this patient population. Future areas of study should investigate the relationship between sexual dysfunction and specific cancer

treatments received, other medical late-effects of cancer treatment, psychological wellbeing, and quality of life.

POSTER # 053 | KNOWLEDGE OF FOLLOW-UP CARE AMONG SURVIVORS AND CAREGIVERS: A QUALITY IMPROVEMENT INTERVENTION

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Background: Today more than 400,000 pediatric cancer survivors live in the United States and greater than 60% experience at least one treatment-related late effect. Studies reveal more than half of survivors do not adhere to recommended long-term follow up care. We hypothesized that the majority of solid tumor and brain tumor caregivers/survivors lack knowledge regarding the need for long-term follow up and risks for late effects.

Objectives: By implementing an educational intervention we will 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: Using quality improvement methods we developed an intervention and surveyed solid and brain tumor caregivers or survivors (16 years and older) treated with chemotherapy and/or radiation and 3-24 months off therapy. Survey questions inquired the length of long-term follow up, the reason for life-long follow up and possible late effects. We then provided subjects with the correct answers (lifelong, risk for late effects, and patient specific side effects, respectively). We also explored whether the 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 and prospectively assessed percent change from baseline of the following: correctly acknowledging need for lifelong follow up care, at least two patient specific late effects, how often anxiety is endorsed and rated > 5 out of 10-point scale.

Results: To date, we completed four PDSA cycles with 52 patients (mean age 12 years, 60% female, 67% solid tumor) with a baseline visit, 38 patients with two and 17 patients with three visits. In the 17 patients with 3 visits average time between the first and third visit was 9.8 months (range 6 – 23 months). In this group, correct responses for follow up duration increased from 31% to 69% and to 94%, respectively. Correct identification of at least two late effects increased from 63% at baseline, to 81% and 94%, respectively. Anxiety was endorsed by 44% at baseline and decreased to 25% and 30% at the second and third visits, respectively. Of those who remained anxious at the third visit, 60% of them rated their anxiety at>5.

Conclusion: Awareness for lifelong follow up care among pediatric cancer survivors and caregivers is poor. Our intervention led to a meaningful increase in knowledge while related discussion provoked significant anxiety.

POSTER # 054 | PRIMARY CARE PHYSICIAN PERSPECTIVES ON TRANSITION OF CARE FOR PEDIATRIC CANCER SURVIVORS

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Background: Increasing numbers of pediatric cancer patients are surviving into adulthood yet remain at risk for therapy-related complications. Most cancer survivors receive long term follow up care from a primary care provider (PCP), however, transition of care from the oncologist to the PCP may be difficult or result in gaps in care due to lack of understanding about potential late effects, inadequate resources, and limited provider communication.

Objectives: This study aimed to assess the ways in which PCPs receive treatment-related information and follow-up recommendations for pediatric cancer survivors during their transition of care and understand their perspectives on ways to improve delivery of information.

Design/Method: Licensed PCPs in Arizona were eligible. Participants completed a 20-item questionnaire regarding care for pediatric survivors and preferences about delivery of treatment-related information. Results were utilized to create a tailored treatment summary for transition of care from the oncology clinic back to the PCP. A subset of participants was recruited to participate in focus groups/interviews to provide feedback about the treatment summary. Descriptive statistics were utilized to analyze quantitative data and qualitative data were audio-recorded, transcribed, coded, and analyzed utilizing thematic analysis.

Results: One hundred fifteen PCPs completed online surveys, including family medicine (37.4%), internal medicine (5.2%), and pediatric (57.4%) providers. Majority of PCPs (69%) reported they felt comfortable caring for pediatric cancer survivors. However, 44% reported dissatisfaction with the information they receive from the oncologist and 88% reported needing more information to provide adequate care. PCPs reported receiving survivorship information from multiple platforms, and a majority (94%) of participants felt that more information about treatment-related side effects would be helpful. A subset (n = 10) provided feedback about the treatment summary and delivery of information in focus groups. PCPs described the complexity of care for pediatric cancer survivors and specific themes were identified related to information desired, including presentation of and access to information, relevant content, limitations in communication, and impact of having treatment information on care of survivors.

Conclusion: This study is a unique evaluation of transition of care for pediatric oncology patients from the PCP perspective. Results suggest that the transition of care for pediatric cancer survivors from the oncology specialty setting to the PCP could be enhanced through using a brief, individualized treatment summary inclusive of diagnosis, significant dates, treatments received, survivorship problem list, vaccination status, ICD-10 coding, and patient-specific follow-up guidance. Improved communication can facilitate better surveillance and monitoring for this vulnerable population.

POSTER # 055 | FINANCIAL TOXICITY IMPACT ON HEALTH-RELATED QUALITY OF LIFE OF RETINOBLASTOMA SURVIVORS & CAREGIVERS

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Background: Retinoblastoma (RB) is the most common tumor of the eye in childhood. The Research Into Visual Endpoints and RB Health Outcomes After Treatment (RIVERBOAT) consortium was established to examine health outcomes, including psychosocial, in the contemporary era of RB therapy.

Objectives: To assess financial toxicity and health-related quality of life (HRQoL) of retinoblastoma survivors and their caregivers.

Design/Method: Eligible patients were diagnosed between 2008-2022 and at least 6 months post-treatment at assessment. Caregivers completed surveys assessing their HRQoL (Medical Outcomes Questionnaire Short Form [SF-36]), their child's HRQoL (Pediatric Quality of Life-Cancer Module [PedsQL]), and financial toxicity (Comprehensive Score for Financial Toxicity [COST]). Medical record abstraction was performed for disease presentation and treatment.

Results: Of 375 patients, 214 had unilateral and 161 bilateral disease. Among 536 eyes, using the International Retinoblastoma Staging System, there were 10% A, 19% B, 12% C, 32% D, 23% E eyes and 4% unclassified. Median age (years) at diagnosis was 1.0 (Quartiles: 0.4∼1.9), and at study enrollment was 5.3 (3.0∼9.1), and median time from diagnosis to enrollment was 3.7 years (1.3∼7.5). Sole treatment included systemic chemotherapy (20%), intra-arterial chemotherapy (19%), enucleation (16%), local ophthalmic therapy (21%) and combinations thereof. The SF-36 was completed by 205 caregivers, with median scores of 53.8 (47.9∼59.3) for physical domain and 47.9 (42.6∼51.7) for the mental domain, where higher scores indicate lower disability. PedsQL was completed by 189 caregivers, with a median score of 79 (66.0∼88.0), where higher scores indicate better HRQoL. Caregiver and patient HRQoL did not differ by patient age, laterality, eye group, time since diagnosis, or treatment type. COST was completed by 218 caregivers and the median score was 28.0 (19.0∼34.0), where higher scores (scale 0-44) indicate lower financial toxicity. Association between higher financial toxicity and eye group was significant for group D ($p = 0.027$). We found a significant association between the SF-36 mental domain in each of PedsQL and COST, where a 10-point increase in PedsQL and COST is associated with an increase of 1.7 and 2.0 points in the expected SF-36 mental domain score, respectively. Additionally, a 10-point increase in COST is associated with an increase of 1.7 points in the expected SF-36 physical domain score.

Conclusion: In this cohort of RB patients and their caregivers, reported HRQoL is normal, but there is an association between financial toxicity and impaired HRQoL among patients and caregivers. With ongoing accrual and cohort follow-up, we will assess if this association persists into longer-term survivorship.

POSTER # 056 | DETRUSOR DYSFUNCTION AND MAST CELL ACCUMULATION IN THE BLADDER AFTER VINCRISTINE EXPOSURE IN MICE

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Background: Cytotoxic chemotherapy is the foundation for treating various childhood malignancies and has contributed to incredible gains in pediatric cancer survival. However, this type of therapy is known to have a variety of deleterious side effects. One common chemotherapy agent in children is vincristine (VCR). Despite well-known VCR-induced peripheral neuropathy (VIPN), the impact of VIPN on lower urinary tract (LUT) function remains to be elucidated. Our recent study showed childhood cancer survivors who received VCR and/or doxorubicin reported higher rates of LUT dysfunction (LUTD) than control cohort, warrant further investigation.

Objectives: The aim of this study was to investigate the effects of systemic vincristine (VCR) exposure on lower urinary tract (LUT) function in childhood malignancies using a murine model.

Design/Method: With IACUC approval, male CD-1 mice (3.5-wk-old) received an ip injection of 750 μg/kg of VCR twice per week for 4 weeks. Control mice received saline. At 1 month after the last treatment, LUT and detrusor function were evaluated by in vivo, awake cystometry and by an in vitro physiological recording using bladder strips, bladder histology and gene expression pattern analysis by qPCR.

Results: VCR exposure induced a 6-fold increase in the number of non-void contractions compared to the control ($p = 0.01$). VCR exposure induced a decrease in the detrusor contractility triggered by depolarization of detrusor muscle and nerves besides an increased responses to carbachol and ATP, suggesting that VCR induced a sensitization of cholinergic and purinergic pathway in the bladder. Bladder histology showed an accumulation of mast cells in VCR group by 2.2-fold ($p < 0.05$) without affecting other parameters examined compared to the control group. VCR exposure induced an upregulation of genes associated with mast cell activation, CD117, and TrpV2 (2.3- and 1.7-fold, $p < 0.05$), besides a downregulation of TGFβ1 (0.17-fold, $p = 0.013$) which is known to suppress mast cell activation.

Conclusion: Systemic VCR exposure in juvenile mice induced LUTD alongside an increased activity of cholinergic and purinergic pathways in the bladder. Our data also suggests an involvement of mast cells in VCR-induced LUTD. Our results indicate that systemic VCR exposure impacts LUT function

and therefore follow-up urological assessment would benefit these children who receive VCR as part of their anti-cancer treatment.

POSTER # 057 | CHARACTERIZING SURVIVOR EXPERIENCES IN A PEDIATRIC CANCER SURVIVORSHIP CLINIC

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Background: Childhood cancer survivors (CCS) are at risk for therapy-related late effects and benefit from risk-based surveillance and counseling provided in cancer survivorship clinics. It is imperative to engage CCS and their parents/proxies early in survivorship care to ensure CCS' participation in appropriate lifelong care. However, little is known about CCS and parent/proxy experiences in pediatric cancer survivorship clinics.

Objectives: This study aims to gain insight into CCS and parent/proxy experiences in a pediatric cancer survivorship clinic to understand how to optimize their experiences in survivorship care.

Design/Method: This study will include a convenience sample of CCS ≥ 1 year off-therapy who were <22 years of age when they presented to their annual pediatric cancer survivorship clinic appointment at Children's Healthcare of Atlanta between 12/6/2022 and 3/31/2023. The optional, anonymous surveys are completed by the CCS and/or their parent/proxy upon conclusion of the visit. Surveys include multiple-choice, Likert-style, and free response questions that evaluate the first and overall survivorship clinic experiences, amount of information provided during the visit, self-report of past and current CCS health, and level of concern about future health. Descriptive statistics were used to summarize cohort characteristics.

Results: Through 1/11/2023, 46 respondents (11 CCS, 35 parents/proxies) have participated. Not all respondents answered every question. Of the CCS represented, mean CCS age at survey completion was 13.6 ± 4.6 years and 34/46 (74%) were female. The most common diagnosis was leukemia (19/46, 41%). This was the first survivorship clinic visit for 18 CCS (18/46, 39%). The majority of respondents (73%) had received information about the survivorship clinic prior to the first visit, most often through their primary oncologists. Thirty-seven of 42 (88%) respondents felt the amount of information presented at the survivorship clinic visit was appropriate, and 39/41 (95%) reported feeling more informed about the long-term health of the CCS after the visit. When evaluating CCS' health, 34/40 (85%) of respondents reported good health prior to the first survivorship visit (responses of "excellent", "very good", or "good"), 45/46 (98%) reported good health at the time of survey, and 23/46 (50%) of respondents noted ongoing concern for the health of the CCS.

Conclusion: Our early findings demonstrate that CCS have positive experiences in survivorship clinic. Characterizing the pediatric cancer survivorship clinic experiences of CCS and their parents/proxies is a critical first step in determining ways to optimize survivorship care delivery, facilitate engagement and retention in survivorship care, and improve CCS' long-term health outcomes.

POSTER # 058 | IMPLEMENTATION OF MENTAL HEALTH SCREENING TOOLS IN PEDIATRIC ONCOLOGY SURVIVORSHIP CLINIC

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Background: Survivors of childhood cancer are at increased risk for depression and anxiety. The Children' Oncology Group Long-Term Follow-Up Guidelines recommend a yearly psychosocial assessment with attention to depression; anxiety; post-traumatic stress; and suicidal ideation. The feasibility of implementing formal psychosocial screening tools in a pediatric oncology survivorship clinic is unknown.

Objectives: The aim of this project was to integrate the use of validated screening tools for anxiety and depression into the workflow of a comprehensive pediatric oncology survivorship clinic.

Design/Method: A review of the literature and consultation with the psychology team identified the Patient-Reported Outcomes Measurement Information System (PROMIS) short forms for anxiety and depression as appropriate screening tools. The survivorship clinic nurse administered the screening tools via the PROMIS iPad application and notified the provider seeing the patient if either assessment was positive. This prompted a conversation between the provider and patient about referral to mental health services.

Results: Among 239 eligible patients over a seven month period, 88 (36.8%) were screened. This included a two month window in which the survivorship clinic did not have nursing support. During the months with a full time nurse, 70 of 132 eligible patients (53%) were screened. Among the 88 patients screened, 44 (50%) screened positive for anxiety and/or depression: 21 (23.9%) for anxiety only; 4 (4.5%) for depression only; and 19 (21.6%) for both. 30 patients who screened positive for anxiety and/or depression had documentation of a conversation about their mental health in the electronic medical record. After this conversation, 11 patients were given counseling referrals or resources; 8 patients were determined to not need counseling; and 7 patients were already established with mental health professionals. The clinic nurses found the PROMIS screening tools easy to administer, and the providers thought the screening results helped initiate a conversation with patients regarding their mental health.

Conclusion: The implementation of anxiety and depression screening tools into pediatric oncology survivorship clinic is feasible when adequate staff is available. The PROMIS iPad application is easy for staff and patients to use and provides immediate screening results. The combination of the screening tool and

conversations with patients allows providers to identify patients who need mental health support and provide appropriate referrals and resources.

POSTER # 059 | CHARACTERISTICS OF CHILDHOOD CANCER SURVIVORS ATTENDING A SURVIVORSHIP CLINIC IN THE DEEP SOUTH

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Background: Childhood cancer survivors carry an inordinately high burden of late-occurring treatment-related morbidity such as subsequent neoplasms and cardiac compromise. Long-term risk-based anticipatory surveillance is critical to allow for early detection and timely management of complications. The Taking on Life after Cancer (TLC) Clinic at Children's of Alabama (CoA) provides risk-based care to childhood cancer survivors, beginning at 2y after therapy completion and has no upper age limit. All eligible survivors are invited to attend the clinic.

Objectives: We sought to examine the demographic and clinical characteristics associated with TLC attendance for children living in the Deep South.

Design/Method: Our cohort included 1,122 TLC eligible patients diagnosed with cancer at CoA between 2000 and 2016. Our outcome of interest was ≥1 TLC visit. Univariable logistic regression modeling assessed cancer type, treatment era, age, sex, race/ethnicity, payer plan, rural/urban residency, and distance from clinic. Significant variables (P <0.1) were retained in multivariable modeling; associations were reported as adjusted odds ratio (aOR) with 95% confidence intervals (95%CI).

Results: For the eligible cohort the median age at diagnosis was 7y (0-19); 47% were females and 69% Non-Hispanic Whites, 25% African Americans, and 6% other races/ethnicities. Cancer diagnoses included ALL (26%), CNS tumors (20%), solid tumors (33%), AML (5%), lymphomas (14%) and other (3%). Fifty-three percent of the cohort (N = 588) attended TLC. Multivariable analysis revealed recent diagnosis era (> 2009: aOR = 3.05, 95%CI = 2.31-4.03, P <0.0001; reference: </ = 2009) to be associated with higher odds of attending TLC. Patients diagnosed with cancer at an older age ($aOR_{\_per\_1y\_inc}$ = 0.89, 95%CI = 0.87-0.91, P <0.0001) were less likely to attend the clinic as were those diagnosed with CNS tumors (aOR = 0.17, 95%CI = 0.11-0.24, P <0.0001; reference: leukemia/lymphoma), solid tumors (aOR = 0.58, 95%CI 0.42-0.79, P <0.0006), or other rare cancers (aOR = 0.32, 95%CI 0.14-0.75, P = 0.009). Those lacking private health insurance were also less likely to attend (aOR = 0.61, 95%CI 0.47-0.80, P = 0.003). Finally, greater distance between residence and clinic ($aOR_{\_per\_25\_mile\_inc}$ = 0.90, 95%CI = 0.84-0.95, P = 0.0007) was associated with lower odds of TLC attendance.

Conclusion: Just over half of the eligible childhood cancer survivors treated in the Deep South attended the specialized survivorship clinic. This study identified several barriers to attendance, including traveling long distances to care and public or no insurance. In addition, older age at diagnosis and those with certain cancer types were less likely to attend. While the underlying reasons for lack of attendance are likely diverse, they do present an opportunity to develop intervention strategies to ensure that all eligible patients receive optimal long-term follow-up care.

POSTER # 060 | CLONAL HEMATOPOIESIS IN CHILDHOOD CANCER SURVIVORS: WHO IS AT RISK?

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Background: Childhood cancer survivors face long-term health effects as a consequence of treatment, namely, an accelerated aging phenomenon and, while rare, treatment-related myeloid neoplasms (tMN). Clonal hematopoiesis (CH) is an aging-related process which in adults is a well-established precursor to myeloid malignancy and independently confers increased all-cause mortality. In an effort to define the rates of CH in childhood cancer survivors, we consented/enrolled a cohort of 305 pediatric patients with a wide variety of diagnoses, exposures, and time from therapy. Cross-sectional analysis completed on 287 patients revealed 22 variants in 7 unique genes among 17 patients (CH rate of 5.9%).

Objectives: To highlight the importance of studying CH in all childhood cancer survivors, not just those perceived to be at greatest risk of tMN, we present the case of a now 15 year old Hispanic male survivor of standard risk pre-B acute lymphoblastic leukemia (ALL) with evidence of traditional clonal hematopoiesis detected six years from completion of therapy.

Design/Method: Genomic DNA was isolated from peripheral blood mononuclear cells and analyzed by a CH-specific targeted NGS panel (Vanderbilt VANTAGE) covering 24 genes commonly associated with adult CH. An average sequencing depth of 400X enabled variant allele frequency (VAF) detection as low as 1%. Raw data was aligned with BWA-MEM and analyzed with Terra Bio CHIP Detection workspace following GATK best practice guidelines; CH calls were manually adjudicated. Patient clinical variables were extracted from the electronic medical record.

Results: While most patients who exhibited CH had a single genetic mutation at varying VAF (1-48%), one patient harbored mutations in ASXL1, TET2, and TP53 with VAFs of 1.2-2.7%. He was initially diagnosed at four years of age and received therapy as per COG AALL0331 (total dosages: 1gm/m2 cyclophosphamide and 75 mg/m2 doxorubicin). His treatment course was uncomplicated and he has no known cardiac toxicity or other late-effects. Family history was significant for a father with polycythemia, paternal uncle with leukemia in childhood (deceased at 28yo), and paternal grandmother with lung cancer.

Conclusion: We present an example of a patient bearing no traditional risk factors associated with tMN who now six years post-therapy has evidence of traditional CH. Further studies are ongoing to define if mutations are co-occurring at the single cell level and may inform the risk of malignant transformation. This case highlights the need for expanded longitudinal sampling of all childhood cancer survivors in order to better understand the risk that CH may portend.

POSTER # 101 | TRANSCRIPTOMICS REVEALS EMT AS A POTENTIAL DRIVER OF MYELOID SARCOMA

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Background: Myeloid sarcomas (MS) are extramedullary tumors of myeloid blasts forming masses, disrupting normal tissue architecture in patients with acute myeloid leukemia (AML). The incidence of MS in pediatric AML is estimated to be as high as 40% with unclear impact on prognosis. Little is known about the critical molecular underpinnings of MS development. Specifically, gene expression changes which promote MS have not been described previously and may have therapeutic implications. Additionally, anecdotal evidence with MS suggests potential resistance to immune based therapies such as allogeneic hematopoietic stem cell transplant (allo-HSCT) emphasizing the importance of better understanding MS development.

Objectives: To determine if there are specific gene signatures present within MS compared to intramedullary/bone marrow AML.

Design/Method: Bulk RNA sequencing was performed on formalin-fixed and paraffin-embedded (FFPE) (adult human, patient-derived) or frozen (mouse) paired MS and bone marrow trephine/whole bone marrow specimens. Differential expression analysis and gene set enrichment analysis (GSEA) was performed. *Npm1*$^{cA/+}$;*Smc3*$^{+/-}$ mice were used which spontaneously generate MS to validate the findings in patient samples with less contaminating tissue sequenced with a known genetic driver mutation.

Results: GSEA was used to identify pathways different between human MS samples and paired bone marrow. The top ranked gene set upregulated in MS was Epithelial Mesenchymal Transition (EMT) . Importantly, a mouse model of AML using *Npm1*^{cA} also had EMT as the most enriched gene set. Key EMT transcription factors were evaluated and demonstrated significantly increased expression of Twist1 in both human and mouse MS.

Conclusion: Both patient-derived and mouse MS compared to bone marrow AML demonstrate an EMT like gene signature independent of AML driver mutation. Whether this is a critical mechanistic driver of MS development or a consequence of microenvironment influence on the leukemic cells is not yet known. Twist1 is not normally expressed by hematopoietic cells and its role in MS is not well described. Our ongoing studies will evaluate the necessity of Twist1 on MS development in vivo and the impact of the MS tumor microenvironment with particular interest in the potential treatment resistance of MS to allogeneic transplantation. Given the high incidence of MS in pediatric AML, understanding the mechanisms of development are key to improving and targeting therapies.

POSTER # 102 | SINGLE-CELL RNA ANALYSIS FOR RISK STRATIFICATION OF INFANT ACUTE LYMPHOBLASTIC LEUKEMIA PATIENTS

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Background: Infants less than one year old suffer poor outcomes when afflicted by Acute Lymphoblastic Leukemia (ALL), largely owing to high rates of relapse. Those cases with genomic rearrangement of the *KMT2A* gene (*KMT2A*-r) have the highest risk of relapse. Despite numerous advancements in the study of ALL, little is understood about the contributing molecular mechanisms of resistance which has limited the ability to predict relapse in infant patients with ALL.

Objectives: In this study, we attempt to improve risk stratification of infant patients with *KMT2A*-r ALL by using single cell RNA sequencing (scRNAseq) to identify cells that may be treatment resistant.

Design/Method: Previous research has identified 84 genes associated with resistance to, and 369 genes associated with susceptibility to, in vitro prednisone treatment of ALL samples. Using scRNAseq, we were able to quantify expression of these genes in each cell individually from our 25 samples. Based on the expression of genes in each list, we assigned "resistance" and "sensitivity" scores to classify cells as "Prednisone Resistant" or "Prednisone Sensitive."

We repeated this process to classify cells as "Quiescent" or "Proliferative" using a published list of 559 genes associated with Hematopoietic Stem Cell (HSC) Quiescence and 466 genes associated with HSC Proliferation.

To explore the relationship between cell cycle phase and treatment resistance, we assigned cells one of three Cell Cycle Phases (G0/G1, S, G2/M) using Seurat's Cell Cycle Phase assignment function.

Results: We confirm that patients who relapse tend to have a higher proportion of "Prednisone Resistant" cells at the time of diagnosis (32% of cells in relapse cases vs 15% of cells in non-relapse cases, $p = 0.012$). We found that patients who relapse typically have higher proportions of "Quiescent" cells at time of diagnosis, evidencing a potential contributing mechanism of resistance (26% of cells in relapse cases vs 13% of cells in non-relapse cases, $p = 0.003$.)

We found that patients with high proportions of G0/G1 cells that are classified as "Prednisone Resistant" were more likely to relapse. By combining Cell Cycle Phase and Prednisone Resistance, we were able to refine our risk stratification such that 100% of the "High Risk" patients were those with relapse, whereas only 50% of the "Low Risk" patients experienced relapse ($p = 0.0052$).

Conclusion: These findings have the potential to improve prediction of relapse risk at time of diagnosis and to allow for more effective treatment of infant patients with ALL.

Candelli *et al*, Leukemia, 2022
Venezia *et al*, PLoS Biol, 2004

POSTER # 103 | ESTROGEN EXPOSURE MODIFIES GLUCOCORTICOID RECEPTOR ACTIVATION IN B-LYMPHOBLASTS

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Background: Adolescents and young adults with acute lymphoblastic leukemia have decreased chemotherapy responsiveness and a dramatically lower overall survival than younger children. A myriad of biological and psychosocial factors is hypothesized to contribute. Our preliminary data suggest that β-estradiol exhibits a biological effect on lymphoblasts. Others have described cross-talk between estrogen receptor alpha (ERα) and the glucocorticoid receptor (GCR) at the chromatin level, suggesting a genomic or epigenomic interaction. We hypothesize that exposure to β-estradiol (BE) in the bone marrow microenvironment alters the chemotherapy responsiveness of lymphoblasts, and that this can be targeted to therapeutic benefit.

Objectives: To determine the impact of BE exposure on cell proliferation and chemotherapy resistance in acute leukemia cells.

Design/Method: Ribosomal-RNA depleted RNA libraries were constructed and sequenced from cells exposed to 10 nM BE versus vehicle control to determine the impact of BE on the lymphoblast transcriptome. Cells were treated with a range of BE doses and quantitative PCR analyses of the GCR and ERα were undertaken. Cell proliferation was measured using MTS and BRDU assays. To specifically assay the effect BE has on GCR activation, western blot analysis was performed on total GCR, phospho-Ser211 GCR, and phospho-Ser226 GCR after exposure to varying concentrations of BE. Immunofluorescence was utilized to track changes in subcellular localization of GCR after drug and hormone exposure.

Results: We identify leukemia cells that endogenously express ERα and ERβ. Surprisingly, we identified negligible transcriptomic effects of physiologic BE exposure, and we specifically find that exposure to both physiologic and supra-physiologic doses of BE does not alter the expression of ERα or the GCR. In addition, exposure of ERα or ERβ expressing leukemia cells does not alter cell proliferation. However, we do find that physiologic doses of BE result in an immediate increase in phosphorylation of Ser211 on the GCR (an activating post-translational modification), and decreased phosphorylation of GCR Ser226 (a repressive post-translational modification) in an ERα expressing leukemia cell line. This corresponds to a trend in increased phosphoERK/ERK, with GCR phosphorylation being a known target of phosphoERK.

Conclusion: It is unlikely that BE is exhibiting a direct transcriptional effect on leukemia cells. However, we present evidence suggesting that BE at physiologic concentrations may impact the glucocorticoid responsiveness of acute leukemia by modifying the activation and function of the GCR. Future studies will examine the impact of β-estradiol on dexamethasone sensitivity.

POSTER # 104 | BEYOND SOLID TUMORS: A PREVIOUSLY UNRECOGNIZED ROLE FOR SIX1 IN PEDIATRIC ACUTE LEUKEMIAS

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Background: The *CALM-AF10* translocation is found in 5-10% of T-cell acute lymphoblastic leukemias (T-ALL) and some acute myeloid leukemias (AML) and is associated with poor outcomes. *CALM-AF10* leukemias, like *KMT2A*-rearranged leukemias found in infants, are characterized by increased *HOXA* gene expression. To identify novel target genes, we performed next generation sequencing on *CALM-AF10* transduced hematopoietic stem cells (HSCs) and murine *CALM-AF10* leukemia cells treated with the CRM1 inhibitor Leptomycin B (LMB), which impairs CALM-AF10 binding to *HOXA* genes. Eleven genes were common to both sets, including 7 *Hoxa* genes and the *Six1* homeobox gene. While SIX1 and its cofactor EYA2 are overexpressed in solid tumors, the role of SIX1 in leukemias is less defined.

Objectives: Evaluate the role of SIX1 in Acute Leukemias

Design/Method: SIX1 gene and protein expression were assessed in *CALM-AF10*, Jurkat T-ALL and NOMO1 AML leukemia cell lines. *SIX1* expression vectors were transduced into fetal liver HSCs and immortalization was assessed using colony assays. shRNAs targeting *Six1* were retrovirally transduced into *CALM-AF10* leukemia cell lines. Cell-Titer-Glo assays were used to assess the effects of shRNAs and an inhibitor of the Six1/Eya2 interaction (compound 8430) on cell proliferation. Synergy was assessed using SynergyFinder2 (https://synergyfinder.fimm.fi/) between the CRM1 Nuclear Export Inhibitor KPT-330 and 8430.

Results: SIX1 gene and protein expression were increased in *CALM-AF10* and Jurkat, but not NOMO1 cells. SIX1 overexpression in fetal liver hematopoietic stem cells was sufficient for immortalization. Six1 knockdown in *CALM-AF10* leukemia cells decreased cell proliferation. Additionally, compound 8430 decreased proliferation and growth of *CALM-AF10* and Jurkat cells, with limited effect on NOMO1 cells. The addition of KPT-330 to 8430 was synergistic in *CALM-AF10* cells and, to a lesser degree, in Jurkat cells.

Conclusion: The *SIX1* homeobox gene is highly expressed during development, and its expression is silenced post-embryogenesis. Through an unbiased screen, we discovered that *Six1* is upregulated in the presence

of CALM-AF10. We showed SIX1 is sufficient for the immortalization of hematopoietic stem cells, and that it contributes to the proliferation of *CALM-AF10* leukemia cells. A role for Six1 in *CALM-AF10* leukemogenesis is further supported by the ability of a SIX1/EYA2 inhibitor to slow the proliferation of *CALM-AF10* leukemia cells. Importantly, based on our observation that 8430 also slows proliferation of Jurkat cells, SIX1 inhibition may be relevant in other leukemias. Finally, our demonstration that 8430 synergizes with the Nuclear Export Inhibitor KPT-330 suggests the possibility of a novel therapeutic approach for *CALM-AF10* and other pediatric leukemias.

POSTER # 105 | DEVELOPMENT & VALIDATION OF CYTOKINE-INDUCED MEMORY-LIKE NK CELL PRODUCT FOR RELAPSED/REFRACTORY AML

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Background: Relapsed and refractory acute myeloid leukemia (RR-AML) is challenging to treat, with 5-year survival of 35%. Hematopoietic stem cell transplant (HSCT) offers the potential for long-term cure when performed in patients who reach significant tumor burden reduction without multiorgan damage before transplant. Cellular therapies may offer the potential of salvaging patients with refractory or relapsed disease after conventional chemotherapy with tolerable toxicity and represent a true alternative as a bridge to transplant. Cytokine-induced memory-like natural killer cells (CIML-NK), which rely on stimulation with IL-12, −15, and −18, have been recently described as a successful approach to induce transient complete remission in adults with AML.

Objectives: The goals of this trial are: 1. To determine the safety and feasibility of the CIML-NK cells infused into young adults with relapsed/refractory AML; and 2. To develop a functional assay potentially capable to predict in vivo efficacy.

Design/Method: This is an ongoing investigator-initiated, open-label, phase 1/2 trial of safety and feasibility of haploidentical donor CIML-NK cells generated in our institution in young adults with RR-AML within a 3+3 dose-escalation study design. Planned dose levels are 1) $1x10^6$ CIML-NK cells/kg, 2) $3x10^6$ CIML-NK cells/kg, and 3) $6x10^6$ CIML-NK cells/kg.

Results: Following two development runs (PQ-0527, −0552), three scaled-up qualification runs (PQ-0562, −0611, and −0572) were performed using the finalized processing procedure for CIML-NK. We have been able to produce therapeutic compliant doses of GMP grade CIML-NK products that satisfactorily reached FDA IND approved release criteria on sterility, stability, cell content and phenotype, viability and NK cell purity as characterized immunophenotypically and functionally in tumor killing assays. Lastly, our preliminary data focus on the development of a new flow cytometry-based killing assay to distinguish between on-target and off-target killing of healthy hematopoietic progenitors, monocytes, B-& T-cells.

Conclusion: In summary, we have been able to demonstrate the feasibility of the production of functionally competent CIML-NK products for human infusion, aiming towards their administration as a bridge to HSCT in RR-AML. The study is open for enrollment and details are available at https://www.clinicaltrials.gov/ct2/show/NCT05580601.

POSTER # 106 | DERIVATIVES OF PLANT ALKALOID LEONURINE HAVE ANTI-LUEKEMIC EFFECTS IN B-ALL AND T-ALL

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Background: Although survival has improved greatly for pre-B cell Acute lymphoblastic leukemia (B ALL) high risk (HR) subgroups continue to result in significant mortality and morbidity of pediatric oncology patients. T ALL is also considered high risk disease with treatment failure. Novel treatment strategies can overcome chemotherapy resistance and imporve toxicity in ALL therapy. Leonurine is a bioactive alkaloid that is naturally occurring only in Herbra Leonuri which has been used in traditional herbal medicine. Traditionally, it has been used for menstrual disorders and more recently research suggests that it scavenges oxygen free radicals, anticoagulation properties, and other anti-inflammatory properties. Thus, its use has been investigated in models including myocardial infarction, stroke, chronic kidney disease, and other inflammatory disorders.

Objectives: We present data that demonstrate the anti-leukemic effect of leonurine derivatives on B and T ALL. We will provide data on mechanism and some early preclinical testing data.

Design/Method: We analyzed multiple derivatives of leonurine and selected a potent candidate based on cell viability assays use for further testing designated as investigational leonurine derivative (ILD). WST1 proliferation studies comparing ILD to vehicle were performed in cell lines Nalm6, 697, Molt4, CEM, and JM1 at multiple time points. Nalm6, 697 and Molt4 were used for mechanistic analysis and early pre-clinical models.

Results: Cellular proliferation studies revealed a 1.2-4.4 uM for IC50 depending on the time and cell line. Apoptosis activity was determined by flow cytometry Anexin/7AAD assays showed increased apoptosis in cell lines treated with ILD for Nalm6, Molt4, and 697 cell lines. Caspase 3/7 activity was increased in cells treated with ILD when compared to vehicle treatment. DNA damage assays were performed which revealed only an increased frequency in single strand breaks and not double strand breaks. Western blot was performed to determine levels of PI3K, p-AKT, BCL2/BCL-XL and caspases. The blots suggest

that apoptosis may be a result of increased activation of PI3K/AKT signaling. We performed RNAseq on cells treated with ILD at the 24-hour time point and present gene ontology data for this analysis. NRG mice were injected with modfied cell lines and treated with Leonurine derivative. Nalm 6 showed minimal difference between treatment and control.

Conclusion: In summary, we expect that leonurine derivatives will have a significant clinical effect however further investigation into mechanisms and pharmacokinetics/dynamics will be more revealing. Development of these principles will result in further translational opportunities to improve high risk ALL treatment.

POSTER # 107 | ANALYSIS OF BIVALENT CHROMATIN IDENTIFIES PROGNOSTICALLY RELEVANT LNCRNA IN PRE-B ALL

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Background: Evidence suggests a powerful role for lncRNA in maintaining embryonic stem cell (ESC) pluripotency and regulating ESC lineage commitment, including differentiation to hematopoietic stem cells (HSCs). Published data shows that lncRNA are deregulated in acute myeloid and lymphoid leukemia and demonstrates prognostic potential of lncRNAs. We hypothesize that bivalent marking of lncRNA in early hematopoietic development may provide prognostic indicators for acute leukemia.

Objectives: To develop a novel pipeline identifying lncRNAs with pathological or prognostic significance in preB-ALL utilizing bivalently marked lncRNAs in HSCs.

Design/Method: We utilized publicly available RNASeq data from three ESC cell lines and HSCs from healthy donors. Data was aligned to hg38 and DESeq2 was used for differential expression (DE) analysis defining significant genes as expression log2 fold-change +/−1 and adjusted p-value <0.05. The Spearman correlation coefficient was calculated for all DE mRNA within 100 kb of a DE lncRNA. mRNA-lncRNA pairs with rho>0.8 or <0.8 were considered to have substantial correlation. ChIP-seq data was retrieved from UCSD Human Reference Epigenome Mapping Project. Consensus peaks were defined for H3K27me3 and H3K4me3 using the intersection of all HSC samples. Prognostic value was determined using Kaplan–Meier survival analysis based on lncRNA expression in the NCI Therapeutically Applicable Research to Generate Effective Treatments (TARGET) ALL dataset.

Results: Geneset enrichment analysis of mRNAs that may be regulated in cis by DE lncRNAs demonstrates that genes upregulated in ESC are enriched in pathways associated with stem cell maintenance and system development; whereas genes upregulated in HSC are associated with immune cell and system development. These results are expected, validating our nearest neighbor analytic approach. We examined lncRNAs within 5 kb of a bivalently marked site and classified these lncRNAs into 1 of 4 groups: up-regulated in HSCs or ESCs or expressed only in either HSCs or ESCs. We identified that 11 of 23 bivalent lncRNAs upregulated in HSCs and 4 of 14 bivalent lncRNAs upregulated in ESCs are prognostically significant when examined in the TARGET-ALL dataset. None of these have previously been described as prognostically relevant in ALL, with only PRDM16-DT having been previously identified as a prognostically significant lncRNA in AML.

Conclusion: We provide a pipeline for integrative analysis of lncRNA expression and bivalent chromatin in HSCs to identify candidate lncRNAs involved in HSC proliferation and differentiation, and potentially malignant transformation. Utilizing this analytical approach, we identified bivalently marked lncRNAs that may be of prognostic importance in pediatric ALL.

POSTER # 108 | MENIN INHIBITION IN PEDIATRIC KMT2AR LEUKEMIA: PHASE 1 AND EXPANDED ACCESS EXPERIENCE WITH REVUMENIB

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Background: Acute leukemias with histone-lysine N-methyltransferase 2A rearrangements (*KMT2Ar*, previously *MLLr*) are aggressive hematopoietic malignancies accounting for the majority of acute leukemias diagnosed before the age of 2 years. Disrupting the KMT2Ar-menin interaction in preclinical models leads to downregulation of *HOX/MEIS1* genes, and reversal of leukemogenesis. Revumenib (SNDX-5613) is a potent, selective inhibitor of KMT2Ar-menin interaction, with demonstrated preliminary anti-leukemic activity in the Phase 1 AUGMENT-101 (NCT04065399) study of relapsed/refractory (R/R) acute leukemias.

Objectives: Here, we report the experience of pediatric patients treated with revumenib.

Design/Method: Patients <18 years of age were enrolled in AUGMENT-101 Phase 1 dose escalation cohorts: patients received revumenib without (Arm A) or with (Arm B) concomitant strong CYP3A4 inhibitors. Patients ineligible for AUGMENT-101 due to young age (prior to protocol amendment) or disease status (e.g., presence of CNS disease) were granted expanded access to revumenib via single patient protocols; data available from the treating physicians are reported. A data cutoff of 31 March 2022 was selected for all patients.

Results: Eight patients aged 9 months to 16 years with R/R *KMT2Ar* leukemia were enrolled in Arms A or B of AUGMENT-101. Of these, 75% had ≥4 prior lines of therapy and 50% had prior hematopoietic stem cell transplant. Four patients had responses (CRh, CRp, 2 MLFS); 2 proceeded to transplant with ongoing remissions at data cutoff. Dose and exposure followed a typical allometric relationship, with no notable differences compared to adults. No dose-limiting toxicities occurred in pediatric patients on AUGMENT-101. No Grade

≥3 treatment-related adverse events were reported; Grade 2 related events were differentiation syndrome (n = 4), QTc prolongation, decreased appetite, nausea, and vomiting (n = 1 each).

Eleven patients aged 14 months to 17.9 years with R/R *KMT2Ar* leukemia received revumenib through an expanded access program. BSA-based dosing was implemented based on standard allometric scaling and subsequently supported by pharmacokinetic data from AUGMENT-101. Investigator-reported responses were achieved in 3 patients (2 CR MRD-negative, 1 CRi in a patient with baseline CNS disease), of which 2 proceeded to transplant. No adverse events led to treatment discontinuations.

Conclusion: Encouraging response rates in these heavily pre-treated pediatric patients, and the opportunity of some to proceed to transplant, highlight the feasibility of including pediatric patients early in clinical development. AUGMENT-101 continues to enroll pediatric patients, with pediatric expansion cohorts included in Phase 2 with the RP2D of 163 mg (95 mg/m^2 if <40 kg) q12h with a strong CYP3A4 inhibitor.

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POSTER # 109 | DEFINING THE GENOMIC AND EPIGENETIC LANDSCAPE OF PEDIATRIC AML IN UGANDA

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Background: While acute myeloid leukemia (AML) typically represents 20% of pediatric acute leukemias, review of diagnoses at a large pediatric hospital in Kampala, Uganda revealed 40% of acute leukemias were AML. The reason for this difference in disease lineage distribution needs to be explored. While the genomics of pediatric AML have been extensively studied in high-income countries and the methylation profiles are becoming increasingly defined, almost no genomic and epigenetic data exists of pediatric AML in sub-Saharan Africa.

Objectives: To comprehensively evaluate the genomic and epigenetic landscape of pediatric AML in Uganda. We hypothesize that the genetic drivers of AML in Uganda mirror what is seen in high-income countries, but that differences in early life nutrition and infectious exposures lead to methylation differences that may impact AML development.

Design/Method: We received frozen diagnostic blood and/or bone marrow from 9 patients with AML diagnosed in Kampala. Cytogenetic data was obtained from two complimentary tests, an RNA-based NanoString panel of fusions known to be associated with hematologic malignancies and a high-resolution chromosome evaluation by OncoScan which comprehensively evaluated for chromosomal gains/losses. Targeted next generation sequencing evaluated for mutations in genes recurrently mutated in hematologic malignancies. Genome-wide methylation analysis was done utilizing the Infinium MethylationEPIC BeadChip array on the 9 Ugandan patients and 7 pediatric AML samples from Texas Children's Hospital tissue repository were used for comparison.

Results: Initial gene fusion data was limited by suboptimal RNA quality, but identified one patient with the rare AML associated NPM1::MLF1 fusion. Our DNA mutation panel identified *NRAS* as the most frequently mutated gene, similar to US data. Other than an absence of *FLT3* mutations, the landscape of likely clinically significant (tier I or II) mutations identified was similar to that described for other pediatric AML cohorts. Conversely, striking differences in methylation profiles were observed between the groups. Unsupervised hierarchical clustering by two methods stratified the patients by country of residence with two exceptions.

Conclusion: Pilot data suggests pediatric AML in Uganda has a distinct methylation pattern compared to pediatric AML patients in the US. We are now working to interrogate our methylation data for known biomarkers of specific environmental exposures. We will also explore these methylation biomarkers in blood samples from healthy patients from Uganda and the US to determine if specific exposures are enriched in our AML cohort. In doing so, we hope to identify environmental factors that may play a role in the development of pediatric AML.

POSTER # 110 | IMMUNE STATUS OF CHILDREN FOLLOWING ACUTE LYMPHOBLASTIC LEUKEMIA THERAPY

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Background: Immune recovery following acute lymphoblastic leukemia (ALL) therapy has been investigated by various tests in children. Many studies have focused on certain aspects of the immune function and reported lasting abnormalities for months or even years in some survivors.

Objectives: To report on immunological status in children with ALL after completing chemotherapy using a comprehensive analysis approach.

Design/Method: Monitoring immune status after completion of ALL chemotherapy guidelines combining immunoglobulin levels, lymphocyte subsets, mitogen responses and vaccine titers were developed to provide better care and has been followed at treating physician's discretion at our institution. A retrospective data collection was undertaken in patients who had immune system monitoring evaluations performed. Available data was determined to be abnormal based on age-normal values and analyzed using the SPSS statistical software. This study was approved by the Institutional Review Board at Wayne State University.

Results: Data was available in 58 patients and majority had B-ALL (77.6%). Thirty-seven cases had immune status evaluation completed within the first year. Eleven patients who received intravenous immunoglobulin supplementation less than 9 months at sampling were excluded from analysis leaving 26 cases which were tested at a median of 2.4 (1-12) months. There were 20 males and 6 females with a median

age of 9 (4-18) years at the time. Serum immunoglobulin levels were low in 19.2%, 11.5% and 57.7% for IgG, IgA and IgM, respectively; 15.4% cases had at least 2 low immunoglobulin subtypes. Among the cases with available data, 12 (46.2%) had low absolute T cell numbers, 13 (50%) low CD4+ T cells, 8 (30.8%) low CD8+ T cells and 8 (30.8%) had decreased CD4+/CD8+ ratio. Only 3.8% had low absolute natural killer cell and 19.2% had low absolute B cell counts. Mitogen responses were low at 19.2%, 19.2% and 7.7% of the cases to phytohemagglutinin, concanavalin A, and pokeweed antigen, respectively. Vaccine antibody titers remined positive in 23.1% for hepatitis B surface antigen, 50% for hepatitis A, 57.7% for measles, 46.2% for rubella, 38.5% for mumps, 46.6 % for varicella, 26.9% for diphtheria, and 46.2 % for tetanus. Pneumococcal titers were low in>50% of 23 serotypes in 6 cases.

Conclusion: These results show both humoral and cellular immunity defects in childhood ALL survivors within one year of treatment completion. While IgM deficiency, lack of vaccine titers for hepatitis B, diphtheria and pneumococcus and fastest recovery of natural killer cells are striking, other correlations are being investigated.

POSTER # 111 | RETROSPECTIVE ANALYSIS OF A HYPERGLYCEMIA SCREENING PROTOCOL IN PEDIATRIC PATIENTS WITH ALL AND LLY

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Background: Approximately 4-35% of pediatric patients undergoing treatment for acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LLy) develop drug-induced hyperglycemia. Hyperglycemia is associated with poor outcomes including increased infections, weight loss, diabetic ketoacidosis, and greater mortality. However, no guidelines for identifying drug-induced hyperglycemia currently exist and the time course of hyperglycemia development remains relatively uncharacterized past induction therapy.

Objectives: The present study aims to evaluate a hyperglycemia screening protocol (HSP) that was implemented to identify hyperglycemia more promptly and to further describe the time course of hyperglycemia during ALL and LLy therapy.

Design/Method: A retrospective medical records review of 154 patients diagnosed with ALL or LLy at Cook Children's Medical Center between March 2018 and April 2022 was performed. The HSP included more frequent blood glucose monitoring, criteria for removal of dextrose from IV fluids, consultation to other providers (case management, patient educator, registered dietitian), and robust care coordination between the hematology-oncology and endocrinology teams. Predictors of hyperglycemia were examined with univariate Cox regression.

Results: The HSP was ordered for 88 (57%) of the patients. Fifty-four (35%) patients developed hyperglycemia: 28 (52%) during induction therapy and 26 (48%) patients after induction therapy. Enrollment in the HSP increased the likelihood of a hyperglycemia diagnosis compared to those not enrolled (41% vs. 27%, HR = 1.76, p <0.050). Age ≥10 years was an independent predictor of hyperglycemia development (HR = 3.72, p <0.0001). Patients who did not gain weight during the induction period were more likely to also have hyperglycemia (weight loss: HR = 5.42, p = 0.001; weight steady: HR = 3.48, p = 0.012). The development of pancreatitis was also associated with drug-induced hyperglycemia (HR = 2.45, p = 0.007). Blood glucose values were significantly more likely to be ≥200 mg/dL during days 5-8 of induction therapy compared to days 1-4 (29% vs. 10%, OR = 4.18, p <0.001). Compared to blood glucose measurements taken in the morning (10%), values were more likely to be ≥200 mg/dL when acquired overnight (20%, OR = 4.42, p <0.001), in the afternoon (16%, OR = 2.34, p = 0.011), and in the evening (38%, OR = 10.57, p <0.001).

Conclusion: Implementation of the HSP helped detect hyperglycemia more frequently in enrolled patients compared to controls and readily identified individuals at greatest risk of developing hyperglycemia. These findings highlight a population of patients that develop hyperglycemia past induction therapy and give guidance on the timing of continued blood glucose monitoring in at-risk patients.

POSTER # 112 | RESPONSE TO REINDUCTION CHEMOTHERAPY IN FIRST RELAPSE PEDIATRIC B-ALL: A SINGLE-INSTITUTION REVIEW

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Background: Despite improved outcomes in pediatric B-cell acute lymphoblastic leukemia (B-ALL), survival in the relapsed setting remains poor, with recent data estimating overall survival rates to be about 50%. First relapse reinduction choices are variable and may be guided by institutional experience.

Objectives: To evaluate practice patterns and outcomes in the management of patients with B-ALL after first relapse.

Design/Method: This is a single-institution, retrospective review of pediatric patients with first relapse of B-ALL between 2018-2022. This timeframe was chosen as no clinical trials were available allowing for observation of clinician preference without bias of an open clinical trial. Descriptive statistics were used. No IRB submission was required per institutional guidelines.

Results: Seventeen subjects experienced first relapse between 2018-2022. The average time to relapse was 634 days (114-1309). Relapse types included isolated marrow (IM, 41.2%), isolated extramedullary (IEM, 29.4%) and combined marrow/extramedullary (29.4%). The majority of reinduction therapies were VXLD (vincristine, dexamethasone, pegaspargase, and doxorubicin, 23.5%) or UKALL-R3 (vincristine, dexamethasone, pegaspargase, and mitoxantrone, 35.3%). VXLD was used in 2/7 of IM, 2/5 of IEM, and 1/6 combined relapses. UKALL-R3 was used in 2/7 of IM, 2/5 of IEM, and 2/6 combined relapses. 7 patients

were minimal residual disease (MRD) negative at the end of reinduction (EOrI; 50% in VXLD group, 66.7% in UKALL-R3 group). 28% (2/7) patients who received VXLD and 0% who received UK-ALLR3 were MRD positive at EOrI, respectively. EOrI MRD negativity did show a significant survival advantage ($p < 0.05$). 5 additional subjects never achieved remission. Post-reinduction therapy included chemotherapy (n = 3), chemotherapy plus HSCT, CAR-T, immunomodulatory therapy, and/or radiation (n = 11), and CAR-T (n = 1). 6 patients had 1 or more subsequent relapses (1, VXLD group; 2, UKALL-R3 group). 5 patients remain disease free (1 VXLD, 3 UKALL-R3). During reinduction, there were 8 deaths (47.1%), including 1 with UKALL-R3 due to infection and 4 due to disease progression (none treated with VXLD/UKALL-R3). The remaining 3 deaths were attributed to cardiac arrest, methotrexate-related necrotizing encephalopathy, and secondary AML. Overall, there was 1 death in the UKALL-R3 group and 2 in the VXLD group; this difference is not significant, likely impacted by sample size.

Conclusion: Outcomes in pediatric B-ALL patients after first relapse are poor, with variable reinduction treatment regimens. EFS and OS are similar between patients who undergo reinduction with VXLD or UKALL-R3, with a difference between EOrI MRD. Ultimately, EOrI MRD may serve as a predictor for probability of survival.

POSTER # 113 | CLINICAL AND GENETIC FEATURES OF PATIENTS WITH NUP214::ABL1-POSITIVE ALL ON TOTAL THERAPY TRIALS

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Background: Ph-like ALL, a subtype with similar gene expression as that of Philadelphia chromosome-positive ALL but without *BCR::ABL1* fusion, is associated with inferior outcomes and has many different genomic alterations. One such alteration is the *NUP214::ABL1* fusion, which has been identified in both B-cell and T-cell lineage ALL. Preclinical data suggests that germline *MCM2* variants predispose to the development of *NUP214::ABL1*-positive ALL in murine models, but this germline alteration has not been described in clinical reports.

Objectives: We sought to compare the clinical and genetic characteristics of pediatric patients with *NUP214::ABL1*-positive (fusion-positive) ALL treated on recent Total Therapy protocols with those of patients lacking the *NUP214::ABL1* fusion (fusion-negative), including somatic gene expression profiles and germline alterations in *MCM2*.

Design/Method: We obtained patient clinical data from research databases of patients treated on St. Jude Total Therapy Studies 15, 16 (all patients), and 17 (fusion-positive patients only). Clinical characteristics were compared using t-test, exact Chi-squared test, or regression analysis, as appropriate. Somatic gene expression profiles by whole transcriptome sequencing (n = 5 fusion-positive patients) were compared using t-distributed stochastic neighbor embedding plots. Germline whole exome sequencing data was examined for alterations in *MCM2* (n = 6 fusion-positive patients).

Results: Of 1097 patients studied, 6 (0.5%, 3 B- and 3 T-lineage) had *NUP214::ABL1* fusion. Compared to fusion-negative patients, fusion-positive patients were older (median age 12.2 vs. 5.5 years, $p = 0.02$), had higher WBC at diagnosis (median 73.5 vs. 12.9 $x10^9$/L, $p = 0.03$; WBC>50 x 10^9/L, 67% vs. 24%, $p = 0.03$), and were less likely to have provisional low-risk classification (0% vs. 57%, $p = 0.007$). Fusion-positive patients were more likely to have mid-induction minimal residual disease (MRD)>5% (67% vs. 11%, $p = 0.003$) and end-of-induction MRD ≥0.01% (83% vs. 15%, $p = 0.0006$), more likely to receive allogeneic hematopoietic cell transplantation (HCT) (50% vs. 5.3%, $p = 0.003$), and less likely to have final low risk classification (0% vs. 46%, $p = 0.03$). Of 6 fusion-positive patients, 1 received dasatinib starting at day 15 of induction therapy, 3 received allogeneic HCT for high end-of-induction MRD (6.74%, 0.218%, and 0.324%, respectively), and 1 patient relapsed following HCT. One patient died in first remission following HCT. All 3 fusion-positive patients with B-cell lineage immunophenotype showed gene expression profiles similar to other Ph-like ALL. No fusion-positive patients had detectable germline *MCM2* alterations.

Conclusion: Patients with *NUP214::ABL1*-positive ALL are more likely to present with high-risk clinical features and poor response to remission induction therapy. These patients should be candidates for treatment with kinase inhibitors and/or immunotherapy.

POSTER # 114 | COVID-19 IN ACUTE LYMPHOBLASTIC LEUKEMIA/LYMPHOMA: ST JUDE CHILDREN'S RESEARCH HOSPITAL EXPERIENCE

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Background: Clinical presentation in patients with the coronavirus disease 2019 (COVID-19) can vary from asymptomatic to severe respiratory distress and multisystem organ failure. Risk factors for mortality have included patients in low-/middle- income countries, older age, low absolute lymphocyte and neutrophil counts, and intensive treatment for comorbidities such as malignancy. Detailed studies of COVID-19 in children with cancers in high-income countries (HICs) are lacking.

Objectives: We evaluated clinical characteristics and management of COVID-19 in pediatric patients with acute lymphoblastic leukemia (ALL) and lymphoblastic lymphoma (LLy) who were treated at St. Jude Children's Research Hospital.

Design/Method: Patients 1-18 years old on St. Jude Total XVII protocol between March 2020 and June 2022 were included. COVID-19 testing was performed weekly for screening, and for exposure or symptoms. Illness was categorized as asymptomatic/pauci-symptomatic, mild-moderate, and severe. Descriptive statistics were used for clinical presentation and demographic variables. Associations between categorical variables were investigated using Chi-square or Fisher's exact

test, and between continuous and categorical variables by Wilcoxon rank sum test or Kruskal-Wallis rank sum test. Due to the exploratory nature, analyses were not adjusted for multiple comparisons.

Results: Of 308 patients, 110 (36%) tested positive for COVID-19. Age at diagnosis of ALL/LLy was significantly higher in positive patients than those who remained negative (6.7 years vs. 5.3 years) (P = 0.018). Median age at diagnosis of COVID-19 was 8.2 years; seventeen (15%) patients were asymptomatic. Most common symptoms were cough, fever, and rhinorrhea. Thirty-five (32%) patients were admitted, mostly with febrile neutropenia. Seven (6.4%) had severe disease, six prior to Omicron variants; 4 patients required ICU admission. Most patients were in continuation phase of chemotherapy (n = 77, 70%). Chemotherapy was held in 95 (86%) patients, including all patients with severe COVID-19 (P = 0.012) for a longer median duration (P <0.001). Severe disease was associated with older age at diagnosis of ALL/LLy (P = 0.005) and COVID-19 (P = 0.009), chest X-ray abnormalities (P = 0.010), lower absolute lymphocyte counts (P = 0.022), concurrent respiratory co-infection (P = 0.018), and recurrent COVID-19. Patients with recurrence (n = 11; 10%) were older at first COVID-19 infection (P = 0.041) and were on the standard-high vs. low-risk arm of Total XVII (P = 0.021). None had severe disease on recurrence. There were no deaths in our study population.

Conclusion: Most patients with pediatric ALL/LLy did not have severe COVID-19. Early detection and better supportive care may account for less severe presentation of COVID-19 in HICs. It is also possible that immunosuppression prevents severe illness by modulating the immune response, especially in younger patients.

POSTER # 115 | STANDARDIZED NEUROLOGIC ASSESSMENT DOCUMENTATION TO ENSURE THE SAFE ADMINISTRATION OF NELARABINE

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Background: Nelarabine has become a key component of therapy for pediatric T-cell acute lymphoblastic leukemia/lymphoma (T-ALL/LLy). AALL0434 demonstrated superior outcomes but>grade 3 peripheral neurotoxicities on the nelarabine arms were reported in 8-9% of patients. Although there was no significant difference from the standard arms, two patients also developed severe central neurocognitive decompensation either during or shortly after nelarabine. Nelarabine is typically given as five daily doses, providing an opportunity for early intervention if neurotoxicity is noted mid-course.

Objectives: We aimed to standardize the neurologic assessment documentation with each dose of nelarabine and to improve the baseline rate of daily documentation from 65.9% to>90% of nelarabine doses administered inpatient and outpatient from June 2021 to November 2022.

Design/Method: Baseline data assessing neurologic exam documentation in progress notes for patients with T-ALL/LLy receiving nelarabine was collected for six months. We then implemented a standard of care treatment guideline with a seven-question neurotoxicity questionnaire to be administered prior to daily nelarabine. This questionnaire was also converted to an electronic medical record (EMR) phrase for provider documentation. Data was monitored for twelve months for PDSA1. For PDSA2, universal access to this questionnaire EMR phrase was granted to all institutional users and data was monitored for an additional six months.

Results: Thirty-one patients with T-ALL/LLy were included. Median age was eight years. Baseline data demonstrated that for six patients over six months, 65.9% (29 of 44) of nelarabine doses administered had a daily neurologic assessment. One planned dose was omitted due to neurotoxicity. PDSA1 included twenty patients over twelve months and 95.1% (234 of 246) of nelarabine doses administered had a daily neurologic assessment. Nine doses (out of fifteen planned for three patients) were omitted due to neurotoxicity. PDSA2 included twenty-one patients over six months and 97.2% (175 of 180) of nelarabine doses administered had a daily neurologic assessment. No doses were omitted due to neurotoxicity. Daily standardized neurotoxicity assessments prompted earlier identification of neurotoxicity (including low-grade neuropathy) and earlier intervention.

Conclusion: The implementation of a standard of care treatment guideline with a neurotoxicity questionnaire that was made universally available in the EMR resulted in successful daily standardized neurotoxicity assessments for pediatric patients with T-ALL/LLy receiving nelarabine. Limitations of this project include that it was conducted at a single institution over a short time frame. Future directions include expanding this approach to other multi-day chemotherapy administrations that pose a risk for interval development of neurotoxicity.

POSTER # 116 | ASSOCIATION BETWEEN ADVERSE EVENTS AND END OF INDUCTION MINIMAL RESIDUAL DISEASE IN PEDIATRIC ALL

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Background: Despite improvements in therapy leading to increased long-term survival, adverse events (AEs) are common during induction therapy for pediatric acute lymphoblastic leukemia (ALL). End-of-induction (EOI) minimal residual disease (MRD) is an important prognostic factor and can determine post-induction treatment regimens. Prior literature has described an association between positive EOI MRD and poorer long-term outcomes such as relapse and death.

However, it is currently unknown if development of AEs during induction has an impact on EOI MRD.

Objectives: To describe the frequency and grade of induction AEs in ALL and describe the association between development of AEs during induction and EOI MRD.

Design/Method: This single institution, retrospective cohort study included patients aged 1-21 years diagnosed with ALL or mixed phenotype acute leukemia (MPAL) treated with ALL therapy at Children's Healthcare of Atlanta between January 1, 2010, and September 1, 2022. Data collected via automated or manual chart abstraction included demographics, induction course dates and regimens, and EOI MRD (positive MRD defined as>0.01%). Presence and grade of clinically significant AEs were abstracted according to National Cancer Institute Common Terminology Criteria for Adverse Events v5.0 using a detailed AE abstraction guide. These AEs included pancreatitis, hepatotoxicity (elevated AST, elevated ALT, or hyperbilirubinemia), acute respiratory distress syndrome (ARDS), hypoxia, hypertension, hypotension, neuropathy, hyponatremia, constipation, hyperglycemia, infection, thromboembolic events, and fever. Association between development of any AE grade (grade 1-5) or severe AEs (grade 3+) and EOI MRD was evaluated using chi square or Fisher's exact tests, as appropriate.

Results: There were 673 patients included in this study; 653 (97%) had at least one AE of any grade and 498 (74%) had at least one severe AE during induction. Hyperglycemia (561, 83.4%), constipation (327, 48.6%), fever (312, 46.4%), ALT elevation (254, 37.8%), and hypertension (244, 36.3%) were the most common AEs experienced at any grade. Hypertension (191, 28.4%), fever (166 24.7%), ALT elevation (156, 23.2%), infection (231, 16.2%), and hyperglycemia (78, 11.6%) were the most common AEs experienced at severe grades. Ten patients died during induction: 8 due to AEs and 2 due to disease progression. There was no association between development of AEs and positive EOI MRD for either any AE grade or severe AEs (p>0.05).

Conclusion: This study identified high rates of clinically significant AEs during induction. However, there was no association between development of an AE and having positive EOI MRD. These results can be used to guide patients and families who experience induction AEs.

POSTER # 117 | IM OUTPATIENT EPINEPHRINE PRESCRIPTIONS NOT NECESSARY WITH IV PEGASPARGASE: A RETROSPECTIVE ANALYSIS

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Background: Pegaspargase is an essential component of pediatric acute lymphoblastic leukemia/lymphoma (ALL/LLy) treatment, and the possibility for severe hypersensitivity reactions warrants immediate access to medical care during administration. At our institution, patients have historically been prescribed intramuscular epinephrine (IM epi) to carry on their person after receiving pegaspargase in the event of delayed hypersensitivity reactions. Out-of-pocket costs for IM epi can be significant and intermittent shortages can limit available supplies. It has been our anecdotal observation that these IM epi prescriptions are not utilized in the home setting, leading to concern for medical waste and unnecessary financial toxicity.

Objectives: The primary objective of this retrospective chart review was to quantify the frequency of self-administration of IM epi off-campus in response to pegaspargase hypersensitivity reaction.

Design/Method: This was an IRB-exempt, single center, retrospective chart review. All patients less than 21 years of age with ALL or LLy being treated by the Mayo Clinic pediatric hematology team from May 2018 – November 2022, and who received at least one dose of intravenous pegaspargase, were eligible for inclusion. Details regarding IM epi prescription(s), pegaspargase administration, and hypersensitivity reactions, if applicable, were manually extracted from the electronic medical record.

Results: Sixty-three eligible patients received pegaspargase during the study period. All pegaspargase doses were given intravenously over 2 hours into a running line of D5 NS infusing at 100 mL/m2/hr, and no patients received pre-medication. Seven patients (11%) developed a hypersensitivity reaction. All seven reactions occurred on-site during pegaspargase infusion, for which 5/7 (71%) were administered IM epi. There were no reports of delayed hypersensitivity reactions, and no patients required self-administration of IM epi off-campus.

Conclusion: In our cohort of 63 children with ALL/LLy receiving intravenous pegaspargase, there were no events of delayed hypersensitivity and no patients required self-administration of IM epi off-campus. When intravenous pegaspargase is administered in a medically staffed and pharmacy-supported care setting, prescriptions for outpatient IM epi are not necessary. At an average wholesale price of $700 per 2-pack of IM epi, omission of take-home IM epi prescriptions would have resulted in cost avoidance in excess of $44,000 for our population over the allotted timeframe. To reduce medical waste and out-of-pocket financial burden, we propose the elimination of outpatient IM epi prescriptions for intravenous pegaspargase. Instead of homegoing prescriptions, measures should be implemented to enhance bedside access of rescue medications and dosing tools to treat hypersensitivity reactions.

POSTER # 118 | A QUALITY IMPROVEMENT PROJECT TO DECREASE PEGASPARGASE REACTIONS IN PEDIATRIC ONCOLOGY PATIENTS

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Background: Receiving pegaspargase in pediatric, adolescent, and young adult patients with acute lymphoblastic leukemia (ALL) and lymphoma is vital, and the risk of associated anaphylaxis and drug reactions is well documented. Erwinia chrysanthemi derived asparag-

inase is substituted for pegaspargase if there is a severe allergy, but patients and families must endure more frequent dosing, potentially higher expenses, and availability can be limited. These reactions also cause significant anxiety in patients, caregivers, and medical staff.

Objectives: The goal of this project was to decrease the incidence of drug reactions related to pegaspargase administration of any grade. We evaluated this measure with a goal of increasing the number of pegaspargase doses between reactions by 50%.

Design/Method: This project utilized the Model for Improvement with rapid cycle PDSAs for testing change ideas. A multidisciplinary team including a physician, APP, nurse navigator, pharmacist, nurse educator, and data analyst convened to advance this quality improvement (QI) work. Change ideas tested include changing chemotherapy orders to infuse pegaspargase over 2 hours, concurrent administration of normal saline into the pegaspargase primary line, nursing education around proper administration of the drug, documenting and grading reactions properly, and universal pre-medication for all patients receiving pegaspargase.

Results: Outcome data was evaluated using a Shewhart control chart (G-chart). The data showed an initial center line of 8 pegaspargase doses between reactions. With many change ideas implemented, our current center line is 23 pegaspargase doses between reactions. We are meeting our goal to increase the number of pegaspargase doses between reactions by 50%.

Conclusion: Implementing previously investigated change ideas has led to fewer pegaspargase reactions, reducing strain on patients and families caused by switching to another drug option that requires more frequent doses and increased expense. This QI project illustrates that utilizing QI techniques with an engaged QI team can positively impact the delivery and value of care, decreasing additional interventions, patient strain, and cost. This project is a unique way to evaluate many of the interventions that have been used to prevent reactions to pegaspargase. Our primary measure, number of pegaspargase doses between reactions, has also not been published in the literature.

POSTER # 119 | RACIAL AND ETHNIC DISPARITIES IN INFANT LEUKEMIA SURVIVAL

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Background: The Surveillance, Epidemiology and End Results Program (SEER) database has been used to study race related differences in outcomes for childhood cancer. Compared to Children's Oncology Group (COG) and Children's Cancer Group (CCG) studies, SEER includes overall a reasonable proportion of racial and ethnic groups. Until now, little is known about the influence of race on outcomes in infants with leukemia. Therefore, utilizing SEER data is critical to understanding disparities in an infant population.

Objectives: Our aims include 1) determining incidence of leukemia by different racial groups over time, and 2) analyzing outcomes for infants diagnosed with leukemia by race.

Design/Method: Our proposal to SEER for access to infant data by months of age has been granted. Variables selected from available SEER version 18 plus data (including further granular data by age in months) included the following (raw): patient ID, age (months), sex, race, ethnicity, overall survival (in months), vital status (alive/dead), leukemia type. To accomplish our aims, initial major statistical methods including incidence and descriptives were utilized in Stata version 17. Kaplan-Meier survival estimate curves were run to demonstrate survival time stratified by race. Subsequently, univariate and multivariate Cox proportional hazard models were performed to investigate the predictor variables of race, age (in months <12), gender, ethnicity, leukemia type to understand effect of mortality (hazard ratios) in different racial groups.

Results: Patients (n = 968) age <1 year (12 months) were included. We first described leukemia incidence stratified by race by percentages and frequencies in years 2000-2013 annually. In K-M curves we note that Black infants have significantly worse survival (unadjusted). Results of univariate models indicate significance in leukemia type variable, age (months at diagnosis), and race (Black infants). When accounting for multivariate modeling, statistical significance remains for an increased hazard ratio in Black infants when using White infants as a reference group.

Conclusion: In cautiously assessing and interpreting results based on these methods, we do see that Black infants diagnosed with infant leukemia will have higher risk of mortality compared to specifically their White counterparts. Analysis into root causes of this disparity, including more disease specific metrics, inclusion of genomic factors as well as social determinants of health are necessary to understand better the reason for differential survival in infant populations with leukemia by race. Inclusion of all race and ethnicities as a priority in pediatric oncology clinical trials is a first step.

POSTER # 120 | MANAGEMENT OF PATIENTS AT RISK FOR TUMOR LYSIS: A QUALITY INITIATIVE TO DECREASE UNNECESSARY CARE

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Background: Tumor lysis syndrome (TLS) is a well-known complication of pediatric acute lymphoblastic leukemia (ALL). Cairo *et al.* 2010 and Xue *et al.* 2021 described risk factors for needing significant interventions such as dialysis. Current preventive and supportive practices include intravenous fluids (IVF), allopurinol, and frequent laboratory monitoring days without risk stratification. This may lead to overtreating low-risk patients, precipitating consequences such as hypertension, fluid overload, and longer admissions. Based on data generated at our

institution, a quality improvement project was designed to improve TLS prevention and management.

Objectives: For new patients with ALL, we aim to decrease TLS-directed supportive care (IVF, allopurinol, laboratory monitoring more than daily) to less than 96 hours duration from the start of intravenous chemotherapy.

Design/Method: Our multidisciplinary team created a process map, simplified failure modes effect analysis, and key driver diagram to analyze our current state and identify areas for intervention. Using risk factors identified in a prior retrospective study (WBC, uric acid, phosphorus, creatinine, potassium, LDH, diagnosis, and age), a risk-stratified clinical pathway was created. Data for initial prospective analysis was obtained through manual chart review for patients with ALL (B and T) treated between March and September 2022 and compared with data generated from retrospective analysis including patients between 2007-2021.

Results: Prospective data from 20 patients were collected in 2022 during the initiation of the project. In the retrospective analysis, ~80% of patients remained on allopurinol and ~95% on any IVF at 96 hours. In the prospective cohort, 40% remained on allopurinol and 45% on any IVF at 96 hours. In the perspective cohort, the median time (hours) after the start of intravenous chemotherapy on allopurinol, IVF, and more than daily labs for patients were as follows based on NCI risk groups standard risk B-ALL: 85,104,104; high-risk B-ALL: 87,108,117; and T-ALL:112,137, 120. Of this cohort, no patients required hemodialysis or rasburicase after the initiation of chemotherapy.

Conclusion: In our current state, TLS support is not effectively risk-stratified. Our early data support a trend toward decreased duration of support without increased complications. These improvements began with early discussion of the project even before the clinical pathway was finalized. We can continue to build on this early improvement with more sustainable interventions. The eventual impact of the work may lead to an improvement in quality of life, reduction in resource utilization, and potential reduction of time in the hospital by reducing unnecessary care.

POSTER # 121 | SALVAGE THERAPIES AND OUTCOMES OF PATIENTS WITH RELAPSE OF B-ALL AFTER CD19 CAR T-CELL THERAPY

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Background: CD19-targeted CAR-modified T cells (CART19) demonstrate remarkable complete remission (CR) rates in relapsed/refractory B-lymphoblastic leukemia (B-ALL); however, approximately 50% of children experience a subsequent relapse. Limited long-term data following post-CART19 relapse are available.

Objectives: To detail interventions and outcomes of children and young adults with post-CART19 relapse.

Design/Method: Patients aged <30 years with B-ALL treated on five CART19 clinical trials (CTL019/tisagenlecleucel or humanized-CART19) between 2012-2019, who experienced relapse after initial CR to CART19, were followed and analyzed until death or last contact. The primary outcome was overall survival (OS) from post-CART19 relapse.

Results: Of 195 trial participants, 185 achieved a CR; 85 subsequently relapsed at a median of 8.8 months. Median age was 10.6 years at post-CART19 relapse; 55% underwent prior stem cell transplant (SCT). Relapse sites included bone marrow (79%), extramedullary (15%), or combined (6%). Relapse immunophenotype included CD19-positive (42%), CD19-negative (49%), lineage switch (LS; 5%), or other/unknown (4%).

With a median follow-up time of 51 months from post-CART19 relapse, median OS was 15.3 months (95% CI, 9-27) and 24-month OS was 43% (95% CI, 32-53). OS at 24 months was better for patients with CD19-positive (56% [95% CI, 38-70]) than CD19-negative disease (36% [95% CI, 22-50]), although not statistically significant (P = 0.199). OS was dismal for LS with no long-term survivors. Relapse within 6 months of CART19 infusion was associated with inferior OS, even after adjustment for CD19-immunophenotype (P <0.0001).

After relapse, 72 patients received salvage treatment with curative intent. First post-relapse therapies and associated CR (minimal residual disease [MRD]-negative CR) rates were: conventional chemotherapy (n = 22), 31% (18%); antibody-based immunotherapy (n = 14), 93% (71%); another CART therapy (n = 26), 65% (58%); or other (n = 8). Notably, inotuzumab led to MRD-negative CR in 10/11 patients; 9 then proceeded to consolidative SCT. Event-free survival (EFS) at 24 months from initiation of salvage was 18% (95% CI, 3-38), 38% (95% CI, 14-63), and 31% (95% CI, 15-49) for chemotherapy, antibody-based immunotherapy, and another CART, respectively.

Thirty-seven patients ultimately proceeded to SCT (1^{st} SCT, n = 19; $\geq 2^{nd}$ SCT, n = 18). At 24-months post-SCT, EFS was 68% (95% CI, 43-84) and 28% (95% CI, 10-49; P = 0.020), and OS was 68% (95% CI, 42-84) and 56% (95% CI, 31-75; P = 0.160), for patients receiving their 1^{st} or $\geq 2^{nd}$ SCT, respectively. Four patients died from transplant-related complications.

Conclusion: Long-term outcomes for children with post-CART19 relapse are poor, but may be improved with novel immunotherapies, frequently as a bridge to SCT. Innovative therapies are needed for this population.

POSTER # 122 | HEMOGLOBIN A1C AND ASSOCIATION WITH TOXICITIES DURING INDUCTION FOR ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Despite high survival rates for pediatric acute lymphoblastic leukemia/lymphoma (ALL/LLy), adverse events (AEs) during induction are common. Development of hyperglycemia is frequent and can have serious morbidity. Measurement of hemoglobin A1c (HgbA1c) or fructosamine at diagnosis may be valuable to identify patients at risk for hyperglycemia.

Objectives: To evaluate the association between HgbA1c and fructosamine levels at diagnosis and development of hyperglycemia in ALL/LLy patients and to evaluate the feasibility and efficacy of a continuous glucose monitor (CGM) for early identification of hyperglycemia in patients with high risk (HR) ALL.

Design/Method: A prospective study of patients with ALL/LLy aged 1-21 years is ongoing at Children's Healthcare of Atlanta (CHOA). After consent, HgbA1c and fructosamine are obtained at diagnosis. Patients aged 5 to 17 years with HR ALL are eligible to consent to wear a CGM during induction. Manual chart abstraction of demographic and clinical data, including other AEs, is performed after completion of consolidation. Descriptive statistics are calculated for all study variables.

Results: From February 11 through December 31, 2022, 26 patients were enrolled. Most patients were less than 10 years (22, 84.6%), female (15, 57.7%), White (17, 65.4%), and Non-Hispanic/Latino (18, 69.2%). Seven (26.9%) had HR ALL. Median BMI at diagnosis was 16.1 kg/m2; the median change in BMI between diagnosis and end of induction was +0.24 (−1.5, 1.3). Median HgbA1c and fructosamine levels at diagnosis were 5.5 mg/dL (Range: 4.0-8.3) and 2.15 μmol/L (Range: 1.80-2.53), respectively.

Among the 18 patients who completed consolidation, all had grades 1+ hyperglycemia. Four (22.2%) had grade 3+ hyperglycemia that required insulin; all were HR and insulin was discontinued before consolidation. Three (16.7%) had grade 3+ infection and 5 (27.8%) had grade 3+ hepatotoxicity (increased alanine or aspartate aminotransferase). Among the 10 patients with baseline elevated HgbA1c ($\geq$5.7 mg/dL), 3 (30.0%) developed grade 3+ hyperglycemia, 2 (20.0%) developed grade 3+ infection, and 3 (30%) developed grade 3+ hepatotoxicity.

Three of 5 (60%) eligible patients with HR ALL consented to the CGM; no patients had AEs (pain or infection) related to CGM use.

Conclusion: Testing for HgbA1c and fructosamine at diagnosis is feasible and may be useful in predicting who develops hyperglycemia or other clinically significant AEs during induction. CGM use during induction is feasible. Once enrollment is complete, further evaluation of HgbA1c and fructosamine levels at diagnosis and the development of AEs will be performed and the utility of CGMs in detecting early hyperglycemia will be assessed.

POSTER # 123 | OPTIMIZATION OF INITIATION FOR HIGH DOSE METHOTREXATE IN B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA PDSA 2

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Background: High Dose Methotrexate (HD MTX) is a critical component of high risk, B-cell acute lymphoblastic leukemia (HR ALL) treatment and typically requires 4 inpatient admissions on COG protocols. Pre-hydration (specific gravity $\leq$1.010) and alkalinization (pH $\geq$ 7) is necessary to prevent nephrotoxicity and delayed excretion. Failure to meet these criteria can delay start time and prolong admissions.

Between baseline and Plan-Do-Study-Act (PDSA) 1, workflow improved by increasing communication between providers and pharmacy to decrease the time to administer pre-hydration fluids. Between PDSA 1 and 2, oral sodium bicarbonate was prescribed to alkalinize urine before admission; fellows were empowered to release pre-hydration fluids and facilitate expedited chemotherapy delivery to the floor.

Objectives: Increase interconnectivity between hospital departments (inpatient, pharmacy, post-op, nursing, outpatient) and optimize supportive care to decrease the time to achieve start parameters, decrease the time to start HD MTX, and decrease discharge time.

Design/Method: This QI project involved a retrospective chart review from 7/2020 – 7/2021, including 55 HD MTX cycles for 20 pediatric patients ages 2-20 to establish a baseline.

PDSA 1 (7/21-1/22) included 19 HD MTX cycles for 6 patients ages 2-9. The post anesthesia care unit (PACU) nursing staff and care providers were educated about the importance of efficiently administering a normal saline and a sodium bicarbonate bolus following the LP, to facilitate starting HD MTX.

PDSA Cycle 2 (4/7/22-present) includes 18 HD MTX cycles for 6 patients ages 1-16. We educated the outpatient team to start normal saline and a sodium bicarbonate bolus in clinic and send the urinalysis before admission. For patients coming from home, families were provided with the amount of fluid to drink and oral sodium bicarbonate. Increased communication between pharmacy and providers attempted to decrease time to initiate HD MTX once urine criteria was met.

Results: The initiation time for pre-hydration fluids to reach the patients decreased by approximately 2.17 hours. On days 1 and 29, the time to start chemotherapy decreased by 1.04 hours and the time to meet pH and spec gravity criteria decreased by 0.65 and 0.83 hours respectively. For days 15 and 43, the time to meet urine pH on decreased by 1.22 hours and discharge times decreased by 0.92 hours.

Conclusion: Increased communication across disciplines and providing education yielded improvement in start times and more efficient use of resources to optimize patient care during routine chemotherapy admissions for the patient and the family as well as hospital bed flow.

POSTER # 124 | CPX-351 ASSOCIATED RASH IN PEDIATRIC PATIENTS WITH ACUTE MYELOID LEUKEMIA: A CASE SERIES

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Background: CPX-351 (a liposomal formulation of cytarabine and daunorubicin) is a chemotherapeutic agent for treatment of acute myeloid leukemia (AML). Efficacy and safety of CPX-351 for adult AML therapy is established, and a phase 3 clinical trial of CPX-351 in pediatric AML (NCT04293562) is ongoing. Adult studies report that rash with CPX-351 is a frequent adverse event (~39% of patients). However, the features of cutaneous side effects in the pediatric population associated with CPX-351 including appearance, course, and management have not been well-described in the literature.

Objectives: The objective was to describe the characteristics and management of CPX-351 associated rash in the pediatric population.

Design/Method: This is a retrospective case series of 45 patients who received CPX-351 at Texas Children's Hospital from 2018-2022. Data was collected via manual chart abstraction with approval from the Baylor College of Medicine IRB.

Results: Mean patient age was 9 years (range 0.1-19 years) with 42% identifying as Hispanic, 33% White, 13% Black, and 11% Asian. Eighty percent of patients developed rash. Words used to describe the rash by providers were "maculopapular" (56%), "macular" (22%), "papular" (19%), and "nodular" (3%). The rash was almost universally noted as diffuse although in some instances started on the face, trunk, or extremities prior to becoming generalized and eventually transforming from erythematous to hyperpigmented. Time to onset of rash after CPX-351 administration was 1-8 days. Once present, mean time to rash resolution was 32 days (range of 3-115 days). Forty-two percent of patients had pruritus associated with the rash. Pain was not a symptom ascribed to any patient's rash. Histopathology studies of skin biopsies from 4 patients showed nonspecific findings with perivascular lymphocytic inflammation.

Conclusion: Our pediatric case series demonstrated that rash associated with CPX-351 is significantly more common than what is reported for adults receiving CPX-351 or cytarabine. Additionally, patients had prolonged time to resolution. Based on our data, the rash is generally asymptomatic and resolves without intervention. However, some patients experience significant pruritus, which is an issue for these immunocompromised patients at risk of life-threatening infections secondary to skin breakdown from excoriation. Supportive measures including emollients, topical steroids and systemic antihistamines can be helpful for symptom alleviation. Our case series contributes to the limited data available on CPX-351 associated rash, and it is expected to be helpful in counseling families on this frequent side effect from CPX-351.

POSTER # 125 | RECURRENT HYPOGLYCEMIA FOLLOWING ASPARAGINASE THERAPY FOR LYMPHOID MALIGNANCIES IN CHILDHOOD

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Background: Asparaginase (ASP) is a cornerstone pediatric acute lymphoblastic leukemia (ALL) and lymphoma (LLy) therapy. Hyperglycemia following ASP is described, but hypoglycemia is infrequently reported as a complication. Following hypoglycemic events in children receiving ASP therapy at Texas Children's Hospital, we evaluated associations and outcomes.

Objectives: Determine the risk factors, prevalence, duration, severity, recurrence, and outcomes of children developing ASP-induced hypoglycemia.

Design/Method: Retrospective cohort study using electronic medical records to identify all patients who received ASP (PEGylated or non-PEGylated) and had diagnosis of hypoglycemia between 6/1/2017 and 6/30/22 at Texas Children's Hospital. We defined ASP-induced hypoglycemia as blood glucose (BG) <70 mg/dl 2-8 weeks after ASP administration, without alternative causes. If hypoglycemia evaluation was completed, hyperinsulinism was defined by: BG <50 mg/dL; insulin > 2 mIU/mL; or other parameters as standardly defined. Demographic and clinically relevant data were collected. Univariate regression models using Stata16 were analyzed.

Results: 721 patients received ASP, with 55 (7.6%) having ASP-induced hypoglycemia and a cancer diagnoses of ALL (n = 50) and LLy (n = 5). Median age was 4.4 years (InterQuartile Range [IQR]: 2.6 – 8.1), with 46% Hispanic and 59% male. Median BMI z-score was +0.4 (IQR: −0.3 - 1.2). Initial hypoglycemia event was during Induction or Reinduction therapy in 86% (n = 48), with median time from ASP to hypoglycemia episode of 11 days (IQR: 6-15). Median lowest BG was 51 mg/dL (IQR: 43-57) with median duration 11 days (IQR: 7-19). Management included dietary change (52%, n = 29), cornstarch (29%, n = 16), and continuous enteral feedings (13%, n = 7). Continuous BG monitoring was utilized in 9 patients (16%).

Full hypoglycemia workup was performed in 18 patients (32%), with all evaluations consistent with hyperinsulinism. Recurrent hypoglycemia with subsequent ASP doses occurred in 42 patients (74%), with a median duration 14 days (IQR: 8-21; max: 56 days). Overall survival following ASP-induced hypoglycemia was 80% (85% if excluding patients with relapsed disease), with 3 years' median follow up. Severity of hypoglycemia (lowest BG, number of events, or length of events) was not associated with age, sex, ethnicity, or BMI z-score in univariate analysis.

Conclusion: ASP-induced hypoglycemia is relatively common, often recurs with subsequent dosing, and may be severe, requiring intensive management. Prospective screening of patients receiving ASP may be appropriate to detect and manage events. Reassuringly, patients completed chemotherapy without change in survival at 3 years' follow-up. Further studies to elucidate prognostic factors of ASP-induced hypoglycemia are needed.

POSTER # 126 | A DAILY SYMPTOM CHECKLIST MAY REDUCE HOSPITAL READMISSIONS IN NEWLY DIAGNOSED LEUKEMIA PATIENTS

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Background: At Phoenix Children's, 70-90 patients are diagnosed with acute lymphoblastic leukemia (ALL) yearly. Induction therapy for these patients has significant medical and emotional complications. Readmission rates during induction have historically reached 50%, with approximately 45% of readmissions considered potentially preventable. Reducing induction morbidity is one significant strategy for decreasing readmission rates.

Objectives: We propose to evaluate the feasibility and implementation of a daily texting interface to improve symptom management for patients newly diagnosed with ALL. We also aim to decrease caregiver distress, improve overall satisfaction with the medical care team, and decrease readmission rates for newly diagnosed ALL patients during their first month of treatment.

Design/Method: Phase I of the study (approximately 20 participants) evaluates outcomes via a weekly distribution of electronic questionnaires during induction that measure distress, burden, and quality of life. In Phase II (approximately 40 participants), caregivers will receive daily texts during induction. They will be prompted to complete assessments and answer additional questions regarding symptoms and medication compliance. Pre-defined responses will automatically alert a member of the clinical team for intervention. Phase I data will be compared to Phase II to determine effects of the daily texting interface on distress, burden, and readmission rates.

Results: Phase I data showed the following average self-reported distress scores (maximum = 10): Day 8 = 6.67 (95% CI [5.48-7.86]); Day 15 = 4.59 (95% CI [3.03-6.16]); Day 22 = 4.44 (95% CI [3.04-5.85]); and Day 29 = 4.06 (95% CI [2.69-5.43]). Six of 18 patients (33.33%) were seen in the Emergency Department (ED) without hospital admission. Eleven of 18 patients (61%) were readmitted for a total of 123 inpatient days, and 27% of days were spent in the pediatric intensive care unit (PICU). Two patients were inpatient for the duration of their induction therapy. Phase II data is currently being collected.

Conclusion: Our data suggest that caregivers of patients with ALL experience a moderate amount of distress and that many patients were readmitted to the hospital during induction therapy. Initial feedback from families participating in the daily texting was positive, and most caregivers submitted surveys weekly. Therefore, we anticipate high compliance rates during Phase II. With prompt intervention from a clinical team, Phase II may alleviate caregiver distress and ultimately reduce readmission rates. This may have implications not only for leukemia patients but also other populations undergoing intensive treatments.

POSTER # 127 | EVALUATING PREVALENCE AND CAUSES OF PSYCHOSOCIAL DISTRESS AMONG PEDIATRIC PATIENTS WITH LEUKEMIA

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Background: A Leukemia diagnosis causes psychosocial distress in a significant number of patients. When this psychosocial need goes unattended, it can negatively affect their course of treatment. To prevent this issue, the Distress Thermometer (DT) allows a quick and valid way for patients/parents to self-report distress on a scale of 0-10, including identification of the distress source.

Objectives: This study aims to contribute the Leukemia-distress knowledge by describing the findings from a convenience sample of patients with leukemia that completed the DT from 2020-2022 to see if there is an association/difference between demographic groups such as ethnicity (Hispanic vs. non-Hispanic), gender (Male vs. Female), Leukemia type (ALL vs. AML), and age (0-5, 6-12, 13-18, 19-up).

Design/Method: Patients with Leukemia who completed the DT at least once will participate in the study. Then the data will be analyzed using descriptive statistics and Chi-square. The first comparing method will look at distress levels in three categories: Low (0-3), Moderate (4-7), and High (8-10) across the demographic groups. The second method will use the suggested cut-off value for distress, where a score less than three indicates low or no distress, and a score greater than 3 indicates significant distress.

Results: One hundred and thirteen patients meet the inclusion criteria with age ranges from 0 to 30 with an average age of 9.5. There were 56 Males (49.6%), and 57 (50.4%) were females; 47 were Hispanic (41.6%) and 66 non-Hispanic (58.4%); 89 had ALL (78.8%), and 19 had AML (16.8%). Fifty-eight participants (51.33%) indicated low, 45 (39.82%) were moderate, and 10 (8.85%) had high distress levels. When using the three categories of distress, there was no significant association of distress with gender, Leukemia type, or age, except with ethnicity ($p = 0.032$), which originated from the moderate category. When using the cut-off value of 3 of distress, there was no significant association with any demographic group. The most selected sources of distress were: Worry and Anxiety (38, 36.5%), followed by boredom, apathy, or Irritability (37, 35.6%), and Fatigue (30, 28.8%) in third place.

Conclusion: The DT is a helpful tool for distress screening in a pediatric oncology department. A significant portion of patients with Leukemia experience distress. Despite not showing a significant difference across demographic groups, the statistics show there might be a significant association between moderate distress levels and

ethnicity, where non-Hispanics show a slightly higher distress prevalence over Hispanics. Future studies need to explore this further probable association.

POSTER # 128 | PREDICTORS OF NAUSEA DURING EARLY TREATMENT IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Chemotherapy-induced nausea and vomiting (CINV) remains one of the primary drivers of reduced quality of life among patients diagnosed with pediatric cancer. Current guidelines for CINV prophylaxis focus on the chemotherapeutic agents prescribed due to a lack of identified patient-specific risk factors. Suboptimal management of CINV can cause anticipatory nausea and a reduced quality of life. Apart from the use of granisetron in place of ondansetron in patients with *CYP2D6* genotypic variations, pharmacogenomic factors have not been considered when managing CINV in children.

Objectives: The primary objective was to identify patient-specific clinical risk factors for the development of nausea during induction and the first cycle of high-dose methotrexate (HDMTX) in children with newly diagnosed Acute Lmphoblastic Leukemia (ALL), using the number of doses of antiemetics prescribed as a surrogate for nausea. Further analyses evaluated germline genomic features associated with nausea.

Design/Method: This retrospective cohort study included 576 patients who were treated for newly diagnosed ALL on St. Jude Children's Research Hospital's Total Therapy XVI trial. Patient and disease characteristics were obtained from the clinical trials research database. The primary outcome measure was the sum of the total doses of antiemetics administered to patients either inpatient or in the outpatient infusion center and outpatient prescriptions for antiemetics during the first 8 weeks of therapy encompassing 7-drug induction and the first cycle of HDMTX. Previously generated genomic data from peripheral blood specimens obtained during remission were used for genome-wide association studies of CINV. Associations of CINV with clinical risk factors and genomic features were determined using linear regression models.

Results: Antiemetic use varied widely with a median of 34 doses (interquartile range 27-46). Older age (1.2 extra doses per year of age, 95%CI 0.7-2), female sex (8.7 doses, 95%CI 5-12.5), receipt of 5 g/m^2 vs. 2.5 g/m^2 of HDMTX during consolidation (7.4 doses, 95%CI 3.6-11), and receipt of 6 vs. 3 intrathecal chemotherapy doses during induction (5.9 anti-emetic doses, 95%CI 2-10), were associated with greater antiemetic use in both univariate and multivariate analyses. Patients requiring more antiemetics during early therapy also lost more weight during this time. Evaluation of genomic predictors of nausea are ongoing at this time and will be reported at the meeting.

Conclusion: Despite similar treatments, children with newly diagnosed ALL experience wide variations in the degree of nausea during early therapy. Knowledge of patient-specific risk factors could allow more targeted interventions to improve quality of life.

POSTER # 129 | PROCEDURE SEDATION PRACTICES IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA TO REDUCE ANESTHESIA EXPOSURE

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Background: Pediatric acute lymphoblastic leukemia (ALL) is the most common cancer in children with current event-free survival (EFS) rates>90%. An important advancement in treatment has been central nervous system (CNS) -directed therapy involving multiple doses of intrathecal (IT) chemotherapy delivered directly to the cerebrospinal fluid (CSF) via lumbar puncture (LP). Multiple methods of providing sedation are available to improve patient comfort and successful IT therapy delivery. Recent studies show possible adverse neurocognitive effects associated with repeated anesthesia exposure

Objectives: Evaluate if conscious sedation administered in the the Jimmy Everest Center for Cancer and Blood Disorders (JEC) by pediatric hematology oncology faculty is safe with minimal adverse sedation events, associated with effective delivery of IT chemotherapy and with rate of traumatic LPs similar in comparison to general anesthesia and other institutional sedation alternatives.

Design/Method: We used a retrospective cohort study of patients ages 0-24 years diagnosed with ALL between January 1, 2019 and December 31, 2021 who received treatment at the JEC. Sedation practices and patient characteristics were collected for LPs performed during Maintenance phase of therapy. Descriptive statistics were gathered and generalized linear regression models were used to assess for potential risk factors that may lead to procedure complications.

Results: Study population included 58 patients and 352 LPs during Maintenance therapy. Seventy-six percent of patients received moderate sedation with ketamine and midazolam while the remainder received alternative forms of sedation. Successful delivery of IT chemotherapy and collection of CSF for analysis was achieved in > 99% of LPs in this population. There were no statistically significant differences in rates of traumatic LP between different modes of sedation and were favorable when compared to historical controls. Serious complications due to sedation were extremely rare.

Conclusion: Conscious sedation administered in the JEC by pediatric hematology oncology faculty was not associated with lower rates of successful delivery of IT therapy or higher rates of traumatic LPs compared to other institution sedation methods. Moderate IV or inhaled sedation administered in the outpatient clinic had a comparable procedural safety and efficacy profile compared to general anesthesia with a low rate of adverse sedation events which were not severe. The model

used in the JEC allows for decreased exposure to general anesthesia which may have important neurologic implications for long-term survivors.

POSTER # 130 | REAL-WORLD DATA OF THE USE OF RIVAROXABAN IN PEDIATRIC PATIENTS WITH HEMATOLOGIC MALIGNANCIES

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Background: In Canada, rivaroxaban was approved for the treatment of thromboembolism (TE) in children in January 2021. Anticoagulation is particularly challenging in children with hematologic malignancies, as frequent procedures and thrombocytopenia put the patients at high risk of bleeding. Real-world data are scarce regarding the use of rivaroxaban in children with hematologic malignancies.

Objectives: Describe the effectiveness and safety of rivaroxaban in children with hematological malignancies

Design/Method: We performed a retrospective cohort study of children and adolescents aged 21 years or younger diagnosed with leukemia or lymphoma who received rivaroxaban at the CHU de Québec and the CHU Sainte-Justine. Main outcomes were TE resolution, categorized as: complete/partial/progressive disease, and major (MB) and clinically relevant non-major bleeding (CRNMB), defined as per ISTH criteria. Rivaroxaban dosing is not available in our jurisdiction and could not be collected.

Results: Among 11 eligible patients (median age: 13 years [25-75th percentile: 10-16.5], 55% male), eight patients (73%) had acute lymphoblastic leukemia [ALL], 2 (18%) non-Hodgkin lymphoma, and one (9%) Hodgkin lymphoma. All patients had a CVC in place (55% Port-A-Caths, 45% PICC lines), as well as additional prothrombotic risk factors, most commonly asparaginase exposure (73%), mediastinal mass (46%), and obesity (36%).

Rivaroxaban (standard weight-based dosing) was used for VTE treatment in 10 patients, because of deep vein thrombosis (n = 4), pulmonary embolism (n = 1), cerebral sinus venous thrombosis (n = 3) or multiple TEs (n = 2). Rivaroxaban was started after a median of 27 days (25-75th percentile: 14-86) after TE diagnosis following treatment with unfractionated or low molecular weight heparin. Interruptions of anticoagulation were necessary in 9 (90%) patients, due to thrombocytopenia or lumbar punctures. Complete TE resolution was achieved in 8 (80%) patients. One patient with a CSVT sustained an asymptomatic TE progression, despite adequate compliance and absence of interruptions. Rivaroxaban was used for as primary thromboprophylaxis post-operatively in one patient with several prothrombotic risk factors; no TE occurred.

During a combined exposure of 50.7 months, no MB or CRNMB episode was encountered. No patient stopped rivaroxaban due to adverse events. Three out of 16 lumbar punctures performed during rivaroxaban treatment were traumatic, which was not significantly different than LPs performed during treatment with other anticoagulants (19% vs 36%, p = 0.236).

Conclusion: Rivaroxaban was safe in children and adolescents with hematological malignancies. While our data and subgroup analyses from the pediatric randomized controlled trial EINSTEIN-JR suggest its effectiveness in children with cancer, ongoing surveillance is required, especially for subgroups at higher thrombotic risk.

POSTER # 131 | ADHERENCE TO MERCAPTOPURINE AND HABIT STRENGTH IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Rates of adherence to mercaptopurine (6-MP) below 90% have been associated with increased relapse in pediatric patients with acute lymphoblastic leukemia (ALL). Habit strength has been associated with medication adherence through multiple mechanisms, including self-efficacy and social norms.

Objectives: The goal of this study was to investigate the relationship between habit strength, adherence to 6-MP, and health-related quality of life domains.

Design/Method: This was a single center, cross-sectional study. A total of 52 participants, including 11 patients (ages 12-23, mean age 16 ± 4, 45% Female) and 41 parents/caregivers (ages 25-43, mean age 37 ± 5, 80% Female) of patients with ALL under the age of 18. Participants completed the Visual Analogue Scale (VASdose), PROMIS Medication Adherence Scale (PMAS), Self-Regulated Habit Index (SRHI), and PROMIS quality of life measures (PROMIS-CAT). Spearman's rho correlations were used to assess relationships between variables. Eleven semi-structured interviews of patients and caregivers were conducted and analyzed using Grounded Theory coding and thematic analysis.

Results: Overall, 81% (n = 42/52) of participants surveyed had high adherence to 6-MP (VASdose ≥95%); 91% (n = 10/11) of patients and 78% (n = 32/41 of parents/caregivers reported high adherence. The median VASdose and PMAS score were 100% (IQR 3) and 39.5 (IQR 2) across all participants, respectively. Participants with higher adherence, VASdose ≥ 95% and PMAS ≥ 39.5, reported less physiological stress (p = 0.02), and better cognitive function (p = 0.09) and peer relations (p = 0.08), compared to those with lower adherence. No significant correlation was found between medication adherence rate and habit strength.

Emerging themes from qualitative coding included the influence of routine and automaticity on 6-MP as well as adherence strategies. Strategies such as reminders, care team communication, and developing personalized tools were cited by participants as potentially improving adherence in taking or administering 6-MP. Other facilitating participant characteristics included experience with medication

administration, self-efficacy, and access to social support. Financial burden, scheduling conflicts, and medication access were common barriers cited by participants.

Conclusion: One-fifth of our participants reported lower adherence to 6-MP (VASdose <95%), which increases risk of relapse. Medication adherence to 6-MP was not associated with habit strength, but our results show preliminary associations between adherence rates and quality of life outcomes, such as physiological stress. Behavioral interventions are needed to better optimize adherence to 6-MP and improve health outcomes in pediatric ALL.

POSTER # 132 | TREATMENT HETEROGENEITY OF HIGH-RISK CLASSICAL HODGKIN LYMPHOMA IN PEDIATRIC AND AYA PATIENTS

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Background: Classical Hodgkin lymphoma (cHL) remains a prevalent diagnosis among pediatric and adolescent and young adult (AYA, aged 15-39 years) patients. With multiple efficacious treatment regimens and nearly all patients surviving into adulthood, novel approaches seek to maintain rate of cure while minimizing long-term side effects. These include risk of cardiovascular and pulmonary toxicity, secondary malignancies, and infertility.

Objectives: This project compared the various treatment regimens of high-risk (HR) cHL (stages 3 and 4) within a single academic institution. Primary outcomes included overall survival (OS) and relapse-free survival (RFS) rates. Secondary outcomes included need for radiation, cardiovascular toxicity, pulmonary toxicity, secondary malignancy, and infertility.

Design/Method: Retrospective chart review identified patients with HR cHL treated at a tertiary care center with large pediatric and adult hematology/oncology practices from 2012 to July 2022. Patients 39 years and under were included. Baseline demographic data, disease specific information, treatment regimen, treatment location, remission status, cardiovascular and pulmonary toxicity, secondary malignancies, infertility, and survival were collected.

Results: Seventy-seven eligible patients were identified, with 11 in the pediatric and 66 in the AYA age group. Patients were treated with 9 different regimens, including ABVD (48%), BEACOPP (28%) and ABVE-PC (6%), among others with 1-2 patients each. OS was 96%, and overall RFS was 82%. Twenty-two percent of patients required radiation. Only one patient developed a secondary malignancy (initially treated with BEACOPP) and ultimately died secondary to treatment-related toxicity. Fourteen percent of patients developed pulmonary toxicity and 3% of patients developed cardiovascular toxicity. Fertility was inconsistently evaluated, precluding collection of meaningful data. Data by regimen:

ABVD: RFS 28/37 (77%), radiation 3/37 (8%), pulmonary toxicity 3/37 (8%), cardiovascular toxicity 1/37 (3%).

BEACOPP: RFS 17/21 (81%), radiation 9/21 (43%), pulmonary toxicity 6/21 (29%), cardiovascular toxicity 1/21 (5%).

COPP-ABV: RFS 3/4 (75%), radiation 1/4 (25%), pulmonary toxicity 1/4 (25%), no cardiovascular toxicity.

ABVE-PC: RFS 5/5 (100%), radiation 1/5 (20%), no toxicities.

A-AVD: 4/4 (100%) RFS, no toxicities.

Conclusion: Our single institution data demonstrates that historically used regimens, including BEACOPP and ABVD, have good survival rates but result in high toxicity rates. Newer regimens so far have acceptable relapse-free survival and toxicity rates. Oncologists should therefore consider the toxicity profile when selecting a regimen to treat patients with HR cHL. The multitude of regimens also suggests the need for reassessment of group practices as new data becomes available to allow for continued success in treating cHL with minimal treatment toxicity.

POSTER # 133 | TARGETED IMMUNOTHERAPY IN CHILDREN, ADOLESCENTS & YOUNG ADULTS WITH LYMPHOMA: RADICAL HODGKIN COHORT

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Background: Significant chronic health conditions increase over time among pediatric, adolescent, and young adult (CAYA) classical Hodgkin lymphoma (cHL) survivors. Targeting the tumor microenvironment and tumor-specific antigens is emerging as effective and safe treatments for cHL patients which may help reduce toxicity. We completed a phase 2 trial evaluating the use of an antibody-drug conjugate targeting CD30 (brentuximab vedotin, Bv) and anti-CD20 antibody targeting regulatory B-cells (rituximab, RTX) added to risk-adapted chemotherapy in newly diagnosed cHL CAYA patients. The combination was safe and resulted in reduction of toxic chemotherapy and radiation therapy, while maintaining superior outcomes (5-year OS/EFS 100%; Hochberg/Cairo, JITC, 2022). Adding the checkpoint inhibitor nivolumab to chemoimmunotherapy with Bv + RTX may allow further anthracycline dose reduction and reduce the need for RT in intermediate-/high-risk cHL in CAYA.

Objectives: To assess the safety and feasibility of adding nivolumab to chemoimmunotherapy with Bv + RTX in intermediate-/high-risk cHL in patients age ≥ 3 and ≤ 39 years. (NCT05253495).

Design/Method: This is a multicenter study for intermediate- and high-risk cHL. Intermediate-risk patients receive 2 cycles of Bv, doxorubicin, vinblastine, dacarbazine, and RTX (Bv-AVD-R). Rapid early responders (RER) or slow early responders (SER) by FDG-PET scan receive 2 or 4 cycles of Bv, vinblastine, dacarbazine, nivolumab, and RTX (Bv-NVD-R), respectively without further anthracycline (max dose 100 mg/m2). High-risk patients receive 2 cycles of Bv-AVD-R. RERs receive 4 cycles of Bv-NVD-R; SERs receive 2 cycles

of Bv, nivolumab, doxorubicin, vinblastine, dacarbazine and RTX (Bv-NAVD-R), followed by 4 cycles of Bv-NVD-R. Radiotherapy is given only to patients not achieving CR at the end of planned chemoimmunotherapy based on FDG-PET, regardless of early response assessment.

Results: Nine patients have been treated to date including 4 intermediate- and 5 high-risk patients. Median age 17 yr (10-23 yr). Male:female ratio = 5:4. On FDG-PET following 2 cycles of Bv-AVD-R, all 4 intermediate-risk patients and 3 high-risk patients have been RER. Two high-risk patients have been SER. All 9 patients have completed therapy and are in CR. No patient has required radiation therapy to date. There have been no unexpected AEs related to therapy and no dose limiting toxicities with the addition of nivolumab. Accrual is ongoing.

Conclusion: The addition of nivolumab to a backbone of reduced toxicity chemoimmunotherapy is safe and feasible. Targeting the tumor microenvironment and PD1/PD-L1 axis is a promising approach in CAYA with cHL which may maintain overall outcomes while limiting anthracycline and radiation exposure.

POSTER # 134 | INTERIM PET-CT, PREDICTIVE MARKER AND TOOL FOR THERAPY MODIFICATION IN PEDIATRIC HODGKIN LYMPHOMA

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Background: Hodgkin lymphoma (HL) is one of the highly curable malignancies in children. Given its high sensitivity, specificity, positive and negative predictive value, interim PET-CT becomes a promising tool for predicting outcome in patients with HL. In this study, we shared our experience with interim PET-CT in the management of pediatric patients with HL treated at our institute.

Objectives: 1. To analyze the role of Interim PET-CT in children with Hodgkins Lymphoma treated with ABVD chemotherapy and or radiation.

2. Discuss the result and the effect of other factors on the outcome.

Design/Method: This is a retrospective study of pediatric patients diagnosed with HL treated from September 2017 to February 2022. Patients were diagnosed and managed as per ESMO clinical practice guidelines.

Results: Total children were 23. Median age was 9 years. There were 17 males (70%) and 6 females (30%). Consolidation radiotherapy was delivered to 9/23 patients. Interim PET-CT was done after 2 cycles of ABVD, twenty patients (86.9%) showed a complete metabolic response (CMR), 3 (13%) patients showed partial response. At a median follow up of the 29 month event free survival was 95.7% (CI- 95%) and overall survival was 100%. All 20/23 patients whose interim PET-CT showed CMR, continued to be in remission on followup. One of three patients whose interim PET showed partial response and received 4 more cycles of ABVD showed progression at the end of therapy PET CT, which was confirmed by biopsy. The patient was salvaged with Brentuximab, Gemcitiabine and autologous transplant. Two of three patients with partial response on interim PET-CT were given escalated BEACOPP and showed complete remission in post treatment PET CT. Univariate analysis showed no statistically significant correlation with patient characteristics or lab parameters with outcomes. Findings of Interim PET-CT was not associated with outcome when the whole cohort (n = 23) was taken for analysis, but when 21 patients who were uniformly treated without modification of therapy analyzed and showed findings of Interim PET-CT had statistically significant association with outcome $p < 0.0476$. This excludes 2 patients who had a partial response (interim PET CT) and further treated with escalated BEACOPP.

Conclusion: Interim PET-CT response is prognostically important, CMR in interim PET-CT is associated with prolonged remission status, justifying the use of limited treatments. Patients with positive interim PET-CT have a higher chance of relapse and need augmentation of therapy. A surveillance scan is not required during follow-up in patients where the interim PET-CT was in CMR.

POSTER # 135 | REVIEW OF CLINICAL EVIDENCE IN FRONTLINE TREATMENT OF NEWLY DIAGNOSED HIGH-RISK PEDIATRIC CHL

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Background: Multiagent chemotherapy (CTX) and targeted therapy (e.g., brentuximab vedotin [BV]) treatment regimens for pediatric patients with classical Hodgkin lymphoma (cHL) are largely determined by risk (i.e., low, intermediate, high) and adapted based on early treatment response. Understanding clinical evidence within the high-risk population is critical for the evolution of treatment and reduction of late effects.

Objectives: To identify clinical evidence for the efficacy and safety of frontline treatment for pediatric patients with high-risk cHL in the United States.

Design/Method: A systematic literature review (SLR) was initiated in July 2022. Searches were conducted in MEDLINE (via PubMed) and Embase. Existing SLRs, randomized controlled trials (RCTs), prospective non-RCTs, and observational studies of pediatric patients (≤22 years) with cHL treated in the frontline setting in the United States from 2009 were included. Quality assessment of each study was performed.

Results: A total of 4,556 records were identified; 12 unique studies represented across 32 publications were abstracted. Most studies were non-RCTs (n = 5); 2 RCTs investigated the comparative efficacy

of BV+CTX versus CTX. Across all clinical trials, considerable variation was observed regarding study design, inclusion criteria, CTX drugs, sample size, and definitions of "high-risk" disease. Event-free survival (EFS) was the most common primary endpoint. The RCTs reported EFS or progression-free survival (PFS) for BV+CTX versus CTX. Both studies reported significantly higher 3-year EFS/2-year PFS for patients who received BV+CTX; no significant differences in 3-year overall survival (OS) were observed versus CTX. A non-RCT reported 100% 5-year EFS and OS in a small sample (n = 12) of patients who were treated with BV+CTX. A single-arm study reported significantly higher 3-year EFS for BV+CTX versus a CTX historical control (97.4% versus 80.8%); no improvement in OS was observed. Reported 3- and 5-year PFS/EFS (range: 74.4%–94.0%) and OS (95.0%–98.5%) rates were similar for CTX across studies. The proportion of patients who received radiation therapy was reported in six studies and ranged from 13%–100%. Safety data were inconsistently reported across studies; the most commonly reported adverse events across studies for all treatments were hematological and peripheral neuropathy.

Conclusion: Limited and heterogeneous efficacy and safety evidence was identified for frontline treatment of pediatric patients with high-risk cHL. Two RCTs identified indicate an EFS and PFS benefit for BV+CTX relative to CTX. Further prospective studies with longer follow-up are warranted to confirm the benefits of BV in this population, particularly its impact on OS.

This study was funded by Seagen Inc.

POSTER # 136 | EMAPALUMAB TREATMENT PATTERNS/OUTCOMES IN PRIMARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS: REAL-HLH STUDY

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Background: Hemophagocytic lymphohistiocytosis (HLH) is a rare, life-threatening, hyperinflammatory syndrome characterized by overproduction of proinflammatory cytokines, such as interferon gamma (IFNγ). Emapalumab is a fully human monoclonal antibody that neutralizes IFNγ activity. Emapalumab is indicated in the US for treatment of adults and children with primary HLH (pHLH) with refractory, recurrent, or progressive disease, or intolerance to conventional therapy. However, since approval, real-world evidence on emapalumab use in routine clinical setting is limited.

Objectives: To assess real-world treatment patterns and outcomes in patients treated with emapalumab in the US.

Design/Method: A retrospective chart review conducted across 33 US hospitals identified patients treated with ≥1 dose of emapalumab between November 20, 2018, and October 31, 2021. Data extracted for the subpopulation of patients with pHLH from time of emapalumab initiation to end of data availability, death, or study end (December 31, 2021) are presented.

Results: Forty-six of the 105 enrolled patients met the pHLH classification criteria. Most patients were male (61%) and non-white (54.3%). At diagnosis, mean (SD) age was 3.9 (5.3) years, 21.7% (10/46) of patients had CNS involvement, and 90% (27/30) of patients with available data met at least 5/8 HLH-2004 diagnostic criteria. Genetic mutations known to cause pHLH were reported in 40/44 (91%) patients. FHL2-PRF1 (37.5%), FHL3-UNC13D (25%), and CHS-LYST (12.5%) were the most common genetic mutations. Furthermore, 25/46 (54%) patients presented with infection at diagnosis with viral infections (18/25; 72.0%) being the most common. At emapalumab initiation, 35/46 (76.1%) of patients had received prior treatment for HLH, 15/46 (32.6%) were in the intensive care unit, and 11/46 (23.9%) were receiving supportive care (i.e., mechanical ventilation, extracorporeal membrane oxygenation, vasopressors, or dialysis). Median (range) time to emapalumab initiation from HLH diagnosis was 27.5 (2-759) days. Median (range) treatment duration with emapalumab was 71 (1-523) days. Median (range) starting, maximum single and cumulative treatment doses were 1.1 (0.8-9.8) mg/kg, 6.1 (1.0-12.8) mg/kg and 65.6 (1-512.2) mg/kg, respectively. Overall, 73.8% (31/42) of patients who were considered eligible for transplant by their treating physician proceeded to HSCT. Overall survival was 73.9% (34/46) and the 12-month survival probability following emapalumab initiation was 73.1%.

Conclusion: This study describes real-world treatment patterns and outcomes with emapalumab across a diverse patient population with pHLH. Consistent with the results of the pivotal trial (NCT01818492), nearly three-fourths of HSCT-eligible patients treated with emapalumab proceeded to HSCT and 12-month survival probability following emapalumab initiation was 73.1%.

Study and writing supported by Sobi, Inc.

POSTER # 137 | THE PROTECTIVE ROLE OF TRANSCRIPTION FACTOR NRF2 IN MUNRINE HYPERINFLAMMATION

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Background: Hyperinflammatory syndromes like hemophagocytic lymphohistocytosis (HLH) are characterized by organomegaly, multilineage cytopenias, hypercytokinemia, and tissue hemophagocytosis. The mechanisms by which hemophagocytes regulate the hyperactive immune response remain unclear. The transcription factor Nrf2 is an important sensor for inflammatory and redox stress. Downstream of Nrf2 are antioxidant response elements responsible for restoration of redox homeostasis within the cell.

Objectives: Here we aim to characterize the protective role of Nrf2 in a mouse model of hyperinflammation and investigate the mechanisms by which hemophagocytes regulate immune system activation.

Design/Method: Secondary HLH is induced using TLR9 agonist CpG in both wildtype and Nrf2 knockout mice. Mice receive five doses of 50 ug CpG injected intraperitoneally every other day for a total of 10 days. This induces a secondary hyperinflammatory state which

recapitulates the clinical findings of secondary HLH. Complete blood counts are measured before and after CpG-induced HLH. Liver and spleen pathology are analyzed. Serum free heme, ferritin, and cytokines (IL-12, IL-10, TNF, IL-6, IFNg) are measured on collected blood samples. in vivo oxidative stress is measured by MDA assay, glutathione levels, and CellRox green-fluorescent molecular probe. in vitro bone marrow derived macrophages and dendritic cells are used to investigate regulation of CpG-induced cytokine expression by oxidized red blood cells and heme.

Results: Mice with CpG-induced hyperinflammation have evidence of systemic oxidative and nitrosative stress—including increased serum nitric oxide and elevated lipid peroxidation in both whole spleen lysates and peripheral red blood cells. The compound monomethylfumarate (MMF), a known inducer Nrf2, is able to partially rescue mice from hyperinflammatory disease including anemia. In this model, Nrf2 knockout mice develop significantly worse organomegaly, hypercytokinemia, and evidence of bone marrow stress compared to wildtype controls. Interestingly, the hypercytokinemia in the Nrf2 KO mice favors cytokines that are central to HLH physiology: IL-12, IFNg, and IL-10. Nrf2 KO mice also have an increased serum free heme and an anemia with elevated reticulocytosis—demonstrating red cell consumption by intravascular hemolysis. in vitro we have found that oxidized red blood cell lysates and heme itself are both able to suppress IL-12 transcription and protein production from bone marrow derived dendritic cells in a Nrf2-dependent manner.

Conclusion: Together our findings demonstrate hyperinflammatory syndromes are hyper-oxidative states and suggests hemophagocytosis have a protective role in hyperinflammation in part due to Nrf2-mediated suppression of proinflammatory cytokine production. Nrf2 represents a promising target for clinical application.

POSTER # 138 | IMPLEMENTING A MULTIDISCIPLINARY TEAM AND ORDER SET TO TACKLE HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS

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Background: Hemophagocytic lymphohistiocytosis (HLH), a rare condition marked by excessive immune activation, is diagnostically complex and presents similarly to other inflammatory disorders, including sepsis, liver disease/failure, and Kawasaki disease. Consequently, diagnosis is often delayed, and the condition is often underdiagnosed. To decrease mortality and improve outcomes of patients presenting with HLH, prompt recognition and treatment are necessary. A multidisciplinary team approach can aid in improving diagnosis and management.

Objectives: A disease-specific multidisciplinary team was implemented at our institution, and in December 2019, the team established an electronic diagnostic order set to foster uniformity in the diagnostic approach to HLH for providers. The goals of this study are to capture the impact of the multidisciplinary team and diagnostic tool in the diagnosis and management of HLH at our institution.

Design/Method: This is a retrospective study where preliminary data included information on the utilization of the HLH-specific order set since the time of implementation. The information was obtained from the electronic health record (EPIC), including data from the time of implementation of the order set in December 2019 through October 2022. The trends in the utilization of the order set by providers at our institution were analyzed to evaluate the awareness of this diagnostic tool.

Results: The HLH order set was utilized 30 times since implementation, most commonly by hematology/oncology providers (46.7%), followed by rheumatology providers (33.3%) and infectious disease providers (20%). At the time of analysis in October 2022, the order set was utilized 10 times in the year 2020, 12 times in 2021, and 7 times in 2022. The use of the order set was associated with the diagnosis of HLH in 8 patients (26.7%).

Conclusion: Implementation of an HLH-specific order set facilitated a systematic method to approach patients with suspected HLH. The utilization of the order set remained reasonably stable over time among three different specialties, indicating support and awareness of this tool by these providers. A multidisciplinary team can increase awareness and improve the diagnosis and management of this disease, and thus improve outcomes of patients with HLH.

POSTER # 139 | A NOVEL THERAPY FOR REFRACTORY CBFA2T3::GLIS2-associated AMKL USING STRO-002 AND PLERIXAFOR

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Background: *CBFA2T3::GLIS2*-associated AML (CBF/GLIS AML) is an aggressive form of AML often associated with AMKL and recognized by its unique RAM phenotype by flow. It has a very poor prognosis, frequently refractory to standard of care regimens, with extreme marrow localization of leukemic blasts likely mediated by high CXCR4 (CD184) expression. The *CBFA2T3::GLIS2* fusion gene is the most common oncogenic transcript in pediatric AMKL and universally results in high expression of FOLR1 surface antigen. STRO-002, an antibody drug conjugate targeting FOLR1, is currently in Phase I clinical trials for adults with refractory ovarian and endometrial malignancies A summary of 17 patients with refractory *CBFA2T3::GLIS2* AML who received STRO-002 under compassionate use single patient IND reported significant clinical activity with little to no toxicity (7 patients achieved MRD negative remissions). Plerixafor, a reversible CXCR4 antagonist, mobilizes marrow stem cells and leukemic cells and has been investigated in patients with relapsed/refractory leukemia in combination with chemotherapy with modest response.

Objectives: We report a case of complete morphologic and immunophenotypic remission by targeted combination of STRO-002 and plerixafor in a child with refractory CBF/GLIS AML.

Design/Method: Case Report

Results: A 2-year-old female presented with fever, arm pain, and bruising and was diagnosed with RAM phenotype AMKL with FOLR1-positive *CBFA2T3::GLIS2* oncogenic fusion. She was enrolled on AAML1831 Arm A but Induction therapy was unsuccessful as evidenced by 14% residual BM blasts by flow cytometry. She was transitioned to STRO-002 monotherapy (4.3 mg/kg/dose IV every 2 weeks) as an outpatient for 4 cycles. BM was assessed q2wks prior to each cycle. Flow results post Cycles 1-4 were respectively: 2.7%, 2.02%, 1.6%, and 0.36%. Given persistent measurable residual leukemia, Plerixafor was added for leukemic cell mobilization with Cycles 5 and 6 (Plerixafor 0.24 mg/kg/dose 4 h prior and 24 h post each STRO-002 dose). After Cycle 5, MRD was 0.013% by flow and 0.4% *CBFA2T3::GLIS2* fusion expression. After Cycle 6, our patient achieved 0% MRD by flow and 0% *CBFA2T3::GLIS2* fusion expression. She had one episode of transient neutropenia after Cycle 5 while RSV+. Blood counts improved with the addition of plerixafor, and no toxicities were noted. She is currently 3 weeks status-post haploidentical bone marrow transplant awaiting engraftment.

Conclusion: Our patient with refractory *CBFA2T3::GLIS2*-associated AMKL achieved CR with STRO-002 and further reduction in leukemic burden was observed when plerixafor was added in combination. The treatment was well-tolerated by our patient. This initial report of the STRO-002-plerixafor combination supports further evaluation in similar patients.

POSTER # 140 | SMOLDERING LEUKEMIA PRESENTING AFTER PROLONGED PANCYTOPENIA

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Background: Acute leukemia in children commonly presents with abnormal blood counts, which bone marrow examination reveals an infiltration of lymphoblasts or myeloblasts. There have been rare reports of children who present with a "pre-leukemic" phase that is then followed by a temporary normalization of blood counts prior to their diagnosis of more overt acute leukemia.

We present the first case of precursor B-lymphoblastic leukemia (pre-B ALL) preceded by a prolonged but temporary pancytopenia without normalization of blood counts prior to leukemia onset. Clonal B-lineage blasts were identified by serial bone marrow monitoring during the 7 months of pancytopenia and was subsequently followed by a diagnosis of pre-B-ALL.

Objectives: We report on a 7-year-old boy with a 7-month history of persistent immature B cell population in the bone marrow with peripheral pancytopenia and hyperdiploidy on bone marrow analysis.

Design/Method: Case report/ Literature review

Results: Work up for infections, bone marrow failure syndrome, and autoimmune disorders were negative. PET CT was negative. He underwent whole exome sequencing, which showed a heterozygous BRIP1 mutation and compound heterozygous HFE mutations for hereditary hemochromatosis.

The phenotype of his immature B-cell population remained constant during this time and was CD19+ (dim), CD20-, CD22+ (dim), CD10+ (bright), CD34+, CD38+ (dim), cyto CD3-, CD7-, and MPO-. The bone marrow burden of his immature B-cell population increased over three bone marrow evaluations resulting in overt pre-B ALL after a 7-month period. At the time of overt pre-B ALL diagnosis, his bone marrow biopsy was>80% replaced by immature B-lymphoblasts positive for CD19, CD79a, PAX5, CD10, CD34, TdT, CD99, and Bcl2. Cytogenetics and FISH were consistent with hyperdiploidy, including the favorable double trisomy 4 and 10.

The patient was risk stratified as NCI standard risk based on age and presenting white blood cell count and was enrolled on Children's Oncology Group AALL1731. The patient has completed induction and achieved a negative peripheral blood and bone marrow minimal residual disease (MRD) evaluations.

Conclusion: Although there have been rare reports of transient pancytopenia with normalization of blood counts prior to the onset of overt leukemia with or without infection, this is a perplexing, first case of pancytopenia without transient normalization of peripheral blood counts preceding the onset of overt acute leukemia and in which the pre-leukemic clone was documented throughout the 7 months of pancytopenia leading up to the diagnosis of leukemia by bone marrow morphology, flow cytometry and hyperdiploidy cytogenetics.

POSTER # 141 | NEED FOR PNEUMOCOCCAL REVACCINATION AFTER BLINATUMOMAB THERAPY: A CASE REPORT

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Background: Blinatumomab is a bispecific T-cell engaging monoclonal antibody targeting CD19 on B-cells and CD3 on T-cells. It has demonstrated efficacy in patients with relapsed/refractory B-cell acute lymphoblastic leukemia (ALL) and is being studied in patients with standard risk (SR) B-cell ALL with minimal residual disease (MRD) after induction. While blinatumomab use in pediatric patients has been shown to have decreased rates of sepsis and infection when compared to chemotherapy, there are limited data describing specific adverse events (AEs) in the pediatric population.

Objectives: We describe a case of a 3-year-old fully-vaccinated male with SR-average B-Cell ALL treated with blinatumomab who was subsequently found to have subtherapeutic pneumococcal titers.

Design/Method: As presented as a fully-immunized 27-month-old male with B-cell ALL, CNS 1 and neutral cytogenetics. He was treated per Children's Oncology Group (COG) protocol AALL1731, on study.

His day 8 peripheral blood flow cytometry MRD was 0.007% and end of induction bone marrow MRD was undetectable by flow cytometry; high throughput sequencing MRD was detectable. Therefore, his ALL was stratified as SR-average, and he was randomized to two cycles of blinatumomab in addition to standard chemotherapy. Nineteen months after completion of blinatumomab, during maintenance cycle one, he was found to have S.pneumoniae bacteremia. Ten-weeks later, during maintenance cycle two he again presented with S.pneumoniae bacteremia. Recurrent S.pneumoniae bacteremia prompted evaluation of Pneumococcal titers, all of which were low, requiring re-vaccination with Pneumovax 23.

Results: Throughout treatment, IgG levels were <400 mg/dL only twice, the most recent episode was five months prior to the first episode of bacteremia; both times he received intravenous immunoglobulin (IVIG). Otherwise, his IgG levels were normal (> 600 mg/dL), including around presentation of his bacteremia episodes. Notably, he had three negative blood cultures between bacteremic episodes and was not neutropenic during either episode. Four weeks after Pneumovax 23 vaccination, his vaccine titers demonstrated a normal humoral response with a greater than 4-fold increase in>50% of serotypes.

Conclusion: This case represents a rare discovery of diminished protective titers following recurrent bacteremia of a vaccine-preventable illness in a fully-immunized pediatric patient who received blinatumomab for SR-B-cell ALL. It is possible that blinatumomab may decrease the durability of immunity in fully-vaccinated children, further highlighting the importance of research on blinatumomab activity and AEs in pediatric patients, including the need to check vaccine titers and create re-vaccination strategies.

POSTER # 143 | A DE NOVO GERMLINE RUNX-1 VARIANT PRECEDING DEVELOPMENT OF T-ACUTE LYMPHOBLASTIC LEUKEMIA

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Background: Germline variants of the *RUNX1* gene are associated with *RUNX1* Familial Platelet Disorder with Associated Myeloid Malignancies (*RUNX1*-FPDMM), which is characterized by thrombocytopenia and 30-40% increased risk of developing myelodysplastic syndrome (MDS) and acute myeloid leukemia. The role of *RUNX1* gene alterations in the development of childhood acute lymphoblastic leukemia (ALL) is unclear, but findings have been reported in a few patients and appear to portend a poor prognosis.

Objectives: To characterize a rare pediatric case of *RUNX1*-FPDMM that evolved into ALL.

Design/Method: Case report

Results: This 12-year-old girl had been diagnosed at 1 year of age with *RUNX1* variant of uncertain significance and chronic idiopathic thrombocytopenic purpura. She was monitored with serial CBCs for potential development of *RUNX1*-FPDMM. She presented with one-month of diffuse lymphadenopathy and leukopenia.

Lymph node and bone marrow (BM) biopsies were diagnostic of T-ALL with a minor population of abnormal myeloid progenitor cells. She was treated with dexamethasone, vincristine, PEG-asparaginase, and daunorubicin for conventional T-ALL induction therapy, which was complicated by a putamen stroke. At end of Induction, the BM minimal residual disease (MRD) was positive at 1%, but the abnormal myeloid population noted at diagnosis could not be assessed due to a hemodilute sample. Due to persistent cytopenias delaying initiation of Consolidation, another BM aspiration was performed 6 weeks later and revealed an expanded CD34+ progenitor population, consistent with MDS. Her presentation was suggestive of germline *RUNX1*-FPDMM complicated by emergence of T-ALL and MDS. This was attributed to *de novo RUNX1* pathogenic variant, as the abnormality was not detected in family's genetic testing.

Treatment was modified to include allogenic hematopoietic stem cell transplant (HSCT) as potentially curative treatment and inability to tolerate conventional chemotherapy due to prolonged myelosuppression. Single-agent nelarabine was considered but deferred with concern for potential neurotoxicity complicating her recent stroke. She received two cycles of modified maintenance (dexamethasone, vincristine, methotrexate), one cycle of venetoclax and azacitidine, followed by four infusions of daratumumab monotherapy. Due to persistent MRD despite these agents, she received one course of conventional Consolidation chemotherapy (cyclophosphamide, cytarabine, 6-mercaptopurine, vincristine and PEG-asparaginase); subsequent BM was T-ALL MRD-negative. To date, she remains MRD-negative with normal hematopoiesis 3 months post-haploidentical peripheral HSCT.

Conclusion: This patient with *de novo RUNX1* germline variant developed *RUNX1*-FPDMM with emergence of T-ALL. Children with germline *RUNX1* variants should be monitored accordingly. Those who develop MDS and acute leukemia pose complex therapeutic challenges. Allogeneic HSCT in CR1 represents potentially curative treatment.

POSTER # 144 | UNCOMMON GENETIC MUTATIONS IN TRANSIENT ABNORMAL MYELOPOIESIS IN A PATIENT WITHOUT DOWN SYNDROME

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Background: Transient abnormal myelopoiesis (TAM) is seen in infants with Down Syndrome (DS) and associated with GATA1 mutation. This gene promotes proliferation of megakaryocytes. TAM cells acquire N-terminal truncating GATA1 mutations. TAM is at risk for spontaneous conversion to a hematopoietic malignancy such as acute megakaryoblastic leukemia (AML-M7). We present a case of a patient without DS with uncommon genetic mutations associated with TAM.

Objectives: This case report demonstrates a patient without DS with uncommon genetic variants who went into spontaneous remission from TAM.

Design/Method: Single subject case report.

Results: An ex 39-week-old male presented with "blueberry muffin lesions" and hepatosplenomegaly at two days of life. Complete blood count noted a white blood count of 26,000/μL with 27% blasts, hemoglobin 9 g/dL, and platelets of 13,000/μL. Flow cytometry showed 57% CD36+ CD33+ CD117+ myeloid blasts in the peripheral blood. Suspicion for TAM rose with concern for DS, however, karyotype was 46, XY. The patient underwent a bone marrow biopsy, revealing 20% CD117+ myeloid cells. Flow cytometry noted strong expression of CD41 and CD61 on 41% of the blasts, identified as megakaryoblasts (M7). The karyotype of the bone marrow again yielded 46, XY and FISH was negative, without evidence of mosaic DS. Chromosomal microarray did not detect GATA1 abnormality and was negative. Next generation sequencing (NGS) for genes involved in myeloid neoplasms detected variants of clinical significance, KRAS (c.179G>A), 12%, and IKZF1 (c.56C>T), 50%, when tested from the blood. The patient had low risk features: normal bilirubin, transaminases, and coagulation profile, no effusions, no hyperleukocytosis, and no hydrops fetalis. He was closely monitored without interventions and repeated flow cytometry at 5 weeks of age showed no blasts. Most recent blood counts at three months of age were within normal range with no evidence of leukemia. Further, his KRAS resolved and IKZF1 was 52%, suggesting the latter mutation has heterozygous presence in somatic cells.

Conclusion: This case highlights genetic mutations in a patient with TAM without DS and shows the necessity of performing NGS on unclear cases.

Mutations of KRAS are associated with childhood leukemia. Mutations of IKZF1 can cause abnormalities of GATA1 expression in fetal megakaryocytes and thus alter the GATA1 mediated regulation of other transcription factors, ultimately leading to hematopoietic malignancy. Although our patient did not have GATA1 mutation, his IKZF1 gene mutation, which is known to be an upstream regulator of GATA1, may have induced the abnormal megakaryocytic proliferation in this individual without DS.

POSTER # 145 | CHRONIC PAROTITIS AND SIALOCELE: A RARE CAUSE OF FACIAL SWELLING IN A PATIENT WITH RELAPSED LEUKEMIA

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Background: Children with relapsed leukemia are at high-risk of developing life-threatening infectious complications which, unless adequately treated, can cause delays in, or even abandonment of, definitive curative therapy. However, other pathological processes, through which cancer care may continue, can occur in this population and need to be considered in differential diagnoses. Here, we present a challenging case of a patient with relapsed precursor B-cell acute lymphoblastic leukemia (B-ALL) with a unique cause of non-infectious, non-neoplastic persistent facial swelling—obstructive chronic parotitis and recurrent sialocele.

Objectives: To describe a non-infectious, non-neoplastic cause of persistent facial swelling in a patient with relapsed precursor B-ALL.

Design/Method: Case report.

Results: A 5-year-old male with early relapsed precursor B-ALL was receiving re-induction therapy according to AALL1331 at an outside hospital. He was hospitalized on induction day 9 for neutropenic fever. History revealed a recent abrasion injury to the right buccal mucosa while eating a snow crab leg. Chemotherapy was discontinued and broad spectrum antibiotics were initiated. Cultures from a biopsy performed by otolaryngology (ENT) confirmed a polymicrobial infection with extended spectrum beta-lactamase *Escherichia coli*, *Streptococcus constellatus*, *Bacteroides pyogenes*, and *Prevotella melaninogenica*. Despite appropriate antibiotics, clinical symptoms continued to worsen prompting transfer to Texas Children's Hospital on hospital day (HD) 7. Repeat biopsy by ENT demonstrated a necrotic ulcer without salivary flow and inability to visualize a patent Stensen's duct. After prolonged broad spectrum antimicrobial therapy and neutrophil recovery however the patient's swelling persisted. Ultimately, magnetic resonance imaging obtained on HD57 and 67 demonstrated a 2.2 cm septated extension from the right parotid gland, most consistent with a sialocele. After extensive discussion, ENT performed a right total parotidectomy with facial nerve dissection and preservation with subsequent improvement of swelling. During this time, he received anti-leukemic treatment with blinatumomab and achieved minimal residual disease negative remission on HD57. He proceeded to hematopoietic cell transplant 5-weeks post-total parotidectomy without any further associated infectious complications. He has since achieved 100% donor engraftment and remains in remission 100 days after transplant.

Conclusion: This case highlights a non-infectious, non-neoplastic complication after traumatic injury and extensive polymicrobial infection as the cause of prolonged facial swelling in an immunocompromised patient. This rare complication may be initially overlooked by providers given the significant risk of persistent infection in this high-risk population.

POSTER # 146 | PROFOUND HIGH ANION-GAP METABOLIC ACIDOSIS IN A PEDIATRIC LEUKEMIC PATIENT RECEIVING MERCAPTOPURINE

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Background: The purine analog 6-mercaptopurine (6MP) can be associated with myelosuppression, hepatotoxicity, nausea, poor appetite, and rash. Symptomatic hypoglycemia is documented in 7% of pediatric patients receiving 6MP. Despite its infrequency, 6MP-associated hypoglycemia may be more prevalent than the data indicates.

Objectives: We describe a 13-year-old male with high-risk acute lymphoblastic leukemia (ALL) who developed 6MP-associated hypoglycemia with severe metabolic acidosis. We sought to highlight the variability in presentation of patients with 6MP-induced hypoglycemia.

Design/Method: This is a case report and short review of the literature.

Results: A 13-year-old male undergoing maintenance chemotherapy with methotrexate and 6MP for high-risk B-Cell ALL presented with non-bloody and non-bilious vomiting. His labs—severe hypoglycemia (30), ketoacidosis (pH of 7.07, CO2 of 33, base excess of −20), elevated lactate (8.6)—indicated severe disease, yet he was well appearing. Thiopurine metabolite studies revealed elevated 6-Thioguanine Nucleotide (6TGNs) of 585 p/mol/8x108 RBC (nl 235-450) and elevated 6-Methylmercaptopurine nucleotides (6MMPNs) of>52,320 pmol/8x108 RBC (nl <5700). Given this presentation of hypoglycemia with an impressively high anion gap metabolic acidosis and elevated lactate, the prevailing concern was toxicity from 6MP, supported by his remarkably elevated 6MMPNs, the hepatotoxic metabolite of 6MP. He was admitted to the hospital service and oral chemotherapies were held.

As he was found to be a rapid metabolizer of 6MP, his 6MP dose was reduced and allopurinol was initiated to shunt 6MP metabolism and increase thioguanine production relative to 6MMP production. Once his ANC recovered, 6MP was resumed at 30% of the previous dose with the addition of allopurinol 100 mg (56 mg/m2) daily. Subsequent thiopurine metabolites identified a markedly improved metabolic profile with 6TGNs of 371 pmol/8 x108 RBC and 6MMPNs below the limit of detection in the setting of an appropriate degree of myelosuppression.

Conclusion: The metabolite of 6MP produced by the enzyme thiopurine methyltransferase (TPMT), 6MMP, is a known hepatotoxin. Hepatoxicity of 6MMP, with metabolic changes from cancer, may increase the risk of hypoglycemia in patients taking 6MP. As symptoms of nausea and somnolence mirror side effects of many chemotherapies, perhaps these symptoms represent subclinical hypoglycemia, and this phenomenon is more common than believed.

Despite the severity of lab evidence, our patient appeared well and in no acute distress, representing a divergence from documented cases of 6MP-associated hypoglycemia, suggesting a high index of suspicion is needed to ensure adequate detection and prompt treatment of this side effect, as patient presentation is variable.

POSTER # 147 | PEDIATRIC ACUTE MYELOID LEUKEMIA WITH BREAST CHLOROMAS

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Background: Myeloid sarcoma (MS) (chloroma or granulocytic sarcoma) is a rare extramedullary manifestation of myeloid precursor cells. The mass is composed of primitive myeloid cells that can be located in a variety of organs, most commonly the skin, lymph nodes, gastrointestinal tract, bone, and central nervous system. Involvement of the breast is rare, especially in the pediatric population.

Objectives: This case report demonstrates a rare case of chloroma in a teenage Asian American female who presented with bilateral breast masses at the time of acute myeloid leukemia (AML) diagnosis.

Design/Method: Single subject case report

Results: An eleven-year old teenage female patient (Asian-Indian descent) presented with a 1-2 month history of generalized pallor, fatigue, lightheadedness and several episodes of dizziness. She was also noted to have a 1 month history of bilateral breast masses. There were no other associated symptoms including increased bruising/bleeding, fevers, nor recent illnesses. On presentation, her complete blood count demonstrated a white blood cell count of 24,800/cumm, hemoglobin 3.9 g/dL and platelets 19,000/cumm. The lactic dehydrogenase (LDH) level was elevated at 609 U/L and the uric acid level was normal. A bone marrow aspirate/biopsy demonstrated near replacement with sheets of cells with high N/C ratio and round nuclei with single nucleolus present. Auer rods were not present. Erythroid and megakaryocytic elements were decreased, and myeloid elements showed decreased maturation. CD34 and CD117 highlighted approximately 50% of cells. Myeloperoxidase was strongly positive in the majority of cells. CNS 2. Breast biopsies demonstrated pleomorphic cells with CD34 and focal CD117 immunoreactivity with FISH demonstrating the RUNX1/RUNX1T1 t(8;21) variant gene fusion consistent with AML diagnosis. A whole body positron emission tomography-computed tomography (PET/CT) scan demonstrated several nodular masses in both breasts with mild FDG uptakeFDG uptake in both breasts. The patient was treated with 4 cycles of chemotherapy per the St. Jude Children's Research Hospital AML16 protocol. A PET scan performed at the end of therapy demonstrated no evidence for FDG avid adenopathy or masses. At follow-up, this patient has no evidence of disease over 1 1/2 years after completion of therapy.

Conclusion: Chloromas involving the breast as an initial presentation for AML is unusual and remains a diagnostic challenge; therefore, it must be included in the differential diagnosis of a breast mass in children and adolescents. Remission induction using AML therapy remains the standard of care for the treatment of MS, whether isolated or co-occurring with bone marrow involvement.

POSTER # 148 | TRANSFUSION-ASSOCIATED GRAFT VS HOST DISEASE MANIFESTED AS SUSPECTED GRAFT VS LEUKEMIA IN ALL

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Background: Transfusion-Associated Graft Versus Host Disease (TA-GVHD) is a complication of blood product transfusions where the donor T-cells engraft and attack the recipient. This includes attacking the bone marrow, skin or gut, potentially leading to bone marrow aplasia and multiorgan system failure (MOF). This is prevented by treating blood products to inactivate the donor T-cells with irradiation or, more

recently, psoralen and UV light. Given most recipients have a competent immune system, this extra processing is unneeded, but if given to an immunocompromised patient, non-T-cell inactivated products can cause significant morbidity and mortality. Marrow aplasia and MOF are the most reported but no graft versus leukemia has been reported.

Objectives: We describe an 11-month-old who presented with hyperleukocytosis secondary to B- ALL who received a unit of non-irradiated platelets and had a subsequent marked decrease in his lymphoblasts without any cytoreductive therapy.

Design/Method: We reviewed the records from the blood bank regarding the blood products administered and correlated them with the laboratory findings and medication administration data from the medical record.

Results: On admission, white blood cell count (WBC) was 230,000 TH/cmm with 94% lymphoblasts. He was admitted to the pediatric intensive care unit where he received transfusions of both packed red blood cells and platelets. Prior to leukapheresis, his WBC dropped over the next few hours and the need for leukapheresis was averted as he improved clinically, and his total WBC decreased to 94,000 TH/cmm. He received no corticosteroids or cytoreductive chemotherapy during this time. Given his age, initial WBC, and lack of MLL rearrangement, he was stratified as high risk, and began therapy per AALL0232 six days after initial diagnosis. Prior to starting induction therapy, his WBC was down to 6,800 TH/cmm with 18% blasts. After review of the blood bank records, it was discovered that the issued platelets had not been irradiated.

Conclusion: Given that the patient had received no steroids or other cytoreductive interventions, we propose that donor T-cells attacked the recipient's leukemia, decreasing his white count and circulating blasts. Given that TA-GVHD can also give marked marrow aplasia and MOF we suspect the donor T-cells attacked only the leukemia cells and spared the marrow and other organs as the rest of his blood counts improved as well.

POSTER # 149 | CHOLERA INFECTION CONCURRENT TO HIGH-DOSE METHOTREXATE ADMINISTRATION IN AN AMERICAN CHILD

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Background: *Vibrio species*, including *Vibrio cholera*, are motile, Gram-negative bacteria found in marine environments and most often lead to gastrointestinal illness, characterized by profuse, watery diarrhea. The pathogen can be acquired via travel to endemic regions or, rarely, via ingestion or handling of seafood/marine life. Patients with chronic illnesses and immunocompromised states are at increased risk of more severe disease. Infection with *Vibrio species* is extremely rare in the United States (US) and mostly result from travel. High-dose Methotrexate (MTX) chemotherapy requires maintenance of excellent hydration status in order to support MTX clearance. Methotrexate itself can cause mucositis and affect the normal gut microbiome.

Objectives: To report a case of *Vibrio cholerae* infection in the US in a 13-year-old male with Ph-like B-ALL.

Design/Method: Case Report

Results: In June 2022, a 13-year-old male with Ph-like B-cell ALL was admitted for Interim Maintenance chemotherapy with high-dose MTX in New Jersey. The patient's most recent travel was to Alexandria, Egypt nine months earlier, but had been to a water park recently. Patient developed nausea, non-bilious vomiting, and intractable diarrhea several hours after the initiation of MTX infusion, which continued to worsen. He continued to have profuse diarrhea, edema, mucosal ulceration, and signs of acute kidney injury (AKI). He subsequently developed fever and hypotension.

His MTX levels were extremely elevated at 24 hours (1900 mcmol/L), 36 hours (38.83 mcmol/L), and 42 hours (15.83 mcmol/L) and received Glucarpidase (2,000 units) at 50 hours. Full clearance was achieved two weeks later due to AKI.

His cholera, confirmed with stool PCR panel positive for *Vibrio and Vibrio cholerae*, improved with Doxycycline. A repeat stool PCR was negative following treatment. The patient had no known exposure to any infected individuals. His mother was empirically treated with Doxycycline for similar symptoms, which started 24 hours after the patient's, with good results. However, her PCR confirmation was not done.

Conclusion: This case highlights the importance of considering rare differentials of gastroenteritis, including infections not endemic to the region (e.g., *Vibrio cholerae*), in immunocompromised patients on chemotherapy. Particularly, patients with MTX toxicity may be more susceptible to aberrant proliferation of colonized bacteria due to alterations in gut microbiome, leading to more severe presentations of disease. The fluid shifts and dehydration from such infections can lead to significant methotrexate toxicity and require rapid recognition and aggressive management.

POSTER # 150 | UNIQUE CONSIDERATIONS OF TREATING AN INCARCERATED YOUNG ADULT WITH MULTIPLY-RELAPSED LEUKEMIA

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Background: Young adults with acute lymphoblastic leukemia (ALL) have better outcomes when treated on pediatric protocols. Pediatric oncology teams should therefore be aware of unique psychosocial considerations and challenges that young adults face, including incarceration. Over 50% of individuals in correctional facilities in the United States are under age 40[1,2], thus considered young adults as defined by the National Cancer Institute.

Objectives: We describe the multidisciplinary team approach required to care for an incarcerated young adult with underlying psychiatric history and previous therapy abandonment, presenting from a correctional facility with second relapse of ALL.

Design/Method: Patient was a young adult with high-risk pre-B cell ALL. He received standard of care chemotherapy and went into remission, however abandoned treatment after 8 months and was lost to follow up. A year later he presented from a correctional facility with ALL relapse. He received reinduction chemotherapy and again achieved remission but abandoned treatment three months after being compassionately released from incarceration. Cooperation with treatment was limited by unspecified psychotic disorder and antisocial personality disorder, but he refused psychotropic medications. He presented in second relapse seven months later, again incarcerated. Ethical and logistical concerns were considered in selecting a salvage regimen.

Results: At the time of relapse, considerations included inability to demonstrate compliance, antisocial personality disorder including aggression towards hospital staff, and incarcerated state. Due to these factors, he was deemed ineligible for curative destination therapy (bone marrow transplant or CAR-T cells). At second relapse, blinatumomab was selected due to lower toxicity profile and decreased risk of prolonged cytopenias. Given logistical constraints with outpatient administration, the patient remained admitted for the 28-day cycles. The patient started consistently taking psychotropic medications and behavioral outbursts decreased. Frequent meetings with hospital administration, nursing leadership, correctional facility, hospital security, psychiatry, social work, and ethics service were held to address concerns. Written communication with the warden was necessary for permission for medically necessary activities including showering and physical therapy. Close communication with his attorney enabled scheduling court hearings around hospitalizations. Between cycles the patient returned to the correctional facility, where he was housed in the infirmary for close monitoring.

Conclusion: Pediatric teams caring for young adults may encounter incarcerated patients, which presents unique ethical and logistical challenges. A multidisciplinary approach with close collaboration with correctional facility staff is essential to offer the best standards of care to this marginalized population.

1. Minton & Zheng, Bureau of Justice Statistics, 2021
2. Carson, Bureau of Justice Statistics, 2021

POSTER # 151 | COVID-19 ASSOCIATED PANCYTOPENIA IN A 12-YEAR-OLD FEMALE ON MAINTENANCE THERAPY FOR ALL

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Background: Viral infections have long been known to cause cytopenias and rarely pancytopenia; COVID-19 is no exception. There have been documented cases of COVID-19 resulting in pancytopenia of varying severities in the pediatric population; most cases improve without intervention. There is a paucity of literature on the approach to symptomatic pancytopenia associated with COVID-19 and even less so in the acute lymphoblastic leukemia (ALL) population.

Objectives: We report a case of a twelve-year-old female on maintenance chemotherapy for ALL who presented with symptomatic, sudden severe pancytopenia in the setting of COVID-19.

Design/Method: Our patient was originally diagnosed with high risk ALL at 11 years of age. The patient's end of induction minimal residual disease was 0, and she proceeded through treatment to start maintenance in May of 2022. On a routine visit during cycle 2 of maintenance, our patient presented with rhinorrhea and was found to be COVID-19 positive. Her complete blood count (CBC) was stable. Her maintenance oral chemotherapy was not discontinued despite persistent symptoms for several weeks due to her stable CBC. On week three of her illness, our patient suddenly developed spontaneous bruising, petechiae and severe fatigue while looking and feeling unwell. Her CBC revealed severe pancytopenia. Due to concern for relapse, she was admitted for packed red blood cells and platelet transfusions, as well as a bone marrow biopsy and aspiration. Her chemotherapy was held at this time.

Results: Her bone marrow biopsy revealed severe hypocellularity but negative flow cytometry, chromosomal analysis, and FISH for leukemia. After 1 week of watchful waiting, there was no improvement in cytopenias. She was subsequently started on GCSF and given Intravenous immunoglobulin (IVIG). Within a week there was improvement and one month after her initial pancytopenia presentation, she was COVID-19 negative, and her CBC returned to normal. Her maintenance therapy was resumed.

Conclusion: Our literature review documented one other case of pancytopenia in a child with ALL in maintenance secondary to COVID-19 whose pancytopenia improved over one week. However, there are other reported cases of pancytopenia most commonly related to MISC where IVIG is routinely used. The existing evidence is insufficient for the efficacy of IVIG in a setting like our patient's. It is difficult to ascertain whether expectant management improved her pancytopenia, or if the combination of IVIG and GCSF did. However, we believe it is a good option when there is no evidence of relapse, and there is prolonged severe pancytopenia.

POSTER # 152 | A UNIQUE CASE OF TRANSIENT ABNORMAL MYELOPOIESIS

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Background: Transient Abnormal Myelopoiesis (TAM) is a disease classically defined by the presence of circulating blasts that occurs in the first 90 days of life in infants with Trisomy 21 or Trisomy 21

Mosaicism. Clonal mutations in GATA1 are confirmatory, although not required, to make the diagnosis. It is life threatening in up to 25% of patients, and those who survive the neonatal period carry up to a 30% risk of developing acute megakaryocytic leukemia in down syndrome (DS-AML).

Objectives: Many questions remain regarding the pathogenesis, risk stratification, and prognosis of TAM. Here we describe a case with unusual findings, with the goal of highlighting these questions.

Design/Method: Case Report

Results: Our patient had clinically diagnosed Trisomy 21; at 10 months of age she was found to have 5% circulating blasts with a white blood cell count of 12,000 x 103 μ/L; further testing revealed a GATA1 mutation. However, bone marrow biopsy at the time was negative and the peripheral blastemia resolved without intervention. Based on this, despite not meeting the <90 days old criteria, she was diagnosed with TAM. Circulating blasts in the absence of abnormal bone marrow was consistent with a diagnosis of TAM, and brings into question the <90 days criteria that is typically used. 4 months later, on a routine CBC she had a white blood cell count of 2,800 x 103 μ/L with 13% circulating blasts. Bone marrow biopsy at this time had abnormal hematopoiesis and elevated blast count consistent with DS-AML. She was treated on AAML0431 and exhibited negative minimal residual disease at the end of therapy, however her bone marrow continued to exhibit abnormal CD56 expression, a myeloid marker known to mark leukemogenesis in classic AML but interestingly not in DS-AML.

Conclusion: Our case highlights several questions in TAM that have yet to be answered. Long term prognostic indicators continue to be elusive—risk stratifications predict acute complications but have no predictive value for spontaneous resolution or progression to DS-AML. Residual abnormal myeloid expression, genetic aberrations, and timing of onset are potential factors that may correlate with long term prognosis. Lastly, historically infants had to develop peripheral blastemia in the first 90 days of life to meet diagnostic criteria for TAM, but our patient's findings were consistent with TAM at 10 months of age. Should this criteria be re-evaluated, and should screenings be changed based on this finding?

POSTER # 153 | BONE PAIN AS A PRESENTING SYMPTOM FOR DIFFERENTIATION SYNDROME: A CASE REPORT

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Background: Acute promyelocytic leukemia (APML) is a rare malignancy in the pediatric population. Differentiation syndrome is a common but potentially fatal complication of treatment for APML. Common presenting symptoms include fever, dyspnea, weight gain, peripheral edema, hypotension, acute renal failure, pleural and/or pericardial effusions, and cholestasis. Bone pain has not been previously described as a symptom.

Objectives: Describe bone pain as a novel presenting symptom for differentiation syndrome.

Design/Method: Case Report

Results: A previously healthy 8-year-old boy presented with left arm numbness and tingling. Radiologic and laboratory evaluation revealed a right middle cerebral artery infarction and pancytopenia [white blood cell (WBC) 0.9K, hemoglobin 11.2 g/dL, and platelets 98K] with 20% blasts that contained Auer Rods. Due to concern for APML, he was immediately started on all trans retinoic acid (ATRA). Upon confirmation of the diagnosis of APML 2 days later, he began arsenic trioxide (ATO) per standard risk induction therapy per AAML1331. On treatment day 10 of combined ATRA and ATO, his WBC rose to 20.3K and he was started on prophylactic therapy for differentiation syndrome but was continued on ATRA and ATO. The next day, he reported bone pain in his right leg that later migrated to his chest. His pain became significant enough he required treatment with opioid medications. Extensive workup was performed without a clear etiology. On treatment day 13, he developed fevers and respiratory distress requiring supplemental oxygen. The decision was made to treat him for differentiation syndrome with escalation of dexamethasone and cessation of ATRA and ATO, after which his pain resolved within 24 hours. He was subsequently able to resume ATRA and ATO with no recurrence of his pain.

Conclusion: We describe a patient who developed differentiation syndrome with bone pain as a primary symptom. There was a temporal association as he developed bone pain within 24 hours of leukocytosis and other symptoms of differentiation syndrome and did not have bone pain as a presenting symptom. Bone pain has not been described as a symptom associated with differentiation syndrome in the literature. Whereas the patient's bone pain was not very responsive to pain medication alone, it resolved with treatment of his differentiation syndrome. We theorize that the rapid development of leukocytosis in patients with leukopenia at the start of therapy could result in bone pain similar to that experienced by patients receiving filgrastim therapy for chemotherapy-associated neutropenia.

POSTER # 154 | THE USE OF MILRINONE TO SUPPORT A PEDIATRIC PATIENT WITH HR-AML AND HEART FAILURE THROUGH HSCT

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Background: Treatment of acute myeloid leukemia (AML) is associated with high rates of cardiotoxicity. Certain subtypes of AML, such as those with activating mutations of the FMS-related tyrosine kinase 3 (FLT3) receptor are most successfully treated with hematopoietic stem cell transplant (HSCT). Literature describing cardiac support through HSCT for patients with high-risk (HR) AML and concurrent cardiotoxicity is limited.

Objectives: We describe a pediatric patient with FLT3-mutant HR AML with evidence of therapy induced heart failure who was successfully

supported through conventional myeloablative conditioning and HSCT with the use of milrinone.

Design/Method: A 12-year-old female presented with a history of prolonged fatigue. A complete blood count (CBC) was drawn with the presence of peripheral blasts. Flow cytometry revealed that the blasts expressed myeloid antigens CD13, CD33, CD117, and MPO and she was diagnosed with AML. She was initially started on treatment per Children's Oncology Group (COG) protocol AAML1031, arm B, on study. Cytogenetics returned with an increased FLT3/ITD allelic ratio and she was switched to arm C of the same protocol which replaced bortezomib with sorafenib. During induction cycle 2, she developed concern for heart failure with left ventricle ejection fraction (LVEF) of 32% and a left ventricular shortening fraction (LVSF) of 28%. Her pre-treatment echocardiogram had been normal.

Repeat bone marrow assessment after two induction cycles revealed continued presence of disease and she was switched to salvage chemotherapy regimen TVTC+sunitinib with plan to proceed to a matched unrelated donor (MUD) HSCT when in remission (CR1). Her heart failure worsened with decreased LVSF to 23.75% during this. Sunitinib was discontinued and she was started on lisinopril to support her cardiac function. Her cardiac function continued to decline but she achieved CR1. A multidisciplinary approach was utilized to trial a milrinone drip to support our patient's heart failure through a fully myeloablative conditioning regimen and her HSCT which she underwent successfully with limited complications.

Results: Now more than 8 years after her transplant, she continues to remain in CR1 with normalized heart function and is clinically doing well.

Conclusion: Our case presents a pediatric patient with HR AML with pre-existing therapy induced heart failure who was successfully supported through a traditional fully myeloablative HSCT with the use of milrinone. Though unconventional, this should be considered as an option for similar patients in the future rather than opting for a reduced intensity conditioning (RIC) HSCT regimen to give the best chance for cure.

POSTER # 155 | DEVELOPMENT OF SOS AFTER TREATMENT WITH 6-TG: A CASE SERIES

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Background: Sinusoidal obstruction syndrome (SOS), previously known to commonly occur as a complication of hematopoietic cell transplantation (HCT) conditioning or high dose chemotherapy regimen, has been reported following treatment with 6-thioguanine (6-TG) for patients with acute lymphoblastic leukemia ALL. 6-TG continues to be used as a 14-day burst in delayed intensification (DI) included in all de novo ALL therapy protocols in the Children's Oncology Group. Yet, development of SOS following treatment with 6-TG is poorly described and previously reported data regarding correlation with different TPMT genotypes has been conflicting.

Objectives: This case series describes the clinical presentation and management for a cohort of pediatric ALL patients developing SOS following treatment with 6-TG.

Design/Method: We performed a retrospective chart review to identify patients with ALL treated at Children's Hospital of Richmond between 2021 & 2022 and developing SOS after receiving chemotherapy regimen including 6-TG. We extracted data to be included in this descriptive case series. SOS was defined using EBMT, Baltimore, modified Seattle and Ponte di Legno (PdL) diagnostic criteria for SOS, prioritizing EBMT criteria.

Results: During a two-year timeframe, we identified three patients with ALL who developed SOS All three patients were males aged [8 - 21 yrs old] with different forms of ALL; B-ALL, T-cell ALL and Philadelphia like HR B-ALL. Two of the three patients received defibrotide for management of SOS. Two of the patients were noted to be intermediate TPMT metabolizers. The patient with B-ALL and normal TPMT metabolism was noted to have most severe course of illness requiring prolonged PICU stay. All three patients recovered with no residual symptoms including normal hepatic venous flow on repeat imaging.

Conclusion: This case series confirms previously reported relatively mild presentation for SOS associated with 6-TG. While previous studies are conflicting about correlation between TPMT metabolism and development of SOS, there is no clear correlation in our cohort with incidence or severity of presentation.

POSTER # 156 | DISTAL INTESTINAL OBSTRUCTION SYNDROME IN A PATIENT WITH B-CELL ALL AND CYSTIC FIBROSIS

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Background: Multiorgan involvement, such as distal intestinal obstruction syndrome (DIOS) and pseudomonas infection, in cystic fibrosis (CF) patients is a significant risk factor in those with malignancy who are receiving aggressive chemotherapy. DIOS is a common complication of CF, with a prevalence of 5-12 episodes per 1000 patient-years. Genetic mutations causing defects in the CFTR protein cause mucus buildup and in combination with pancreatic insufficiency, leads to malabsorption and increased risk of intestinal obstruction. CFTR gene mutation has been associated with the development of some leukemia's.

Objectives: Our case describes a 17-year-old patient with a history of CF and Pre-B cell Acute Lymphocytic Leukemia (ALL) who developed DIOS during induction chemotherapy. Our aim is to create awareness of the association between the CFTR gene with cancers and demonstrate how such complex cases should be co-managed with the multidisciplinary team.

Design/Method: Chart and literature review of patient with CF, ALL and DIOS.

Results: Seventeen-year-old with CF, recently diagnosed with high-risk ALL admitted to the hospital during induction chemotherapy with a 1-day history of fevers in the setting of severe neutropenia. Physical examination was benign, specifically no abdominal tenderness or distension. Blood culture was positive for Pseudomonas. The patient was treated with cefepime, metronidazole, and vancomycin. Fever resolved and repeat cultures were negative, however the patient remained severely neutropenic. The patient completed induction chemotherapy with vincristine, prednisone and daunorubicin. On Day 25 of induction, patient developed abdominal pain and vomiting in the setting of constipation. Physical examination was significant for distension and diffuse tenderness. Abdominal XR was concerning for an ileus versus small bowel obstruction. Pediatric Surgery was consulted. CT abdomen showed a significant amount of inspissated stool in the small bowel consistent with DIOS. GoLYTELY was slowly administered via a nasogastric tube and titrated up as tolerated. After four days of treatment, the patient began to pass stool. Neutropenia resolved and the patient was discharged from the hospital.

Conclusion: This case demonstrates the occurrence of DIOS in a patient with both CF and ALL. No similar cases have been described prior to this, per our literature review. There is no standard protocol for management of DIOS in patients with both ALL and CF. Surgical intervention is required in severe cases of DIOS, but is associated with a high mortality rate in immunosuppressed leukemic patients, therefore, non-operative management is preferred. This patient was managed successfully using GoLYTELY, demonstrating that severe cases can potentially be managed nonoperatively.

POSTER # 157 | A CASE OF T-CELL LYMPHOBLASTIC LYMPHOMA IN A TEENAGER WITH TRISOMY 21

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Background: Children with Down Syndrome (DS) have increased risk of hematologic malignancies compared to the general pediatric population. The most common malignancies are myeloid leukemia of Down Syndrome and B-cell acute lymphoblastic leukemia. DS-specific protocols have been developed as these patients are at high risk for treatment-related toxicities. T-cell malignancies are rarely seen in DS, with few case reports in the literature. Patients with DS and T-cell disease are treated with standard-of-care therapies with modifications extrapolated from DS-specific B-cell protocols. Due to the rarity of patients with DS and T-cell lymphoblastic lymphoma (T-LBL), no clinical trial data or protocols exist to guide therapy.

Objectives: To report a case of T-LBL in a 13-year-old young man with DS.

Design/Method: Case report and literature review.

Results: A 13-year-old young man presented with an anterior neck mass. Neck and chest CTs were obtained which showed mediastinal and left neck lymphadenopathy with tracheal deviation and nonocclusive left internal jugular thrombus. Biopsies of the cervical node mass showed a clonal population of abnormal precursor T-cells by flow cytometry strongly positive for CD3 and TdT. Bone marrow aspirate showed 2-3% T-lymphoblast involvement. Diagnostic lumbar puncture was negative (CNS1). CT abdomen and pelvis showed bilateral renal lesions. He was treated with induction per modified AALL0434 with bortezomib. End-of-induction bone marrow MRD was negative and PET-CT showed metabolic complete response. He was hospitalized throughout induction, delayed intensification, and periods of neutropenia during other cycles. He has received prophylactic antimicrobials during high-risk phases of therapy including levofloxacin and micafungin in addition to trimethoprim-sulfamethoxazole. To date, his course has been complicated by severe dehydration during consolidation, grade III mucositis with initiation of Capizzi methotrexate in interim maintenance which improved after dose reduction, asymptomatic Covid-19 infection and *S. epidermidis* central line-associated bloodstream infection at the end of interim maintenance. He was treated with supportive care for his acute Covid infection and intravenous vancomycin to salvage his central line which was successful.

Conclusion: T-LBL in DS is a previously unreported entity for which there are no clinical trial data or standard protocols to guide therapy. To date, this patient has demonstrated excellent response to T-LBL treatment and DS-specific supportive care with minimal toxicity or serious adverse events. This case supports using high-risk treatment such as AALL0434 with bortezomib in patients with DS and T-LBL given dismal salvage rates in children with recurrent T-cell disease.

POSTER # 158 | PEDIATRIC PURE ERYTHROID LEUKEMIA—AN ONGOING DIAGNOSTIC AND THERAPEUTIC CONUNDRUM

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Background: Pure erythroid leukemia (PEL) is a rare (<1%) but aggressive subtype of acute myeloid leukemia (AML) defined by a bone marrow with ≥80% immature erythroid cells and ≤20% myeloblasts. Previously known as FAB type M6b, in 2016, World Health Organization classified PEL as the sole type of acute erythroid leukemia (AEL). PEL can arise de-novo or secondary to other tumors. Diagnosis is challenging due to morphological similarities to other malignancies, particularly megakaryoblastic leukemia. In addition, PEL carries a complex karyotype and unique cytogenetics with frequent mutations of NUP98. PEL blasts lack the usual T-, B-, and myeloid cell markers; CD34 and HLA DR are exclusively negative, and CD117 is mostly positive. CD71, ferritin H, and glycophorin A are reliable markers for erythroid lineage. E-cadherin is highly specific and crucial for diagnosis confirmation in glycophorin A negative PEL cases. Prognosis is dismal with a median survival of 1.5 to 6 months.

We describe a complicated pediatric case of NUP98 mutated PEL refractory to standard chemotherapies.

Objectives: To describe a challenging case of PEL and emphasize the need for more therapeutic research.

Design/Method: Case report

Results: We report a 2 year old, previously healthy, girl who presented with oral blisters, fever, poor appetite, fatigue, and petechial rash. Labs showed WBC 16700/uL, hemoglobin 4.9 g/dL, platelets 3000/uL, and 4% blasts on peripheral smear. AML was confirmed by peripheral flow cytometry revealing 14% abnormal blasts with myeloid differentiation and CD71 positivity. Bone marrow aspirate showed 19% blasts, with increased erythroid precursors and dyserythropoiesis in a hypercellular marrow with erythroid predominance consistent with M6 AML/AEL. CD117 and E-cadherin were strongly positive in addition to diffuse PAS positivity; FISH analysis identified NUP98 mutation. She received induction chemotherapy as per AAML1831 with daunorubicin, cytarabine, and gemtuzumab. End of induction MRD was positive (1.5%) and FISH positive for NUP98 (8.5%). Patient's course was complicated by delayed marrow recovery, multiple bloodstream infections, typhlitis, and respiratory failure requiring invasive support. She progressed through three additional salvage regimens including decitabine-CLAG (cladribine, cytarabine), TVTC (topotecan, vinorelbine, thiotepa, clofarabine), and venetoclax/azacitidine. While awaiting enrollment on a phase II trial, patient developed veno-occlusive disease, disseminated fungemia, and hepatic failure finally leading to her demise eight months after initial diagnosis.

Conclusion: Pure erythroid leukemia is an essentially fatal AML subtype often delayed in diagnosis due to its complex morphology and inherent refractoriness to standard AML therapies. More research is needed to understand the disease's pathophysiology and incorporate novel therapies.

POSTER # 159 | CNS-SYMPTOMATIC HYPERAMMONEMIA FOLLOWING RECOMBINANT CRISANTASPASE PSEUDOMONAS FLUORESCENS (RYLAZE)

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Background:FDA licensed in June 2021,recombinantCrisantaspase Pseudomonas fluorescens(rC-P, Rylaze) has been the sole source of Erwinia asparaginase in the US since July 2021. Like all asparaginase formulations, at least subclinical increases in ammonia are expected from hydrolyzation of asparagine. Significant hyperammonemia was not observed in the 25 mg (n = 33) or 25/25/50 mg (n = 51) dose levels but was reported in 3 subjects at the 37.5 mg dose in the registration phase 2/3 trial.

Objectives:To assess rate of central nervous system(CNS)-symptomatic hyperammonemia following rC-P.

Design/Method: Single-center retrospective review of patients treated with rC-P from July 2021 to October 2022. All cases were treated with 25 mg MWF dosing. CNS-symptomatic hyperammonemia was defined by mental status changes with elevated serum ammonia levels requiring inpatient management.

Results: Twelve patients with acute lymphoblastic leukemia(ALL) were treated with 6-for-1 dose interconversion of rC-P for pegylated E.coli asparaginase (PEG). Among these, a total of 47 PEG dose substitutions were attempted, 4 of which were interrupted in 3 patients due to hyperammonemia. None of these previously received Erwinia chrysanthemi asparaginase(Erwinaze). Head imaging was normal except as noted. All showed full neurologic recovery paralleling normalization of serum ammonia levels over 2-5 days.

Case 1

13-year-old female with relapsed B-ALL received rC-P during second retrieval, 4 months after 2 uneventful rC-P courses in 1st relapse. She developed seizures requiring intubation following dose 1/6 in second reinduction. Maximal ammonia level was 395 μmol/L. Imaging showed changes consistent with posterior reversible encephalopathy. She required brief dialysis to manage hyperammonemia.

Case 2

12-year-old transgender female in late consolidation of T-lymphoblastic lymphoma developed altered mental status on dose 4/6. Maximal ammonia level was 279 μmol/L. Lactulose, sodium phenylbutyrate, levocarnitine and arginine were employed in management of 4 days of hyperammonemia. Two months later, she developed a maximal hyperammonemia of 307 μmol/L following dose 1/6 upon rechallenge; subsequent doses were abandoned.

Case 3

16-year-old female with B-ALL developed confusion, fatigue, and poor appetite two days after dose 3/6 rC-P in late delayed intensification(DI) after successfully tolerating courses in late consolidation and early DI. Maximal ammonia was 423 umol/L. She was managed with levocarnitine, sodium benzoate, and sodium phenylacetate over 48 hours.

Conclusion: We observed a 6-9% by course and 25% by individual rate of CNS-symptomatic hyperammonemia following rC-P, exceeding reported initial testing estimates. Clinicians should remain cognizant of this adverse effect, which may vary in frequency or severity along with ongoing shifts in availability of asparagine-depleting agents.

POSTER # 160 | REFRACTORY PTLD WITH DLBCL PHENOTYPE TREATED WITH CD19 CAR T-CELL THERAPY

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Background: Diffuse large B-cell lymphoma (DLBCL) is the most common type of non-Hodgkin lymphoma (NHL) both worldwide and in the United States. One serious complication of solid organ transplants (SOT) is developing post-transplant lymphoproliferative disorder (PTLD). Of this group of disorders, many are B-cell in origin and

express Epstein-Barr virus (EBV) positivity. Pediatric and young adult patients with relapsed/refractory B-NHL often have heterogeneous, aggressive histologies and poor prognosis. Kymriah, CD19 chimeric antigen receptor (CAR) T cell therapy, is approved for treatment of refractory/relapsed NHL in adults but not for pediatric patients.

Objectives: We describe a case of refractory PTLD with a DLBCL phenotype that ultimately achieved remission with Kymriah CAR T cell therapy.

Design/Method: Case presentation

Results: A 16-year-old male with a past medical history of a renal transplant at 3 years of age secondary to obstructive uropathy with posterior urethral valves presented with abdominal pain and fever. He was on immunosuppression at the time. Abdominal ultrasound raised concern for intussusception. Biopsy of the lead-point mass resulted in a diagnosis of PTLD which was EBV-negative, and histologically consistent with monomorphic DLBCL. Flow cytometry showed the tumor expressed CD19+, CD20+, and CD22+ along with neutral cytogenetics. Staging revealed disease on both sides of the diaphragm (stage III) with CNS negativity. After 4-weeks of rituximab mono-therapy a repeat PET/CT showed progression of his disease. He was transitioned to R-CHOP therapy for one cycle. Repeat imaging indicated increased tumor burden. At this time he transitioned to DA-EPOCH-R per COG protocol ANHL1131 and received one cycle with repeat imaging consistent with further progression of disease. Decision was made to undergo Kymriah CAR T cell therapy with leukapheresis done nearly 3.5 months after initial diagnosis. He received a cycle of R-ICE therapy as a bridge during the manufacturing process. Repeat disease evaluation showed a nearly ~25% partial response. He underwent lymphodepletion and Kymriah infusion around 4.5 months after initial diagnosis. 1-month post-infusion, PET/CT showed 35% reduction in tumor burden. 3-month imaging showed a 39% reduction in tumor burden along with a complete metabolic response. 6-month imaging showed a 61% reduction in tumor burden with continued complete metabolic response. Now at 2 years post CAR T infusion, our patient remains in remission.

Conclusion: Kymriah, CD19 chimeric antigen receptor (CAR) T-cell therapy, may be an effective therapy for refractory PTLD/DLBCL in pediatric patients with trials looking to further explore this.

POSTER # 161 | IMPORTANCE OF ALK GENE SEQUENCING IN PEDIATRIC ANAPLASTIC LARGE CELL LYMPHOMA

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Background: Anaplastic lymphoma kinase (*ALK*) gene rearrangements are commonly found in pediatric anaplastic large cell lymphoma (ALCL). *ALK* gene rearrangements encode constitutively activated *ALK* fusion proteins that regulate downstream pathways involved in cell growth, survival, and cell-cycle control. At diagnosis the distinction between ALK positive and ALK negative ALCL is typically made through immunohistochemistry (IHC) and fluorescence in situ hybridization (FISH) looking for classical rearrangements, most commonly with *NPM1*. ALK inhibition is a therapeutic strategy currently being explored in pediatric ALCL. However, IHC and FISH alone do not predict sensitivity to specific *ALK* inhibitors.

Objectives: Therapeutic implications of *ALK* gene sequencing in pediatric anaplastic large cell lymphoma (ALCL)

Design/Method: This is a case report.

Results: A previously healthy 12-year-old boy presented with fevers, pleural and pericardial effusions, skin nodules, lung nodules and parenchymal disease, and diffuse lymphadenopathy. Cervical lymph node biopsy demonstrated ALCL, *ALK* + (via IHC and FISH showed t(2;5) confirming an *NPM1-ALK* fusion protein). He achieved complete remission after 2 cycles with multi-agent chemotherapy (dexamethasone, ifosfamide, methotrexate, cytarabine, etoposide, cyclophosphamide, doxorubicin and brentuximab). After his 4th cycle he relapsed and started monotherapy with crizotinib, a first generation *ALK* inhibitor. He had progressive disease after 3 weeks and was changed to combination chemotherapy with brentuximab and nivolumab with the addition of alectinib, a second generation *ALK* inhibitor. He again had progressive disease within 3 weeks and received therapy with ifosfamide, carboplatin and etoposide with a mixed response. Next generation sequencing (NGS) was done at time of second relapse and demonstrated the already known *NPM1-ALK* fusion, but also found an ALKI1171T mutation. NGS was not done at diagnosis so it is unknown if this mutation was present at diagnosis or was an acquired mechanism of resistance. Based on preclinical studies and limited clinical studies demonstrating that ALKI1171T mutations are resistant to crizotinib and alectinib but may maintain sensitivity to ceritinib, the patient started ceritinib in combination with brentuximab. Within 4 weeks of starting ceritinib he achieved a complete response that was sustained long enough to get him to allogenic hematopoietic stem cell transplant.

Conclusion: Testing for the presence of *ALK* rearrangements via IHC is standard in pediatric ALCL but cannot solely predict sensitivity to specific inhibitors. Consideration should be made for upfront *ALK* gene sequencing as this may drive therapeutic decisions regarding which inhibitor is most likely to result in a clinical response.

POSTER # 162 | Hematopoietic Bone Marrow Transplant to Treat Systemic EBV-positive T-cell Lymphoma of Childhood

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Background: Systemic EBV-positive T-Cell Lymphoma of Childhood (SEPTCLC) is a rare disorder for which a standard of care has not been established. SEPTCLC is associated with primary EBV infection or Chronic Active EBV; beyond that, the etiology remains unclear. Most patients are of East Asian or Latin American descent, suggesting a genetic predisposition. Symptoms include fever, pancytopenia, hepatosplenomegaly, and are often associated with hemophagocytic

lymphohistiocytosis (HLH). Many patients are treated on HLH or non-Hodgkin lymphoma protocols and require transplant. However, no standard approach to conditioning for HSCT exists, and outcomes remain poor.

Objectives: To describe methods by which a patient with SEPTCLC was successfully treated with hematopoietic stem cell transplant

Design/Method: Retrospective chart review, discussion with care team, review of current literature

Results: A 20-month-old female was diagnosed with HLH and began therapy with dexamethasone and etoposide. Bone marrow biopsy demonstrated abnormal, mature clonal T-cells present at 6.4% of non-erythroid cells. These expressed CD8 and showed decreased CD5 expression. PCR detected monoclonal arrangement of T-cell receptor gamma-chain gene. Bone marrow aspirate was referred for a second opinion by a T-cell specialist who made the diagnosis of SEPTCLC. Immunophenotypically similar cells were present at 20% of viable cells on liver biopsy. Therefore, she was treated with dose adjusted Etoposide, Prednisone, Vincristine, Cyclophosphamide, Doxorubicin, and Rituximab (DA-EPOCH-R). Rituximab was not continued for subsequent cycles due to T-cells, not B-cells, harboring EBV in this malignancy. Valganciclovir was added for EBV directed therapy. Bortezomib was excluded due to difficulty in administration during intensive chemotherapy. Intermittently, extra doses of etoposide were given based on inflammatory marker trends. Repeat bone marrow and liver biopsies after two cycles demonstrated no evidence of disease. Chemotherapy was continued until her 9/10, B allele mismatched unrelated donor was identified. Emapalumab was added weeks prior to transplant due to an HLH flare. Conditioning for HSCT consisted of alemtuzumab, fludarabine, melphalan, and thiopeta. During conditioning, another HLH flare occurred. High dose dexamethasone and emapalumab, every 72 hours, were given until Day −1, effectively managing the flare. She engrafted on Day +17. Post-transplant course was complicated by EBV, CMV, and adenovirus viremia, iatrogenic adrenal insufficiency, and hypertension due to prolonged steroid use. At Day +105 status post HSCT, she remains fully engrafted with no signs of recurrence of HLH or lymphoma.

Conclusion: Our patient was successfully treated for HLH and SEPTCLC with modified DA-EPOCH, dexamethasone, emapalumab, valganciclovir, and HSCT.

POSTER # 163 | AN ADOLESCENT WITH GREY ZONE LYMPHOMA TREATED WITH BRENTUXIMAB VEDOTIN AND R-CHP CHEMOTHERAPY

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Background: Grey Zone Lymphoma (GZL) is an aggressive, rare cancer with histochemical and pathologic features of classic Hodgkin lymphoma (cHL) and non-Hodgkin lymphoma (NHL). With only 0.53 cases per million per year, treatment has not been standardized. Progression-free survival remains unfavorable (39%) while overall survival is 88-96%; the latter decreases to 76% with metastatic disease.

Objectives: To describe a treatment approach for GZL in an adolescent with metastatic disease.

Design/Method: Case report.

Results: An 18-year-old female with undifferentiated connective tissue disease presented with neck pain, a palpable 4 x 2 cm cervical lymph node, and erythrocyte sedimentation rate (ESR) of>130 mm/hr. Lymph node biopsy revealed a CD20 negative, CD30 positive B-cell lymphoma with histopathologic features of diffuse large B-cell lymphoma and cHL. No malignant cells were identified on bilateral bone marrow biopsy or lumbar puncture. PET CT revealed multifocal hypermetabolic activity of the axial-appendicular skeleton and lymph nodes (bilateral cervical chain, supraclavicular region, and mediastinum) (Deauville 4-5). A diagnosis of Stage IV-bulk mediastinal GZL was made and confirmed by an external, secondary review.

Common GZL treatment strategies include: 1) doxorubicin, bleomycin, vinblastine, dacarbazine; a cHL approach, 2) cyclophosphamide, doxorubicin, vincristine, prednisone, ± rituximab (CHOP ± R), or 3) dose-adjusted etoposide, doxorubicin, cyclophosphamide, vincristine, prednisone, ± rituximab; a NHL approach. A CHOP regimen was selected given its superior overall response rate, 71%, in GZL. Brentuximab vedotin was added given reported radiographic and clinical remission in adult CD30+ mGZL case series. Vinblastine was omitted to reduce anticipated peripheral neurotoxicity.

After two cycles of brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone (BV-CHP), previous hypermetabolic activity decreased (Deauville 2-3). Following four additional cycles of BV-CHP, no hypermetabolic activity above the background was detected. The patient was also evaluated for immune dysregulation given her medical history. Focused exome sequencing revealed a variant of uncertain clinical significance in the NLRP1 gene. No pathologic variants were reported. Hematopoietic stem cell transplant was not pursued. The patient remains off chemo-immunotherapy with surveillance imaging and labs. ESR has improved but remains above the normal range (54 mm/hr).

Conclusion: Treatment strategies are heterogeneous for GZL. Here we report a favorable tumor response in an adolescent with GZL who was treated with BV-CHP. Given this patient's known rheumatologic disease, underlying immune dysregulation was an important diagnostic consideration.

Pilichowska et al, Blood Advances, 2017
Mallipudi et al, Case Reports in Oncological Medicine, 2019
Bosch-Schips et al, Cancers, 2022
Simon et al, Pathology and Oncology Research, 2021

POSTER # 164 | POST-TRANSPLANT LYMPHOPROLIFERATIVE DISEASE IN A PATIENT WITH SCHIMKE IMMUNO-OSSEOUS DYSPLASIA

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Background: Schimke Immuno-osseous Dysplasia (SIOD) is an extremely rare autosomal recessive disorder due to biallelic SMARCAL1 mutation associated with variable manifestations,

including skeletal abnormalities, short stature, focal segmental glomerulosclerosis causing proteinuria and kidney failure, malignancies including osteosarcoma and non-Hodgkin lymphoma, atherosclerosis, developmental delay, bone marrow hypoplasia, and T-cell immunodeficiency leading to recurrent infections. Treatment is symptomatic, including dialysis and kidney transplant.

Objectives: We report an adolescent with SIOD who developed aggressive post-transplant lymphoproliferative disease (PTLD) after a kidney transplant.

Design/Method: Retrospective medical record review.

Results: A 14-year-old male with SIOD on low-dose tacrolimus and prednisone immunosuppression for a kidney transplant 8 years prior and a history of surgery and methotrexate chemotherapy for non-metastatic tibial osteosarcoma completed 39 months prior, presented with increased work of breathing, diffuse abdominal pain, and loose stools. Laboratory testing showed Epstein-Barr virus viremia and PET-MRI demonstrated extensive generalized lymphadenopathy and a significant mass with intense FDG uptake encasing the bowel. Lymph node biopsy pathology showed monomorphic PTLD with an abnormal B-cell population expressing CD19, CD20, CD22, CD10, and CD38. Fluorescence *in situ* hybridization confirmed MYC gene rearrangement but was negative for BCL2 and BCL6 rearrangements. Due to germline biallelic SMARCAL1 mutations associated with impaired DNA repair and organ toxicity, the patient was at increased risk for chemotherapy complications. Therefore, we adopted a staged approach to treatment by first utilizing agents associated with minimal DNA damage, starting with single-agent rituximab weekly. PET-MRI after three doses of rituximab demonstrated a marked decrease in tumor volume and FDG activity and EBV PCR was undetectable, consistent with a robust treatment response. A combination of steroids and weekly rituximab was administered for an additional month. Unfortunately, repeat PET-MRI showed increased size and metabolic activity of masses within the abdomen suggesting progressive PTLD. Weekly rituximab was continued due to the initially favorable therapeutic response, but a follow-up PET-MRI one month later showed further progression of the abdominal disease. Despite two cycles of more aggressive therapy including cyclophosphamide, methotrexate, vincristine, and steroids, the disease progressed further and he succumbed to his disease 2 months later.

Conclusion: SIOD patients are at a high risk of developing PTLD after kidney transplant due to underlying T-cell immunodeficiency, and chemotherapeutic management is complicated by impaired DNA repair. Early identification of these patients and sequential hematopoietic stem cell and kidney transplants from the same donor may lower the risk of PTLD and the development of other cancers.

POSTER # 165 | PRECURSOR B-LYMPHOBLASTIC LYMPHOMA PRESENTING AS A PRIMARY JAW TUMOR: CLINICAL AND GENOMIC FINDINGS

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Background: Precursor B-lymphoblastic lymphoma (B-LBL) is a well-recognized entity related to B-ALL, often presenting as localized disease in skin, soft tissue or bone. Genomic characterization of B-LBL has been limited in comparison to other B-lineage malignancies.

Objectives: To describe the clinical and genomic findings of a patient with localized B-LBL and extensive jaw involvement.

Design/Method: Case Report

Results: A 15-year-old, previously-healthy young man had progressive, unilateral pain and swelling of his jaw. MRI showed an ill-defined mass involving the buccinator musculature and a majority of the right mandibular bone. Biopsy of the jaw mass revealed a small, round blue cell tumor, consisting of a B-lymphoblast population by immunohistochemical staining, The malignant cells were positive for CD19, CD79a, PAX5, partial TdT, BCL-2 and C-MYC. Flow cytometry and cytogenetic analysis of the biopsy specimen were unsuccessful due to poor viability. Next generation sequencing (NGS) of the jaw mass (Anthology Diagnostics, Edison NJ) detected a dominant abnormal clone with MYC mutation along with KMT2D mutation in a subclone. Staging evaluation including PET/CT and bone marrow aspirate/biopsy demonstrated the primary tumor localized to the jaw with no other sites of invovlement. Cytogenetic analysis and NGS on the bone marrow sample showed no evidence of mutations. He was considered to have stage I, B-LBL by Modified Murphy criteria and was registered on the Children's Oncology Group trial AALL1731 for localized B-LBL. The patient had a complete response by PET/CT at end-Induction and continues to receive protocol chemotherapy.

Conclusion: Our patient presented with an extensive, localized mass of the mandible and surrounding musculature, clinically suggestive of Ewing sarcoma or other sarcoma of soft tissue and bone. However, this small round blue cell tumor proved to be a high-grade, precursor-B non-Hodgkin lymphoma. In contrast to immature T-lineage pediatric malignancies, most precursor-B lymphoblastic malignancies manifest as leukemia. B-LBL is recognized to present with localized disease of skin, soft tissue or bone. The NGS findings are interesting and contribute to our knowledge of B-LBL. MYC mutations are typically associated with mature B-neoplasms including Burkitt leukemia/lymphoma; C-MYC overexpression has also been found by immunohistochemistry in a majority of pediatric T-LBL samples. The finding of C-MYC overexpression by immunohistochemistry in our patient along with MYC mutation by NGS points to a role for MYC in immature B-lineage malignancy as well. To date, our patient has responded well to standard therapy for localized B-LBL.

POSTER # 166 | A 15-YEAR-OLD WITH OVERLAPPING FEATURES OF TWO RARE TYPES OF INDOLENT NON-HODGKIN LYMPHOMA

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Background: Pediatric nodal marginal zone lymphoma (PNMZL) and pediatric-type follicular lymphoma (PTFL) are rare types of non-Hodgkin lymphoma (NHL) in children and young adults. They typically present as slow-growing adenopathy of the head/neck.

Objectives: To describe the clinical and genomic findings of a patient with histologic features of both PNMZL and PTFL in a single lymph node.

Design/Method: Case Report.

Results: A 14-year-old male presented with a 6-month history of an enlarged, non-tender right submandibular mass. MRI showed a single submandibular lymph node (2.0 x 1.2 x 1.2 cm). The lymph node was completely resected; histology (reviewed by Dr. S. Pittaluga at the National Institutes of Health) revealed an atypical lymphoid proliferation with a follicular growth pattern. The follicles appeared variably-expanded with serpiginous outlines.

Immunohistochemical staining for CD20 revealed expanded follicles with numerous interfollicular B-cells. CD10 and BCL-6 revealed fragmented germinal centers with high proliferation index by Ki-67 and were negative for BCL-2. CD21 highlighted a distorted follicular dendritic meshwork. CD3 and CD43 primarily highlighted reactive T-cells. Immunostains for CD30, CD15, and MUM1 were negative.

Molecular testing demonstrated a monoclonal B-cell population in FR1, FR2 and FR3 region as detected by IgH-VDJ-PCR; FISH testing was negative for BCL-2 rearrangement. Next generation sequencing (NGS) of the tumor (Anthology Diagnostics, Edison NJ) detected low-level mutations in the MAP2K1, NSD1, and RIT1 genes along with low level del(9)(p24p13) JAK2-PAX5 fusion. The final diagnosis was most consistent with an atypical lymphoid proliferation with features overlapping between PNMZL and PTFL. Staging with PET/CT revealed no additional lymphadenopathy, and he was considered to have stage I, completely-resected NHL. A watch and wait approach was adopted to follow him with physical exam and ultrasound; there has been no evidence of recurrence early in follow-up.

Conclusion: PNMZL and PTFL are rare, indolent types of NHL in young adults; often resection alone is sufficient for long term cure. Recent case series support the occurrence of "overlapping" PNMZL and PTFL in some patients. MAP2K1 mutations have been found in significant numbers of both PNMZL and PTFL cases. Our patient's NGS revealed MAP2K1 alteration, supporting the hypothesis of PNMZL and PTFL as part of a morphological spectrum of a single entity. Further studies may investigate the role of other genes including NSD1 and RIT1 in the pathogenesis of this rare entity.

POSTER # 167 | A RARE PRESENTATION OF PEDIATRIC B-CELL LYMPHOBLASTIC LYMPHOMA

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Background: B-cell Lymphoblastic Lymphoma (B-LLy) comprises approximately 2-4% of pediatric non-Hodgkin Lymphoma (NHL). Most common sites of disease for B-LLy include lymph nodes, bone marrow (with less than 25% involvement), skin, abdominal organs, and occasionally gonads. Primary testicular lymphoma is an extremely rare entity and is not associated with any specific findings on ultrasound. Treatment failure for infection with the presence of a mass raises concern for an underlying malignant process. Staging criteria for localized testicular involvement are not well defined in both the Murphy Staging System and the International Pediatric Non-Hodgkin Lymphoma Staging System (IPNHLSS). Classifying NHL with involvement limited to the testes as Stage III is suggested by analogy with ovarian localization, which, as retroperitoneal disease, is explicitly defined as Stage III by the IPNHLLSS. Optimal treatment in North America is also unclear, with the most recent and current COG research protocols for localized B-LLy (AALL0932 and AALL1731) specifically excluding B-LLy with testicular involvement.

Objectives: We report an unusual case of isolated primary testicular B-cell lymphoblastic lymphoma presenting in a 10-year-old boy.

Design/Method: Case report.

Results: A 10-year-old boy with no pertinent past medical history presented to our clinic with a 2-day history of abdominal pain, decreased appetite and right testicular swelling. Ultrasound showed a complex intratesticular hypoechoic collection concerning for an abscess. Testicular and epididymal enlargement with hyperemia were noted suggesting epididymo-orchitis. Multiple rounds of antibiotics were given without improvement. Testicular germ cell tumor markers (LDH, b-HCG, AFP) were negative. As he had continued redness and pain, a radical inguinal orchiectomy was performed, revealing B-cell lymphoblastic lymphoma. Bone marrow aspirate, CSF evaluation, and PET-CT scan were negative for disease elsewhere. His disease was classified as Stage III and treatment with intensive acute lymphoblastic leukemia/lymphoma chemotherapy per AALL1131 was started to prevent recurrence.

Conclusion: Isolated testicular presentation of B-cell lymphoblastic lymphoma is very rare but should be considered in pediatric patients with atypical testicular masses. Given its rarity, the optimal treatment regimen is unclear. Nevertheless, if classified as Stage III disease, treatment with intensified acute lymphoblastic lymphoma/leukemia type treatment to avoid recurrence is reasonable.

POSTER # 168 | PEDIATRIC-TYPE FOLLICULAR LYMPHOMA IN A CROHN'S DISEASE PATIENT RECEIVING ANTI-$\alpha 4\beta 7$-INTEGRIN THERAPY

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Background: Patients with autoimmune conditions treated with systemic immunosuppressants are at risk of developing malignancies such as lymphoma. Crohn's disease, a type of auto-inflammatory bowel disease, is caused by activated T-lymphocytes migrating into intestinal tissue. Vedolizumab, a monoclonal antibody binding to $\alpha 4\beta 7$-integrin, uniquely inhibits T-cell migration into the bowel, thereby reducing

local inflammation for disease control. Unlike other biological treatments for Crohn's, vedolizumab is believed to have an insignificant immunomodulatory effect outside the gastrointestinal system.

Objectives: We report a case of pediatric-type follicular lymphoma (PTFL) in a 27-year-old Crohn's disease patient on vedolizumab. The patient exhibited systemic immune suppression from reduced T-cell proliferation and circulation.

Design/Method: The patient case was reviewed in Cleveland Clinic Children's EPIC electronic medical record system. Literature review for similar cases/etiologic explanation was performed through searches of PubMed and Cochrane library.

Results: A 27-year-old male with Crohn's disease noted a painless mass in the right mandibular fossa about 5 years after starting vedolizumab therapy. Computed tomography confirmed the mass within the parotid gland and encasing the facial nerve, as well as involved submandibular and cervical lymph nodes. Mass biopsy demonstrated neoplastic infiltrate with a follicular pattern and immunophenotype consistent with PTFL. Pre-therapy immune system testing revealed reduced numbers of CD3+CD4+-T cells (27%; 304 cells/uL; normal: 34-61%; 533-1674 cells/uL) and CD3+CD8+-T cells (14%; 151 cells/uL; normal: 10-41%; 175-958 cells/uL) in peripheral blood. Response to in vitro mitogen stimulation with phytohemagglutinin (PHA)(174K counts per minute (CPM); normal 190K CPM) and concanavalin A (ConA)(49K CPM; normal 81K CPM) was also suppressed. The tumor was not amenable to surgical resection or local radiation therapy; therefore, 6 cycles of R-CVP (rituximab, cyclophosphamide, vincristine, prednisone) chemo-immunotherapy were administered, concurrently with monthly vedolizumab. Repeat assessment at 12 months off-therapy revealed complete remission for both PTFL and Crohn's disease, yet persistent suppression of peripheral blood T-cells (CD3+CD4+ 32%, 526 cells/uL; CD3+CD8+ 18%, 293 cells/uL; PHA: 125K CPM; ConA: 93K CPM). Ongoing immune suppression at this clinical stage may only be attributed to continued vedolizumab therapy.

Conclusion: PTFL is a rare type of non-Hodgkin lymphoma. This case illustrates PTFL in a patient with preexisting inflammatory conditions on long-term biologic therapy rendering strong local (bowel) but not systemic immune modulation. The role of immunosuppresion in PTFL pathogenesis has not been established, but routine immune system workup in patients with PTFL may help reveal an etiologic correlation.

POSTER # 169 | BURKITT LEUKEMIA WITH AN UNDERLYING DIAGNOSIS OF LYNCH SYNDROME: ASSOCIATION OR COINCIDENCE?

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Background: Lynch Syndrome (LS) is a cancer predisposition syndrome causing a spectrum of adult-onset malignancies, predominantly, colorectal and endometrial cancers. It is inherited in an autosomal dominant fashion by monoallelic loss of function mutation in DNA mismatch repair (MMR) genes. Hematological malignancies (HM) are not typically observed in LS. However, in cases of biallelic inactivation as in, constitutional mismatch repair deficiency syndrome (CMMRD), HM are frequently reported.

Objectives: To describe a case of childhood leukemia in a family with LS and to evaluate potential molecular mechanism of carcinogenesis.

Design/Method: Case report.

Results: A previously healthy male was diagnosed with Burkitt leukemia at age 12. He presented with leukocytosis and tumor lysis syndrome. Bone marrow evaluation revealed a hypercellular marrow involved by high-grade B-cell lymphoma, comprising over 90% of marrow cellularity. Flow cytometry was positive for CD10, CD19, CD20, CD22 and CD45 with FISH studies demonstrated low-level MYC rearrangement (9%) and negative for BCL2 and BCL6 rearrangement. Acute leukemia NGS panel (65 genes) revealed a Tier 1 somatic variant in PHF6 with variant allele frequency of 66%. RNA sequencing did not detect any additional fusions. His chemotherapy course was complicated by significant toxicities including prolonged count recovery, severe peripheral neuropathy, neurotoxicity, acute kidney injury and several infectious complications. Due to extensive family history of cancers in the maternal side including colorectal, duodenal, brain and skin cancers, a germline cancer predisposition panel was sent and identified a heterozygous pathogenic variant in MSH2 (c.942+3A>T) consistent with LS. IHC staining of the bone marrow aspirate revealed intact expression in MLH1, PMS2, MSH2, MSH6. Additional tumor profiling through whole exome sequencing to delineate the landscape of somatic mutations, tumor mutational burden and microsatellite instability status is currently pending.

Conclusion: We describe a case of HM in a child with LS. The contribution of germline pathogenic variant in MSH2 in carcinogenesis in this patient is unclear since expression of MMR protein in the tumor tissue was intact. However, there is increasing evidence to suggest that germline MMR deficiency may impact the mutation burden of tumors that may have therapeutic implications.

POSTER # 170 | EARLY UNFAVORABLE CLASSIC HODGKIN LYMPHOMA TREATED WITH A+AVD IN A PEDIATRIC PATIENT

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Background: Historically, standard therapy for classic Hodgkins lymphoma (cHL) in children is doxorubicin, bleomycin, vincristine, etoposide, prednisone, cyclophosphamide (ABVE-PC) which yields excellent survival albeit associated with long term adverse effects that affect overall QoL such as risk of secondary cancer, small risk of infertility and more. Brentuximab vedotin (BV), an anti-CD30 antibody–drug conjugate, has been shown to improve outcomes in relapsed refractory advanced cHL and is being more commonly used for these cases. Some studies such as the BREACH trial[(1)] compared the standard treatment with ABVD (used in adults cHL) to A+AVD (both followed by

radiotherapy) in 170 patients, ages 18-60 years. The study demonstrated the efficacy of 4 cycles of A+AVD (Brentuximab, Doxorubicin, Vincristine, Dacarbazine) followed by radiotherapy as first-line treatment for patients with early-stage unfavorable Hodgkin lymphoma with the hope for future trials with A+AVD that will eliminate radiotherapy.

Objectives: To describe a case of Classic Hodgkins Lymphoma treated with less toxic chemotherapy with great response.

Design/Method: Case Reoport

Results: We present a case of Stage II bulky disease cHL successfully treated with A+AVD without radiotherapy in a pediatric patient. Our patient is an 8yo male who presented with stage 2A bulky disease cHL. Initial PETCT scan showed confluent cervical nodal mass in the left mid neck measuring 6.8 x 3.5 cm as well as involvement of left supraclavicular lymph nodes, with a Deauville 5-point score of 5. Histology revealed large cells that are mostly CD30 +, CD15+ PAX5 dim, a subset positive for EBER and rare CD20 + cells. Due to bulky disease, the patient was started on A+AVD therapy. The patient completed 4 cycles of A-AVD with minimal adverse events. PETCT performed after cycle 2 demonstrated complete metabolic response and good anatomic response to treatment (Deauville score = 1). After cycle 4, his end of therapy PETCT showed no FDG avid lymphoma (Deauville score = 1). He will be monitored clincially per NCCN protocol.

Conclusion: A+AVD should be considered a viable option with great efficacy for early unfavorable cHL including bulky disease as demonstrated in our patient. Using drug substitution, this regimen offers several advantages including high efficacy with minimal adverse effects (brentuximab vedotin), and omission of consolidation radiotherapy [(2)]. A+AVD is a promising regimen with potential to increase event free survival (EFS) in patients with early unfavorable cHL.

POSTER # 171 | DIAGNOSTIC UNCERTAINTY DUE TO PRE-BIOPSY STEROIDS TO TREAT MALIGNANT SUPERIOR VENA CAVA SYNDROME

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Background: Malignant mediastinal masses, most commonly caused by lymphomas and germ cell tumors, can result in superior vena cava syndrome (SVCS) due to compression of the superior vena cava. Clinical features include chest pain, cyanosis, dyspnea, and swelling of the face, neck, and upper torso. SVCS is a medical emergency, and treatment options include rapid high dose irradiation, chemotherapy, and corticosteroids. However, giving emergent corticosteroids to an undiagnosed patient prior to obtaining a biopsy can be challenging as these can affect the diagnostic accuracy of the biopsy by distorting cellular morphology.

Objectives: Our aim is to describe a distinctive case of a 17 year old male with a mediastinal mass who presented with SVCS that was emergently treated with corticosteroids prior to a biopsy, resulting in diagnostic uncertainty.

Design/Method: Single subject case report

Results: A 17 year old boy who presented with SVCS due to a mediastinal mass was rapidly started on dexamethasone due to worsening clinical features and received three doses prior to a diagnostic biopsy. Results were delayed due to difficulty in reading the slide specimens, however the initial diagnosis resembled metastatic embryonal carcinoma, and so a generic chemotherapy therapy regimen was started consisting of ifosfamide, etoposide, and cisplatin (VIP) via ACGT1532 to cover high grade carcinomas, germ cell tumors, and classic Hodgkin lymphoma. He received one course of VIP however he required tumor debulking due to persistent SVC compression. He started a second cycle of chemotherapy with bleomycin, etoposide, and cisplatin (BEP) per AGCT1532 however, again, had poor response. Next generation sequencing eventually revealed an EML4:ALK fusion which is often associated with anaplastic large cell lymphoma (ALCL), however he was found to be CD30 negative. Due to poor response despite multiple lines of therapy, he began treatment for what was now presumed to be ALCL. He received triple intrathecal chemotherapy once followed by treatment per ANHL12P1 with crizotinib, dexamethasone, ifosfamide, methotrexate, cytarabine, and etoposide with good response.

Conclusion: This case report details the adverse effects on pathological diagnosis from treatment with corticosteroids. This patient's poor response after multiple lines of chemotherapy may be due to diagnostic uncertainty secondary to emergent corticosteroid treatment prior to his biopsy. Providers should be aware of the potential adverse effects of corticosteroids on biopsy results, which may lead to misdiagnoses, delays in management, and incorrect treatment regiments.

POSTER # 172 | DIFFUSE LARGE B-CELL LYMPHOMA OF THE OVARIES PRESENTING WITH A PARANEOPLASTIC SCLEROTIC SKIN LESION

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Background: Pediatric non-Hodgkin lymphoma (NHL) accounts for 8% of childhood malignancies with diffuse large B-cell lymphoma (DLBCL) comprising 10 to 20% of NHL. Extra-nodal NHL is rare and most frequently found in the bone. Primary ovarian NHL accounts for 0.5% of all NHL and 1.5% of all ovarian tumors. The most common ovarian NHL reported is Burkitt lymphoma. Paraneoplastic syndromes have been reported with lymphomas and also with ovarian tumors including nephrotic syndrome, encephalitis, among others. There are also reports of paraneoplastic morphea which can occur in all age groups and has occurred in cases of ovarian malignancy.

Objectives: To present an unusual case of bilateral ovarian DLBCL in an adolescent presenting with a skin lesion.

Design/Method: Case report.

Results: A previously healthy 15-year-old female presented with a progressive neck lesion for 2-3 months. It started as a 2-cm erythematous lesion on the right neck and worsened over four months, becoming

more indurated, tender and extending down to the midsternal region. The induration significantly restricted the neck range of motion. The patient also had mild dysphagia and six months of amenorrhea. On exam, patient was obese with a large keloid-like lesion in the lower neck. The skin around the posterior neck, shoulders and proximal chest was hard and indurated. Palpation of lymph nodes and spleen was difficult due to body habitus. Laboratory work up showed LDH of 454 and Uric Acid of 6.8 with mild transaminitis. Head and neck CT showed a non-specific infiltrative process within the soft tissues of the neck. Full-thickness skin biopsy showed predominantly T-cell lymphocytic dermatitis. CT of the chest, abdomen, and pelvis, to assess for an occult neoplastic process, showed large bilateral ovarian masses with retroperitoneal and mediastinal adenopathy. Serum tumor markers showed elevation of CA125 with normal AFP, bHCG, inhibin, and CEA. Left ovarian biopsy was inconclusive; and follow-up left oophorectomy showed DLBCL with CD138 expression. The patient had very good partial response to COP therapy with significant improvement of the skin lesion and range of motion. Patient is currently undergoing R-COPADM.

Conclusion: This case illustrates a unique occurrence of bilateral DLBCL of the ovaries with associated paraneoplastic keloid-like skin induration as the leading presentation and cautions physicians to consider primary ovarian cancer in patients initially presenting with atypical symptoms that cannot be explained by standard workup.

POSTER # 173 | A CASE OF T-LYMPHOBLASTIC LYMPHOMA IN A PEDIATRIC PATIENT WITH A GERMLINE RUNX1 MUTATION

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Background: The runt-related transcription factor 1 (*RUNX1*) gene is vital to the process of normal hematopoiesis.[1-4] Germline mutations in this gene lead to familial platelet disorder with associated myeloid malignancy (FPD/AML), a condition with a significant predisposition to hematological malignancies.[5] The most common neoplasms associated with FPD/AML are of myeloid origin; however, the impact of various disturbances in the *RUNX1* gene and their contribution to the development of distinct categories of malignancies is not completely established.[1-2,6] Due to the phenotypic heterogeneity displayed by this disorder, it is essential to identify patients with germline *RUNX1* mutations for further monitoring, although evidence-based guidelines for the management of patients with FPD/AML have yet to be defined.[5]

Objectives: We describe the diagnosis and management of T-lymphoblastic lymphoma (T-LBL) in a 10-year-old patient with a previously identified germline RUNX1 mutation. We believe that the description of the patient's mutation is crucial to increasing understanding of the result of different germline RUNX1 variants.

Design/Method: This is a case report that examines the diagnosis and management of one patient. The electronic medical record of this patient was accessed via a secure network, and no patient identifiers were obtained.

Results: A 10-year-old male initially presented with isolated thrombocytopenia (12,000/mm^3). Bone marrow biopsy demonstrated megakaryodyspoiesis but no evidence of acute leukemia. These histologic findings, along with a family history of chronic thrombocytopenia, prompted further genetic testing, which demonstrated a nonsense mutation in the *RUNX1* gene (Y414X). The patient was found to be heterozygous for a single nucleotide variant (fraction of 56%) that resulted in a premature stop codon at amino acid position 414 (p.Tyr414Ter). The mutation was concluded as likely pathogenic as the same mutation and a similar nonsense variant were found in several patients with FPD/AML. One year after the initial presentation, our patient was diagnosed with T-LBL via biopsy of a mediastinal mass found on imaging. The patient underwent hematopoietic stem cell transplantation (HSCT) from a haploidentical donor to attend to his T-LBL and the risk of developing hematological malignancies in the future.

Conclusion: The case described emphasizes that specific RUNX1 genetic disturbances may predispose to various types of hematological malignancies. This study also illustrates the importance of defining the impact of unique RUNX1 mutations on the prognosis of patients and the use of HSCT as a prophylactic measure for FPD/AML. Further studies are necessary to investigate how additional somatic mutations affect the range of malignancies associated with germline RUNX1 variants.

POSTER # 174 | NEPHROTIC SYNDROME AND HODGKIN LYMPHOMA: TWO CASES WITH A GREAT DIFFERENCE IN CLINICAL PRESENTATION

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Background: Nephrotic syndrome (NS) is a known paraneoplastic finding, especially with Hodgkin lymphoma (HL). NS can be diagnosed concurrently with HL, precede an occult HL, or follow years after HL treatment.

Objectives: To describe two young adults with HL and NS with widely-different clinical presentations.

Design/Method: Case Report

Results: Case #1: A 17-year-old female presented with asymptomatic adenopathy 4 years after successful treatment of steroid-sensitive minimal-change NS. Cervical node biopsy was diagnostic of HL, nodular sclerosis subtype. She was successfully treated with 4 cycles of ABVD chemotherapy and remains in remission, without evidence of NS recurrence.

Case #2: A 17-year-old female presented to a nephrologist with edema and proteinuria and was diagnosed with minimal-change NS (biopsy-proven). She did not respond to steroids and progressed rapidly to renal failure requiring hemodialysis. Her NS did not

respond to rituximab. Three months after NS diagnosis, while undergoing hemodialysis, she developed fever and supraclavicular adenopathy. Biopsy was diagnostic of HL, nodular sclerosis subtype; evaluation was consistent with stage IIB. She was treated with doxorubicin/vinblastine/dacarbazine plus brentuximab vedotin; doses were modified in cycle 1 for renal failure/hemodialysis. Her renal failure resolved, and full dosing commenced at cycle 2. HL evaluation with PET scan after cycle 2 showed a complete metabolic response; she received 4 cycles total. Her steroid-resistant NS has shown partial response to HL treatment, with continued proteinuria during short-term follow-up.

Conclusion: NS is a rare disorder in young patients; the majority of cases are idiopathic. It is suspected that immune dysregulation is involved in the pathogenesis and corticosteroids are the mainstay of treatment. For decades, NS has been associated with an occult cancer diagnosis, especially hematologic malignancies such as HL and multiple myeloma. In a large Danish population-based study, the 5-year risk of any cancer was 4.7% in NS patients; this association was highest within 1 year of NS diagnosis but remained elevated for years after (1). In some case series, NS associated with HL is steroid-resistant but remitted with successful HL treatment.

Most cases of NS and HL are idiopathic but may represent disorders of immune dysfunction. Our 2 cases demonstrate a clinical spectrum of the association between NS and HL. In the first, HL followed 4 years after successful NS treatment with steroids. The second case more typically illustrates steroid-resistant NS presenting months before HL. Pediatric oncologists should be aware of this rare but important association.

(1) Christiansen et al, American Journal of Medicine, 2014

POSTER # 175 | OSTEOLYTIC BONE LESION MIMICKING SARCOMA AS A PRESENTATION OF B-CELL LYMPHOMA

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Background: Non-Hodgkin Lymphoma accounts for approximately 7% of cancers in the adolescent population. As an unusual presentation, lymphomas can involve bones either as a primary bone mass or metastasis. Primary bone lymphomas are rare entities and are only considered in the absence of lymph node or soft tissue involvement. Whereas, disseminated secondary lymphomas to the bone represent extranodal involvement of the primary disease. Aggressive lymphomas have been reported to present as solitary bone tumors that can be initially misdiagnosed as sarcomas.

Objectives: We report a case of an adolescent with a mature B-cell lymphoma presenting as a primary soft tissue mass with multifocal osteolytic bone metastases.

Design/Method: Chart review, multi-department collaboration and literature review.

Results: A 15-year-old girl presented with a right thigh mass for the past year; diagnosed as a lipoma by a physician in her home country. In addition to the slow growth of this mass, she has had progressively worsening left hip and leg pain for three months. Initial x-rays identified a right lateral thigh soft tissue mass and a proximal left femoral diaphyseal osteolytic lesion concerning for a bone tumor. PET-CT demonstrated a lobular FDG avid soft tissue mass measuring 6x7x8cm in the right groin, and lytic lesions on the left femur, sacrum and spine corresponding to areas of increased radiotracer uptake. To identify if the soft tissue mass and bone lesions originated from the same entity, biopsies of the mass and femur were performed. Both histopathologies showed small blue neoplastic cells, positive for CD45, CD20, PAX5 and BCL-6 with a high Ki-67 proliferation index. FISH studies were negative for myc, bcl-6 and IGH/bcl2 rearrangements; consistent with an aggressive mature B-cell lymphoma. Both bone marrow biopsy and CSF studies were negative for lymphoma. Patient was classified based on St Jude's (Murphy's) Staging as Stage III primary B-cell lymphoma of the thigh with diffuse bone metastases. She received chemotherapy as per Children Oncology Group protocol, ANHL1131 with Rituximab, Vincristine, Cyclophosphamide, High-dose Methotrexate, Doxorubicin, and Prednisone. End of treatment evaluation with PET-CT identified a non-FDG avid residual right thigh mass with the largest diameter of 3 cm. All original lesions were non-FDG-avid. An excision biopsy of the residual mass was negative for B-cell lymphoma.

Conclusion: We describe a rare case of B-cell lymphoma presenting as a soft tissue mass and bone metastases mimicking sarcoma or primary bone tumor. Although imaging studies can be helpful in characterizing bone lesions, histopathology will provide a definite diagnosis.

POSTER # 176 | APPENDICITIS MIMICKING PROGRESSION OF DIFFUSE LARGE B-CELL LYMPHOMA

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Background: Appendicitis has long been known as the "great mimicker" but few case reports in the pediatric population have demonstrated chronic appendicitis mimicking cancer progression on PET imaging.

Objectives: To discuss a unique case of appendicitis mimicking disease progression of diffuse large B-cell lymphoma (DLBCL).

Design/Method: Case Report

Results: A 16-year-old male presented with 3 weeks of periumbilical abdominal pain. CT scan demonstrated a retrocecal mass thought to be an appendiceal abscess.

Further imaging showed irregular bowel wall thickening in the ileocecal region and a mesenteric soft tissue mass. Pathology report demonstrated DLBCL, germinal center type. PET scan revealed hypermetabolic lymphadenopathy throughout the abdomen, pelvis, cecum, and terminal ileum. Chemotherapy per the Children's Oncology Group protocol ANHL1131 was initiated. PET scan after reduction phase evidenced significant decrease in extent and degree of abnormal FDG

consistent with a marked partial response to therapy. However, an end of therapy PET scan exhibited concern for disease progression with increasing focal uptake in the right pelvis. Biopsy of a regional lymph node showed no evidence of lymphoma. Inflammation was noted around the cecum and appendix at laparoscopy. Due to reassuring findings, the patient was observed and had a subsequent PET scan 3 months later that continued to show persistent but decreasing focal FDG which appeared to localize to the appendix. Given the decrease in FDG uptake while off therapy, localization of FDG to the appendix, and the operative report with inflammation in this region, a diagnosis of chronic appendicitis was considered. An appendectomy was performed which confirmed chronic appendicitis without evidence of lymphoma. Follow-up PET/CT scan showed no FDG evidence of recurrent or residual lymphoma. He remains disease free 12 months off therapy.

Conclusion: This case is unique given the patient had hypermetabolic uptake on PET imaging, leading to suspicion of relapsed/refractory DLBCL but was due to chronic appendicitis. Cancers such as Burkitt's lymphoma or colonic-adenocarcinoma have been shown in the literature to mimic appendicitis at initial diagnosis but few cases of appendicitis mimicking cancer recurrence or progression have been reported and none in the pediatric population. Though rare, this case demonstrates a potential for re-analyzing the role of early appendectomy particularly in patients with primary cancer located near the appendix. This could alleviate the misconception of suboptimal treatment response and potentially decrease surgical interventions. Further research is needed.

POSTER # 177 | HYPEREOSINOPHILIA DURING RADIATION THERAPY IN A PATIENT WITH HODGKIN LYMPHOMA: A WARNING SIGN?

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Background: Peripheral eosinophilia is a reported but uncommonly recognized side effect of radiation therapy. Previously, clinical significance was believed to be unlikely. More recently, eosinophilia has been studied as a potential prognostic marker for progression-free survival of oncology patients undergoing immunotherapy, likely attributed to aiding in T-cell recruitment into the tumor microenvironment. Peripheral eosinophilia can lead to multi-organ system dysfunction due to the pro-inflammatory downstream effects. When organ eosinophilia is present and limited to the esophagus, for example, it is termed eosinophilic esophagitis. The contribution of transient radiation induced eosinophilia on long-term organ dysfunction and development of eosinophilic disorders is unknown.

Objectives: Describe a case of an adolescent / young adult (AYA) oncology patient with a 10-year remote history of dysphagia who was found to have a transient peripheral hypereosinophilia during radiation therapy and presents in remission with food impaction, found to have severe esophageal stricture and eosinophilic esophagitis (EoE) on endoscopic biopsies.

Design/Method: Case report

Results: A 21-year-old female with a history of stage IIA nodular sclerosis classic Hodgkin Lymphoma presented 17-months after completion of chemotherapy and superior mediastinal/left cervical radiation with acute onset food impaction. She underwent endoscopy with findings notable for chronic esophagitis and esophageal stricture. Biopsies confirmed a diagnosis of eosinophilic esophagitis. She has required repeated esophageal dilations, significant dietary restrictions, and medical EoE management. She had a remote history of dysphagia without prior intervention and known food allergies. During radiation therapy, she complained of significant nausea and vomiting, and was noted to have new hypereosinophilia with absolute eosinophil count greater than 4,000 cells per microliter following one week of radiation therapy. She was treated with a course of oral steroids with improvement in her eosinophilia and GI symptoms. Following completion of radiation, GI symptoms completely resolved, and eosinophil count returned within normal limits.

Conclusion: Transient eosinophilia is a documented effect of radiation therapy without well-known clinical significance. Eosinophils are important mediators in the natural immune response via amplification of inflammatory cascades while carrying the potential for cytotoxic damage to a patient's own body. The possible adverse effects associated with transient peripheral hypereosinophilia during radiation therapy should be further investigated to better understand associated morbidity, including potential contributing impact related to other eosinophilic disorders, such as EoE.

POSTER # 178 | DELAY IN DIAGNOSIS OF AN ADOLESCENT WITH HODGKIN'S LYMPHOMA PRESENTING AS A NECROTIZING PNEUMONIA

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Background: Hodgkin lymphoma often presents as painless lymphadenopathy, systemic symptoms, or respiratory compromise from a mediastinal mass. Pulmonary cavitation is seen in less than 1% of Hodgkin lymphoma cases that have pulmonary involvement.

Objectives: In this report, we present a case of nodular sclerosis Hodgkin lymphoma that presented as a necrotizing pneumonia resulting in delay of diagnosis and treatment.

Design/Method: The electronic medical record of one patient was accessed through a secure network. No patient identifiers were collected.

Results: A 15-year-old girl presented with a chronic cough and occasional mild hemoptysis that began approximately 6 months earlier. Within that time frame, she also experienced a significant weight loss equivalent to 15% her body weight. She experienced no night sweats, fever, or shortness of breath. The patient lived with her father who was incarcerated more than once over the past several years. She had an

initial chest x-ray ordered by her primary care provider showing airspace disease in the right upper lobe with cavitation. Her ESR was 67, WBC was 33,000 with a high neutrophil count, platelets were 670,000, and Hgb was 9gm/dl. Due to concern for tuberculosis, she was seen by our emergency department where a repeat chest x-ray confirmed the above findings.

The patient was admitted by infectious disease where an extensive workup to rule out tuberculosis and other infectious etiologies was done. Respiratory cultures were negative, acid-fast bacilli smear and serological tests for TB were negative, and bronchoalveolar lavage was non-diagnostic. Computed tomography of the patient's chest and abdomen showed substantial mediastinal, subcarinal, and bilateral hilar adenopathy with central necrosis in the right perihilar region and upper lobe. During her hospital stay, the patient was found to have an enlarged right supraclavicular lymph node on exam. After 3 weeks of extensive negative workup for infectious etiology, the node was biopsied and confirmed to be nodular sclerosis Hodgkin lymphoma. A subsequent PET scan showed stage 4A Hodgkin lymphoma. The patient was started on chemotherapy regimen and had a rapid and significant response.

Conclusion: Hodgkin lymphoma presenting as a cavitary lung lesion can cause a delay in definitive diagnosis due to rarity of this presentation and time spent ruling out more common differentials. From this case, we learned that supraclavicular lymphadenopathy in the presence of a cavitating lung lesion should raise concern for neoplasm in adolescents. Lymph node biopsy should be performed in concurrence with other etiologic work up.

POSTER # 179 | COMPLETE REMISSION POST R-COP REDUCTION IN BURKITT LEUKEMIA MEASURED BY TUMOR-SPECIFIC CELL-FREE DNA

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Background: Burkitt leukemia is a rare aggressive B-cell lineage hematological neoplasm that requires intensive chemoimmunotherapy. Bone marrow assessment for detection of minimal residual disease (MRD) was previously shown to have prognostic value in a small number of patients. Bone marrow flow cytometry remains the preferred method, but the MRD limits (positive vs. negative) have not been introduced into uniform practice. The longitudinal assessment of the cell-free circulating tumor DNA (ctDNA) encoding the patient- and tumor cell-specific rearranged heavy or light (kappa/lambda) chain Immunoglobulin-G, could be used for the treatment response and early recurrence monitoring in patients with other B-cell neoplasms. The ClonoSEQ assay is an FDA-approved NGS-based test capable of detecting MRD at levels below $1x10^{-6}$ cells, the greatest depth achievable by testing today.

Objectives: Report results of longitudinal ctNDA testing in a case of Burkitt leukemia in a pediatric patient with stage IV Burkitt Leukemia and his treatment response as measured by ClonoSEQ evaluation.

Design/Method: Electronic medical records review; literature review for similar cases through searches of PubMed and Cochrane library.

Results: A previously healthy 12 year old male was admitted for severe abdominal pain and upper gastrointestinal bleeding in the setting of severe thrombocytopenia, anemia, and leukocytosis with circulating lymphoblasts. Bone marrow flow cytometry revealed lymphoid proliferation of B-lymphoblasts expressing CD10, CD19, CD20, CD22 and CD45 but lacking TdT, suggesting mature B-cell lineage. Cytogenetic analysis by FISH revealed presence of (8;14)(q24;q32) IGH/MYC rearrangement, and the absence of a primary lymphoid mass. ClonoSEQ assay of the bone marrow identified 3 highly-unique dominant Ig sequences (two IgH and one IgL) with sample clonality of 0.77 (value closer to 1 indicates clone dominance). R-COP reduction as per Inter-B-NHL/COG ANHL1131, group C3 was initiated, resulting in severe tumor lysis syndrome. Post R-COP reduction MRD assessment by clonoSEQ revealed absence of previously identified dominant clonotypic sequences, and remained negative through the rest of the treatment.

Conclusion: Given the rare nature of Burkitt Leukemia, there is currently limited information regarding MRD prognostic relevance. Long-distance Polymerase Chain Reaction (LD-PCR) and Immunoglobulin gene rearrangement strategies have been used, in addition to classical flow cytometry, with similar sensitivities approaching detection of $1x10^{-3}$-10^{-5} cells. Studies by Mussolin et.al.'s group (PMID: 18024872, 32080837) revealed a significant negative prognostic impact of MRD positivity utilizing these methods. ClonoSEQ's robust sensitivity to detect $1/10^{-6}$ cells (thus far studied in ALL, MM and CLL), may help further prognostication in Burkitt Leukemia with increased accuracy.

POSTER # 180 | EVIDENT CLONAL EVOLUTION OF B-CELL ACUTE LYMPHOBLASTIC LEUKEMIA INTO WIDESPREAD HISTIOCYTIC SARCOMA

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Background: Histiocytic sarcoma (HS) is a rare often very aggressive hematopoietic neoplasm with an incidence 0.17 per 1,000,000. Approximately 70% of patients present with disseminated disease which portends a poor prognosis.

Objectives: Describe a case of precursor B-cell acute lymphoblastic leukemia (B-ALL) with evidence of clonal evolution into HS.

Design/Method: Case report.

Results: A 12-year-old male initially presented for epistaxis was found to have a white blood cell count of 36,000 with 80% circulating blasts. Flow cytometry was consistent with a B-cell phenotype with aberrant expression of CD15. He was diagnosed with very high-risk B-ALL CNS3 with PDGFRB+ 5q32, del 7q, t(4:8). He was treated per standard high-risk chemotherapy with a negative end of induction minimal residual disease (MRD).

Therapeutic complications included methotrexate neurotoxicity, moderate peripheral neuropathy and juvenile xanthogranulomas (JXG). He had intermittent severe leg pain with imaging suggestive of avascular necrosis and thus commenced maintenance therapy without steroids. He developed severe abdominal pain and fevers with imaging revealing multiple areas concerning for metastatic disease in his kidneys, liver, spleen and lungs. He ultimately underwent biopsies of his kidney as well as his cuboid and tibial bones which were negative for leukemia and infection but showed significant histiocytic infiltration. Bone marrow aspirate (BMA) and CSF studies were negative for recurrent leukemia. Positron-emission tomography and computed tomography (PET-CT) revealed hypermetabolic nodal, renal, hepatic, pulmonary and innumerable osseous metastases. Immunohistochemical staining on his cuboid, tibia and kidney tissues were diffusely positive for CD163 and CD68 and negative for Langerhans, dendritic and leukemic cells consistent with the diagnosis of HS. Genetic testing from his initial B-ALL diagnostic BMA revealed a CDKN2A/CDKN2B loss and KRAS p.G12V mutation. Genetic testing on his JXG and tibia also revealed losses in CDKN2A/CDKN2B. His cuboid and tibia also harbored mutations in KRAS p.G12V and RAF1 p.R391W, mutations commonly seen in HS.

He began treatment with Trametinib monotherapy. PET-CT after 3 weeks of therapy revealed significant interval decrease in hypermetabolism, size and number of all visceral and bony lesions. We transitioned to cycles of 3 weeks of Trametinib followed by 5 days of Clofarabine and have discontinued B-ALL directed chemotherapy apart from every 12-week intrathecal methotrexate. He has been referred for hematopoietic stem cell transplantation.

Conclusion: This case provides evidence of clonal evolution from a lymphoid malignancy into widespread histiocytic sarcoma with characteristic mutations in RAS/MAPK pathway genes. Targeted therapy with Trametinib has shown an excellent response in combination with Clofarabine chemotherapy.

POSTER # 181 | NOVEL USE OF TRAMETINIB IN PH-LIKE B-ALL WITH DISSEMINATED JUVENILE XANTHOGRANULOMATOSIS AND HLH

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Background: Ph-like B-lymphoblastic leukemia (ALL) is associated with poor outcome harboring either ABL-class mutation or JAK-STAT pathway alterations. Juvenile Xanthogranulomas (JXG) are typically benign, self-resolving histiocytic proliferations in the skin that rarely disseminate and are associated with MAPK pathway mutations.

Objectives: We report the first case of simultaneous Ph-like B-ALL and disseminated JXG with secondary hemophagocytic lymphohistiocytosis (HLH) responding to targeted therapy with trametinib.

Design/Method: Case report

Results: A 12-year-old male presenting with a leukocytosis of 549,000 cells/mcL was diagnosed with Ph-like B-ALL with a t(Y;14) producing CRLF2/IGH rearrangement. Further molecular testing was positive for KRAS G12D. His craniospinal fluid was positive (CNS3). He underwent four drug induction chemotherapy with end of induction bone marrow (BM) minimal residual disease (MRD) by flowcytometry positive at 0.02%. After four weeks of augmented consolidation chemotherapy, he suffered persistent pancytopenia. BM aspirate flow cytometry showed 18% B-lymphoblasts. Concurrently, he developed multiple cutaneous nodules, fever, hyperferritinemia, hypofibrinogenemia, elevated soluble interleukin-2 receptor (IL2R) levels, and hepatosplenomegaly consistent with secondary HLH. The nodules were characterized as CD1a negative, S100 negative, CD68 positive, factor 13a positive, and BRAF V600E negative histiocytic proliferation, consistent with JXG. Molecular testing was positive for BRAF G469R, MTOR S2215Y, and most notably KRAS G12D. Because of rapid deterioration with coagulopathy, intractable gastrointestinal bleeding and hemorrhagic shock, the patient was stabilized with dexamethasone (10 mg/m2 daily), anakinra and two doses of methotrexate (100 mg/m2). Repeat BM was MRD negative by flowcytometry but revealed extensive infiltration with JXG. Trametinib was added while weaning dexamethasone and anakinra leading to remission of B-ALL and JXG. B-lymphoblasts were undetectable by flowcytometry (MRD negative); however, next generation sequencing (NGS) still showed presence of low-level disease. He was bridged with blinatumomab and trametinib prior to maternal haploidentical hematopoietic stem cell transplant.

Conclusion: This case highlights the complexity of a child with multiple live-threatening hematologic processes and the use of molecular analysis to guide therapy, in this case the MEK inhibitor trametinib.

POSTER # 182 | REMISSION WITH AN ADULT REGIMEN IN A TEENAGER WITH BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM

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Background: Blastic Plasmacytoid Dendritic Cell Neoplasm (BPDCN) is a rare but aggressive hematologic malignancy. Due to its rarity, induction chemotherapy regimens vary across institutions, with pediatric acute lymphoblastic leukemia (ALL)-based regimens being the most recognized treatment option in the pediatric population.

Objectives: By describing a pediatric patient with an aggressive presentation of BPDCN who was able to achieve remission and undergo bone marrow transplant, we propose Hyper-CVAD (cyclophosphamide, vincristine, cytarabine, doxorubicin, dexamethasone, methotrexate) with venetoclax as a treatment option for this population.

Design/Method: Case report.

Results: A 16-year-old male with no significant past medical history presented with cervical lymphadenopathy, rash, bilateral periorbital ecchymosis, and conjunctival hemorrhage. The presenting labs revealed a white blood cell count (WBC) of 6.2 K/μL with absolute neutrophil count of 0.7 K/μL, hemoglobin of 9.9 g/dL, platelet count of 33 K/μL, creatinine of 1.23 mg/dL, and uric acid of 7.6 mg/dL. Peripheral blood and bone marrow flow cytometry both revealed the blasts positive for CD4, CD38, CD56, CD123, and HLA-DR and negative for CD2, CD7, CD19, CD20, CD22, CD34, CD46, MPO, and TdT. Cerebral spinal fluid resulted with a WBC of 3 cells/mcL but cytospin was positive for blasts. Computed tomography of the chest and abdomen showed lymphadenopathy and splenomegaly. Magnetic resonance imaging of the brain showed enhancement suggesting leukemic involvement of bilateral lacrimal glands, adenoids, and parotid glands.

Steroids were initiated emergently due to superior vena cava syndrome. He subsequently developed significant tumor lysis and acute disseminated intravascular coagulation. Continued renal replacement therapy was initiated and the patient was stabilized. Since PEG-asparaginase in pediatric ALL-based regimens increases the risk of coagulopathy, the decision was made to treat with the adult BPDCN regimen, hyper-CVAD with venetoclax, along with intrathecal chemotherapy. The patient was able to achieve complete remission after the first cycle, with no aberrant plasmacytoid dendritic cell neoplasm cell population identified on flow cytometry of bone marrow aspirate. The patient received this regimen for 3 cycles and was able to proceed with a matched sibling allogeneic stem cell transplant and remains in remission 100 days post-transplant.

Conclusion: Hyper-CVAD with venetoclax and intrathecal chemotherapy was an effective and tolerable treatment regimen for this pediatric patient with aggressive BPDCN.

POSTER # 183 | SUCCESSFUL TREATMENT OF MALIGNANCY-ASSOCIATED HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS IN A TEENAGER

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Background: Malignancy-associated hemophagocytic lymphohistiocytosis (M-HLH) is a rare but potentially fatal syndrome characterized by immune dysregulation, uncontrolled hyperinflammatory response and end-organ damage. Novel therapy combinations such as ruxolitinib, anakinra and tocilizumab have been used together to control immune dysregulation caused by COVID-19, but their concurrent use has not been reported in M-HLH.

Objectives: To describe the use of combination therapy with high dose ruxolitinib, anakinra and tocilizumab in a patient with two active malignancies and M-HLH.

Design/Method: We describe an 18-year-old male with primary mediastinal germ cell tumor (PMGCT) and associated acute myeloid leukemia (AML) who developed M-HLH during induction chemotherapy for his leukemia. On day 15 of induction with cladribine, idarubicin, cytarabine (CLIA) and venetoclax, despite clearance of peripheral blasts, the patient began to clinically decline with acute jaundice and respiratory distress. Initial labs showed white blood cell count 0.1K/μL , hemoglobin 6.4gm/dL, platelet count 4K/ μL, ferritin 34,014 ng/dL, triglyceride 147 mg/dL, fibrinogen 88 mg/dL, soluble CD25 (sCD25) 2812.6 pg/mL (reference range 175.3 to 858.2 pg/mL), IL-6 23.6 pg/mL (reference range less than 2.0 pg/mL), and direct bilirubin up to 18.6 mg/dL. With clinical symptoms of fever and hepatosplenomegaly, along with laboratory findings, criteria for M-HLH was met. He rapidly progressed to respiratory failure requiring intubation and hypotension requiring vasopressor support. He developed gastroenterological bleeding with refractory thrombocytopenia and coagulopathy needing massive transfusions which in turn, lead to fluid overload requiring continuous renal replacement therapy (CRRT). Therefore, the patient was started M-HLH treatment with anakinra 400 mg every 12 hours, ruxolitinib 5 mg every 12 hours, dexamethasone 10 mg every twelve hours. Tocilizumab was added for 4 doses during period of severe cytokine storm and clinical distress. Ruxolitinib was gradually increased to 50 mg every 12 hours with positive clinical response.

Results: Ten days after the M-HLH therapy, he was extubated to room air and was weaned off of CRRT and vasopressors. Ferritin improved to 1013 ng/dL, direct bilirubin to 0.6 mg/dL, sCD25 to 2184.1pg/mL fibrinogen 232 mg/dL. High dose steroids were tapered down, and anakinra was discontinued with the increased dose of ruxolitinib. Unfortunately, the patient was not able to achieve remission, but M-HLH remained controlled despite persistent AML and active GCT. Ruxolitinib has been weaned to 25 mg every twelve hours while the patient continues AML directed therapy.

Conclusion: In this patient, M-HLH was controlled and remained stable with high dose ruxolitinib, anakinra and tocilizumab plus dexamethasone in a patient with active malignancy.

POSTER # 184 | MULTIMODAL MANAGEMENT WITH IMMUNOTHERAPY AND RADIATION OF HISTIOCYTIC SARCOMA FOLLOWING B-ALL

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Background: Histiocytic sarcoma (HS) is a rare and aggressive non-Langerhans cell histiocytosis that comprises less than 1% of hematolymphoid neoplasms.[1-2] Most cases of HS present in adult white males, with a median age at diagnosis of 63 years.[2] At present, no standardized treatment regimen for HS exists. HS can arise sporadically or can be clonally related to other hematologic malignancies, including acute lymphoblastic lymphoma (ALL) and follicular lymphoma.[2,3] Select cases of HS presenting concurrently with ALL have been reported in the literature, with the majority of cases

demonstrating trans differentiation, in which the histiocytic lesion shared molecular and cytogenetic features with the leukemia.[4]

Objectives: We aim to demonstrate that a multimodal treatment regimen of immunotherapy and radiation therapy may be a safe and effective option for HS that develops after the diagnosis and treatment of B-ALL and/or is refractory to traditional therapies.

Design/Method: The electronic medical record of this patient was accessed via a secure network, and information regarding his presentation, diagnosis, and management was collected. No protected health information was obtained.

Results: A four-year-old male was diagnosed with B-ALL in 2013 with an initial white blood cell count of 41,000/mm^3, CNS1 status, and unremarkable cytogenetics. He remained disease-free for four years after the completion of induction, consolidation, and maintenance chemotherapy per COG protocol AALL1131. In 2017, he presented with chest pain and respiratory distress secondary to a positron emission tomography (PET)-avid anterior mediastinal mass and a significant left pleural effusion. Biopsy of a region of pleural thickening confirmed a non-Langerhans cell histiocytosis with positive CD163, CD68, CD14, factor 13a, and fascin, low/negative S100, and negative CD1a. Therapy with prednisone and clofarabine failed to reduce the size and PET-avidity of the mediastinal mass, so dual immunotherapy with nivolumab and ipilimumab was initiated in addition to proton beam therapy directed at the mass and left chest wall. Due to recurrent reaccumulation of pleural fluid, the patient was referred to palliative care but was able to tolerate the continuation of dual immunotherapy in an outpatient setting and remains clinically stable.

Conclusion: Dual immunotherapy and proton beam radiation achieved clinical stability in a pediatric patient that developed HS refractory to therapy with prednisone and clofarabine four years after he was diagnosed and successfully treated for B-ALL, allowing him to return to school full-time and participate in extracurricular activities.

POSTER # 185 | A CASE OF SEVERE CYSTIC LUNG DISEASE IN RISK ORGAN POSITIVE MULTISYSTEM LCH

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Background: Pulmonary Langerhans cell histiocytosis (LCH) is typically an isolated presentation of LCH in adults but occurs only in 7-16% of pediatric LCH, most commonly as a component of multisystem disease. Pediatric patients with pulmonary LCH often present with respiratory distress and, in severe cases, pneumothoraces secondary to confluence of cysts. Management of pneumothoraces includes chest tube placement or pleurodesis, while patients undergo systemic treatment for LCH. The current standard of care for multisystem LCH is vinblastine/prednisone +/- mercaptopurine for risk organ (bone marrow, liver, or spleen) positive patients. Treatment with cytarabine/cladribine and MAPK pathway inhibitors can be effective for patients with refractory disease.

Objectives: To describe a unique pediatric case of multisystem, risk organ positive (liver) LCH with severe cystic lung disease, highlighting early interventions with pleurodesis and escalation of systemic therapy.

Design/Method: Retrospective chart review through an electronic medical record system.

Results: A 4-year-old previously healthy, Amish male presented with acute respiratory distress, diffuse cystic lung disease, and a significant right-sided tension pneumothorax. He subsequently underwent chest tube placement and right lung wedge resection. Pathology was consistent with LCH. ALK and BRAF-V600E were negative by immunohistochemical staining. Workup for infectious etiologies was negative. PET scan showed uptake in several pulmonary cysts and the left hepatic lobe. Treatment was initiated with vinblastine and prednisone. After 4 weeks of standard treatment with vinblastine and prednisone, he transitioned to cladribine due to recurrent pneumothoraces requiring surgical intervention and hospitalization. He ultimately underwent bilateral doxycycline pleurodesis and bilateral talcum pleurodesis, and trametinib was initiated. Subsequently, molecular tissue testing revealed BRAF-N486_P490del. Surveillance PET scans to date have shown stable pulmonary cystic lesions, resolution of hepatic avidity, and no new avid lesions. At the time of this abstract, he has completed 5 cycles of cladribine and continues daily trametinib with no progression of disease or dose-limiting toxicity.

Conclusion: We describe a case of a pediatric patient with multisystem, risk organ positive (liver), ALK/BRAF-V600E negative LCH with severe cystic lung disease who was treated with pleurodesis for recurrent pneumothoraces and systemic therapy with cladribine and trametinib, currently with no progression of disease or dose-limiting toxicity. Pulmonary LCH in children is rare, and surgical intervention with pleurodesis should be considered early to prevent the development of recurrent pneumothoraces and overall morbidity. In patients with severe clinical disease, we suggest considering early escalation of systemic therapy with a combination of chemotherapy and MAPK inhibition, especially for patients with known targetable mutations.

POSTER # 186 | TREATMENT OF SYSTEMIC JUVENILE XANTHOGRANULOMA IN A NEONATE WITH ACUTE FULMINANT LIVER FAILURE

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Background: Juvenile xanthogranuloma (JXG) is a non-Langerhans cell histiocytic disorder of childhood that typically manifests as benign cutaneous papules or nodules that regress over several years. However, there is systemic involvement in a small number of cases that may be associated with significant morbidity and mortality, without standardized treatment protocols.

Objectives: To describe successful treatment of a patient with systemic JXG and fulminant liver failure.

Design/Method: Retrospective chart review of patient's demographic information, clinical presentation, disease course, and treatment response as well as review of current literature.

Results: A newborn male was diagnosed with cutaneous JXG at birth and discharged home. He presented 1 month later in acute fulminant liver failure; a liver biopsy confirmed histiocytic invasion of the liver and led to diagnosis of systemic JXG. Additionally, he had lesions found on his heart and spleen after ECHO and CT imaging. Hepatic failure required high volume plasma exchange and continuous renal replacement therapy (CRRT) as adjunct supportive therapy. Targeted oncologic therapy was initiated with methylprednisolone. Importantly, an adapted dosing regimen of vinblastine was used due to concern for hepatotoxicity with full dose vinblastine. Due to his age, he required a fifty-percent dose reduction of vinblastine to 3.0 mg/m2. However, given the degree of infiltration and concern for risk of liver necrosis with the rapid destruction of histiocytes, the decision was made to further reduce the dose of vinblastine to twenty-five percent and administer at 1.5 mg/m2 with a second dose given three days later. He responded extremely well to targeted therapy and has since been successfully transitioned to outpatient management for ongoing treatment.

Conclusion: To our knowledge, this is the first report of successful treatment of acute liver failure from systemic JXG using vinblastine. This approach was complicated by our patient's young age, as well as need for high volume plasma exchange and CRRT, which affected the pharmacologic properties of the drug. The modified dosing regimen we used had not been previously described, but fortunately was successful in treating our patient's systemic disease with complete recovery of hepatic function.

POSTER # 187 | HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS IN A PATIENT WITH GERMLINE RB1 MUTATION

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Background: Retinoblastoma and Hemophagocytic Lymphohistiocytosis (HLH) are both rare pediatric diseases that have strong genetic etiologies. Here we present a patient with a history of retinoblastoma and germline RB1 gene mutation who was later diagnosed with HLH in association with ruptured appendicitis. On further genetic testing a heterozygous variant of unknown significance (VUS) of UNC13D (c973G>A) was discovered with only 1 submission in the ClinVar database (variation ID: 1023637).

Objectives: To demonstrate a possible association between RB1 mutation and HLH, further elucidate a VUS in UNC13D, and to raise the question if an HLH risk can arise from a combination of mutations.

Design/Method: Retrospective chart review. Literature search and review.

Results: Our patient was diagnosed at 18 months of age with bilateral retinoblastoma and treated with enucleation of the left eye and chemotherapy. Serum testing found a pathogenic germline RB1 variant, c.1333C>T. Two years after completion of chemotherapy (now 4 years old) he was diagnosed with ruptured appendicitis and sepsis that was treated with antimicrobials and surgery . He continued to have fevers and developed anemia, hepatosplenomegaly, transaminitis, ferritin 30,170 ng/mL, hypofibrinogenemia, hypertriglyceridemia, elevated s-IL2R, and hemophagocytosis in bone marrow. HLH was diagnosed and treated with Etoposide and Dexamethasone. Patient clinically improved after the initiation of treatment. Genetic testing revealed a heterozygous VUS in UNC13D (c973G>A).

Since completion of HLH-94 treatment, he has been doing well with no evidence of HLH or retinoblastoma recurrence, though he continues to have signs of inflammation with thrombocytosis and leukocytosis.

Initial literature search of the terms "RB1" or "retinoblastoma" with "hemophagocytic lymphohistiocytosis" revealed no pertinent findings. Multiple articles reviewing the genetic variation of primary HLH do not implicate RB1 gene mutations as a predisposing factor, or include the unique UNC13D mutation found in this patient.

Conclusion: While there is not currently a significant body of evidence connecting RB1 mutations and HLH, this case provides a unique situation in which both have occurred. The rarity of these diseases, along with our ever-evolving knowledge of genetics could mean that a link between the two does exist, but is only now starting to come to light. The presence of the UNC13D VUS in our patient also helps to provide data that this variation may be a full disease-causing mutation, or perhaps one that leads to increased HLH risk when present in combination with additional mutations, such as the RB1 mutation.

POSTER # 188 | A NOVEL CASE OF ROSAI-DORFMAN DESTOMBES (RDD) DISEASE IN A PEDIATRIC PATIENT

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Background: Rosai Dorfman-Destombes (RDD) is a rare non-Langerhans cell histiocytosis. Patients classically present with enlarged, tender cervical lymphadenopathy and associated constitutional symptoms including fever. RDD is typically a self-limited disease that resolves in 20-50% of patients whose disease is limited to the lymph nodes. It can also be a chronic, relapsing disease depending on involvement of extra-nodal sites and presence of systemic symptoms where there is no uniform approach to treatment.

Objectives: To present a pediatric patient diagnosed with RDD characterized by chronic, relapsing disease with current treatment regimen of multiple therapies including Prednisone, MTX, and 6-MP.

Design/Method: Case Report

Results: We present a 9-year-old previously healthy male who initially presented to his pediatrician with tender, right sided cervical lymphadenopathy. Despite a trial of an antihistamine and antibiotics, his lymphadenopathy persisted. He was hospitalized for painful

lymphadenopathy and was noted to have elevated inflammatory markers (ESR 107, CRP 9.9) and a microcytic anemia. Neck CT revealed enlarged parotid and upper cervical lymphadenopathy without evidence of abscess and biopsy was negative for malignancy. He was discharged with further antibiotics but was re-admitted for development of fever, weight loss and fatigue without improvement of his lymphadenopathy. ENT performed an adenotonsillectomy and tissue pathology was sent which confirmed the diagnosis of RDD (mixed inflammatory infiltrate with noted emperipolesis; BRAF mutation analysis is pending). He was placed on corticosteroids which initially improved his symptoms (fever, fatigue); unfortunately his symptoms returned once corticosteroids were weaned. Due to multiple failed attempts to wean the corticosteroids, methotrexate and mercaptopurine were added to his current treatment regimen, and we have been able to institute a slow wean of his corticosteroid. The goal is to completely wean off corticosteroids. If unable to do so, we will consider use of a MEK inhibitor.

Conclusion: The initial presentation of lymphadenopathy has a broad differential diagnosis; included in this differential is RDD, which is very rare and only seen in about 100 new cases per year in the United States. Currently there is no standard of care for the treatment of RDD and thus must be managed based on the patient's individual presentation. Without systemic symptoms, management is typically observation alone. However, in this case we see that there can also be significant complications and morbidity when there are associated systemic symptoms which may require multiple therapies. Further research is needed to determine if molecular guided therapy can guide our management in patients requiring treatment beyond observation.

POSTER # 189 | LUMPS AND BUMPS: A RARE CASE OF BLASTIC PLASMACYTOID DENDRITIC CELL NEOPLASM IN AN ADOLESCENT MALE

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Background: Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a malignant disease that most often affects men in their sixth decade of life. It is a hematologic malignancy known for frequently affecting other organs such as the spleen, central nervous system, and skin. It is a rare malignancy in adults and is even less common in children.

Objectives: This case highlights our experience with the treatment of this rare malignancy in a pediatric patient.

Design/Method: A case report of the presentation and management of an adolescent male patient with BPDCN.

Results: A 16-year-old male presented to the Orthopedics department of Children's Hospital of New Orleans for evaluation of a 2-month history of a non-tender lump below his left knee in addition to lymphadenopathy of his left groin and unintentional weight loss. On physical exam, a walnut-sized mass fixed to the overlying dermis was noted distal to the left fibular head. Complete blood count (CBC) at presentation was normal. Magnetic resonance imaging of bilateral tibias/fibulas showed skip lesions concerning for lymphoma and computed tomography revealed diffuse lymphadenopathy. Biopsy revealed an atypical CD4+, CD56+, CD123+ cell population consistent with BPDCN. Patient subsequently developed diffuse skin lesions to the back, chest, abdomen, and face with CBC showing anemia, thrombocytopenia, and elevated white count of 21,000 with 62% blast cells.

Remission with 0% minimal residual disease (MRD) was achieved via acute lymphoblastic leukemia (ALL) 4-drug regimen with the addition of weekly PEG-asparaginase. The patient started on CD123 targeting agent tagraxofusp as bridge treatment to allogeneic hematopoietic stem cell transplant (HSCT) and completed three cycles before relapse with new skin lesions consistent with BPDCN and bone marrow showing 0.1% MRD. He subsequently received re-induction therapy with a relapsed ALL regimen consisting of etoposide, cyclophosphamide, and high-dose methotrexate and achieved a second remission with no blasts on morphology (M1 marrow) and MRD of 0.02%. HSCT was delayed due to donor Covid infection and the patient again relapsed with bone marrow with 41% blasts. He is now undergoing a third induction with a 4-drug ALL regimen and weekly PEG-asparaginase with plan for myeloablative treatment with allogeneic HSCT.

Conclusion: BPDCN is an exceedingly rare form of leukemia and there is no consensus on treatment. This case illustrates how intensive ALL treatment is effective in inducing, but not maintaining, remission in this aggressive disease. Further research is needed to determine optimal treatment in pediatric patients to improve long-term event-free survival.

POSTER # 190 | A DIAGNOSTIC CHALLENGE: A DIFFICULT CASE OF REFRACTORY HLH SECONDARY TO FUNGAL INFECTION

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Background: Hemophagocytic lymphohistiocytosis(HLH) is a rare, life-threatening hyperinflammatory syndrome characterized by fever, cytopenias, hepatosplenomegaly, coagulopathy, and elevated inflammatory markers. Primary HLH results from mutations in cytotoxic T-cell regulatory genes, whereas secondary HLH is usually triggered by infection, rheumatologic disorders, immunodeficiencies, or malignancy.

Objectives: Describe the presentation and management of secondary HLH due to fungal infection.

Design/Method: Single subject case report

Results: A 2-year-old female presented with pancytopenia prompting extensive work up at an outside institution for infection, bone marrow failure, and hematologic malignancy which was negative. Bone marrow aspirations/biopsies showed 100% cellularity with atypical lymphohistiocytic infiltrate consistent with reactive inflammation, but

no hemophagocytosis. Ferritin was not elevated at that time. She was treated for presumed autoimmune cytopenias with intravenous immunoglobulin (IVIG) with poor response, then 3 days of pulse steroids and discharged with 1 week of prednisone. Upon discontinuation of steroids, fever recurred, and she presented to our emergency department with pancytopenia and abdominal pain. Initially, she met 4 of 9 criteria for HLH with fever (> 38.5 ^{0}C), pancytopenia (WBC 2.90K/mm3, hemoglobin 5.7 g/dL, platelet 2K/mm3), splenomegaly, and hypertriglyceridemia (triglycerides 341 mg/dL). Initially ferritin was slightly elevated at 445 ng/mL. Clinically she deteriorated with rapidly rising ferritin (peak of 13,433 ng/mL), markedly elevated soluble IL-2 receptor (sIL-2R, 31,000U/mL), and decreased NK-cell function. She met criteria for HLH and was started on dexamethasone(10 mg/m2/day) and etoposide(150 mg/m2/dose) per HLH-94 protocol. Interestingly, CXCL9 was within normal limits. No known primary HLH gene mutations were identified. After 2 weeks of therapy, no significant improvement was noted, therefore secondary causes of HLH were aggressively explored. No evidence of rheumatologic disorder or malignancy was found, but urine histoplasmosis antigen was positive suggesting a possible etiology for secondary HLH. During this time, a maculopapular rash developed and skin biopsy confirmed Trichosporon spp. infection. Given the diagnosis of HLH secondary to fungal infection and lack of response to therapy, etoposide was transitioned to anakinra. Amphotericin B was started and transitioned to itraconazole for histoplasmosis and Trichosporon infection. After this change in therapy, her clinical status and cytopenias improved and immunosuppression was weaned.

Conclusion: The signs and symptoms of HLH are nonspecific, often leading to delay in diagnosis and increased mortality. This case highlights the importance of keeping a broad differential and high index of suspicion for atypical infectious triggers especially in a patient pretreated with steroids. Refractory disease in absence of genetic causes of primary HLH, requires broad investigation for secondary causes.

POSTER # 201 | RNA DEMETHYLASE AS A NOVEL DRIVER OF OSTEOSARCOMA

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Background: Osteosarcoma is the most common bone tumors in children and adolescents. Despite intensive chemotherapy, patients with advanced disease still have a poor prognosis, illustrating the need for alternative therapies. The 5-year survival rate for the triple-combination therapy regimen has demonstrated an improvement of 50%–70% or more when the tumor is localized. However, survival for patients with metastatic or relapsed osteosarcoma has remained virtually unchanged over the past 30 years, with an overall 5-year survival rate of about 20%. Virtually no new drug has been approved for treating osteosarcoma in the last three decades. Therefore, identification of novel drivers of osteosarcoma and robust approach to target osteosarcoma with novel therapies are urgently needed.

Objectives: We recently showed that the gene encoding m^{6}A demethylase ALKBH5 is amplified in osteosarcoma patients (> 40% of OS patients). Furthermore, we showed that ALKBH5 supports osteosarcoma growth and progression. Using gene expression and functional studies, we found that ALKBH5 mediates its pro-tumorigenic function by regulating histone deubiquitinase USP22. Given the tumor-intrinsic USP22 is reported to block the infiltration of T cells and NK cells and promote the infiltration of myeloid suppressor cells in pancreatic cancer, we propose that ALKBH-USP22 signaling plays a critical role in inhibiting anti-tumor immunity in osteosarcoma.

Design/Method: To address the role of ALKBH5-USP22 signaling in shaping anti-tumor immunity and address whether ALKBH5-USP22 and associated immune markers may have prognostic significance, tissue microarray was performed on tumor samples from osteosarcoma patients presented with early stage and metastatic disease using antibody against ALKBH5, CD4, CD8, CD11b, CD11c, CD47, ALKBH5 and FOXP3. In addition, expression and Me-RIP analyses were performed to determine the expression correlation between ALKBH5, RNA methylation and immune markers in osteosarcoma patients.

Results: Our analysis revealed that higher ALKBH5 expression correlated with lower infiltration of CD4, CD8 and M1 macrophage in osteosarcoma patients. Furthermore, our analysis showed that increased ALKBH5 expression correlated with increased population of myeloid derived suppressor cells in osteosarcoma patients. Experiments are currently underway to validate these findings in larger cohorts of osteosarcoma patients.

Conclusion: Our results indicate that RNA demethylase ALKBH5 may inhibit anti-tumor immunity in osteosarcoma patients.

POSTER # 202 | CAN DASATINIB RESTING BE COMBINED WITH CXCR EXPRESSION TO IMPROVE CAR-T CELLS AGAINST OSTEOSARCOMA?

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Background: Two strategies to enhance chimeric antigen receptor (CAR)-T cell efficacy against pediatric osteosarcoma (OS) include chemokine-receptor (CXCR)-mediated homing and dasatinib resting during manufacture. The effect of combining these strategies is unknown.

Objectives: To characterize endogenous and transgenic CXCR expression and efficacy of CXCR.B7H3.CAR-T cells +/- dasatinib.

Design/Method: We serially evaluated endogenous expression of CXCR2, CXCR3, CXCR4, CXCR6, and CXCR7 by flow cytometry on activated T cells in culture +/- dasatinib (50 nM). Using lentiviral transduction, we produced 4 B7H3.CAR-T cell products: 1) CXCR2-modified, 2) CXCR6-modified, 3) B7H3.CAR, and 4) B7H3.Stop (nonfunctional) +/- dasatinib. We compared CXCR expression,

transduction, expansion, CD4/CD8 expression, and activation/memory phenotype +/- dasatinib. We evaluated IL-2 and IFN-γ production by CAR-T cells cocultured with LM7 OS cells using ELISA. We assessed CAR-T cell homing and cytotoxicity in 3D OS spheroid assays. Finally, we injected $1x10^5$ $143B^{+ffluc}$ OS cells (IV) into NSG mice, treated with $1x10^6$ CAR-T cells (5 mice/group), and assessed survival. Statistical analysis included paired t-tests, two-way ANOVA, and Kaplan-Meier curves. N = 4 donors, $p < 0.05$ significant.

Results: We found no differences in endogenous or transgenic T cell CXCR expression or transduction +/- dasatinib. Dasatinib enhanced expansion in CXCR2.B7H3.CAR (12.6 vs 9.2 fold change; $p < 0.05$) and CXCR6.B7H3.CAR (12.6 vs 9.1 fold change; $p < 0.05$) T cells with similar trends in all groups. CD4/CD8 expression was unchanged. Naïve-like T cells were increased by dasatinib in CXCR2.B7H3.CAR (8.4% vs 2.4%, $p < 0.05$), CXCR6.B7H3.CAR (8.4% vs 2.3%, $p < 0.05$), and B7H3.Stop (7.3% vs 2.4%, $p < 0.05$) cells with similar trends in all groups. T cells +dasatinib produced greater IFN-γ and IL-2 than untreated cells, although not achieving statistical significance. T cells +dasatinib demonstrated similar homing but increased proliferation after OS spheroid engagement as untreated cells. While CXCR2- and CXCR6.B7H3.CAR-T cells +dasatinib exhibited delayed spheroid killing (~10 hours), overall cytotoxicity was not decreased. Preliminary in vivo studies suggest dasatinib may enhance survival in CXCR6.B7H3.CAR ($p < 0.05$) and B7H3.CAR ($p < 0.05$) treated mice with confirmatory studies pending.

Conclusion: Endogenous and transgenic CXCR expression are unchanged by dasatinib resting. CXCR-modified CAR-T cells +dasatinib exhibit increased naïve-like phenotype, enhanced proliferation after OS spheroid engagement, and potentially improved antitumor activity in vivo. These findings support combining dasatinib resting with CXCR-mediated homing strategies. However, CXCR-based strategies that leverage rapidity of killing as their primary advantage may be ineffective, as the killing delay caused by dasatinib may negate early homing.

POSTER # 203 | ARMORED GLYPICAN 3-CAR T CELLS CO-EXPRESSING INTERLEUKIN-15 FOR PATIENTS WITH SOLID TUMORS

David Steffin, Nisha Ghatwai, Chunchao Zhang, Purva Rathi, Amy Courtney, Carlos Ramos, Premal Lulla, Tannaz Armaghanny, Bambi Grilley, Leonid Metelitsa, Helen Heslop, Malcolm Brenner, Pavel Sumazin, Andras Heczey

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Background: Glypican 3 (GPC3) is specifically expressed by solid cancers. We previously optimized a GPC3-CAR with the 41BB costimulatory endodomain and showed that co-expression of interleukin 15 (IL15) with this CAR enhances the antitumor properties of transduced T-cells. We hypothesized that IL15 co-expression (15.GPC3-CAR) would enhance CAR-T cell expansion and boost antitumor activity in patients with GPC3+ solid tumors. To determine if IL15 co-expression indeed modified the activity of GPC3-CAR T cells in patients, we compared two phase I studies, one evaluating GPC3-CAR T cells (GAP: NCT02932956; GLYCAR: NCT02905188, and the other evaluating the same CAR but with co-expressed IL15. (AGAR: NCT04377932; CATCH: NCT05103631).

Objectives: To explore the safety, persistence and antitumor activity of GPC3-CAR or 15.GPC3-CAR T cells in patients with relapsed/refractory solid tumors.

Design/Method: Six patients were infused with $3x10^7$ GPC3-CAR T cells and six patients with $3x10^7$ IL15.GPC3-CAR T cells. Toxicity was monitored using the Common Terminology Criteria of Adverse Events v5. in vivo persistence was quantified using RT-PCR and flow cytometry. Antitumor activity of CAR-T cells was defined between weeks 4 and 6 post-infusion by standard 3D imaging using RECIST v1.1 as well as changes in serum alpha-fetoprotein levels.

Results: IL15.GPC3 CAR T cells had higher peak expansion (mean 6.77 x 10^7 versus 3.71 x 10^3 copy number/mcg DNA; $p = 0.0156$) and comparable effective tumor trafficking (mean 4.76 x 10^4 versus 4.30 x 10^3 copy number/μg DNA; $p = 0.0702$) than GPC3-CAR T cells as measured by RT-PCR in the peripheral blood. Increased expansion in the IL15 GPC3 group was associated with a higher incidence of adverse events (161 versus 84 total events), including cytokine release syndrome (one patient grade 2, two patients grade 4 versus one grade 2 event). The increased expansion was also associated with a higher response rate; in patients treated with GPC3-CAR T cells, two had progressive disease (PD) and four had stable disease (SD). In patients treated with IL15.GPC3-CAR T cells, three had PD but three had partial responses (including resolution of lung metastases) via imaging, with response rates of 0% versus 50%, respectively.

Conclusion: Based on results from phase I studies in patients with liver cancer, IL15 co-expression in GPC3 CART induces superior expansion, associated both with increased but manageable toxicity) and greater antitumor activity.

POSTER # 204 | TUMOR-INFORMED CIRCULATING TUMOR DNA IN FIBROLAMELLAR CARCINOMA IN ADOLESCENTS AND YOUNG ADULTS

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Background: Fibrolamellar Carcinoma (FLC) is a rare form of primary liver cancer (100 cases/year), affecting healthy Adolescents and Young Adults (AYA). The established standard of care is surgery. However, recurrence is 80% even with R0 surgery, suggesting that FLC is a systemic disease not only a surgical disease. Systemic therapies in retrospective studies show immunotherapy and chemotherapy combinations have shown success in management of other cancers. Our retrospective study of 51 patients is the first report of ctDNA in FLC.

Objectives: Analyze ctDNA in FLC.

Design/Method: All patients consented to blood draws on a 1-3 monthly basis and had regular imaging reviewed by the FibroFighters Foundation National Tumor Board. Complete response (CR), Partial response (PR) (>30% decrease), Progressive Disease (PD) (>20% increase), and Stable Disease (SD) (neither PD/PR/CR) were determined according to the Response Evaluation Criteria in Solid Tumors (RECIST)1.1. The imaging closest in time to the blood draw was used for correlation purposes. "Negative" is defined as a value = 0.00 mean ctDNA molecules/ml and "Positive" as > 0.00. "Monthly Slope/Trend" is defined as 30*(difference between consecutive values)/(days). PPV/NPV/sens/spec refer to positive/negative predictive value/sensitivity/specificity.

Results: Fifty-one FLC patients (24 M, 27F, median age 22, range 10-56), 92% stage (III/IV), contributed 214 samples (mean 4.2/patient, range 1-11). Negative values correlated with no evidence of disease (NED) on imaging 65% of the time, positive values with disease 48% [PPV/NPV/sens/spec of 0.65/0.48/0.35/0.76]. NPV and sens increased to almost 100% with a ctDNA threshold of > 1.0 at the expense of a lower PPV and spec. However, consecutive negative ctDNA values correlated with radiologic NED 87% [PPV/NPV/sens/spec = 0.87/0.88/0.78/0.93] without a single PD in this cohort (n = 58). A "downward slope" predicted Objective Response (CR+PR) and Disease Control (CR+PR+SD) at 65% and 96% [PPV/NPV/sens/spec of 0.65/0.48/0.35/0.76 and 0.96/0.27/0.36/0.94, respectively], while an "upward trend" predicted relapse 55% [PPV/NPV/sens/spec = 0.55/0.98/0.94/0.81]

Conclusion: In this first report of 51 AYA FLC patients, and 214 tissue-informed cell free ctDNA data points, positive and negative values performed well for predicting "disease" or "NED" respectively, especially for consecutive values of zero, where no PD were observed. A downward trend performed better than an upward trend to predict objective response or relapse.

POSTER # 205 | HEREDITARY PARAGANGLIOMA/PHEOCHROMOCYTOMA SYNDROME TUMOR DIAGNOSES IN CHILDREN

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Background: Pathogenic variants (PVs) in the *SDHA*, *SDHB*, *SDHC*, and *SDHD* (*SDHx*) genes predispose to paraganglioma/pheochromocytoma (PPGL), renal cell cancer, and gastrointestinal stromal tumors (GIST). Recommendations for beginning *SDHx*-related tumor surveillance range from age 10 to 15 years, and the study institution initiates surveillance at age 10. There is minimal information on the long term follow up of children diagnosed with an *SDHx* related tumor.

Objectives: Define and describe the diagnostic process and outcomes for children with an *SDHx*-related tumor under the age of 18 years.

Design/Method: A prospectively maintained database at an academic medical center identified individuals with *SDHx* PVs with an *SDHx* related tumor at or below 18 years of age. Patient data was abstracted from electronic medical records and genetic test results to identify demographics, kindred, clinical diagnostics, and genomic information. Descriptive and comparative analyses utilized R*Stats and Excel.

Results: Of 310 individuals with *SDHx* PVs, 24 (7.7%) individuals across 17 kindreds were diagnosed with an *SDHx* tumor prior to the age of 18 years. Most individuals were assigned female at birth (n = 17, 70.8%), and are all known to be living, ranging from age 14 to 73 (median 23 years). Their age at diagnosis ranges from 10 to 18 years. Over half of the individuals had a PV in *SDHB* (n = 13, 54.2%), while an additional 37.5% (n = 9) had *SDHD* PVs. Ten individuals had head and neck PGLs, of which 7 had *SDHD* PVs. Seven individuals had abdominal PGLs (5 *SDHB*, 2 *SDHD)* and five were diagnosed with pheochromocytomas. Nineteen individuals (79.2%) had one tumor, while six individuals had multiple tumors (5 *SDHB*, 1 *SDHD)*. Approximately 71% of the cohort had a benign *SDHx*-related tumor (n = 17). Seven individuals from unique kindreds had malignant tumors (one GIST and six PPGL), including individuals with PVs in each of the *SDHx* genes (*SDHA*, *SDHB*, *SDHC*, *SDHD)*. The presentation of metastases ranged from a single affected lymph node to widespread metastatic bony lesions

Conclusion: The long-term follow up of individuals diagnosed with an *SDHx*-related tumor in childhood is highly variable in presentation and length of follow-up. The diagnostic presentation of pediatric PPGL *SDHx* tumors in individuals align with penetrance risk estimates previously reported in the *SDHB* and *SDHD* genes, though malignant *SDHx* tumors across individuals with a PV in each of the *SDHx* genes is unique. Additional research is needed to evaluate the long-term outcomes of individuals with *SDHx* PVs diagnosed with tumors in childhood.

POSTER # 206 | EARLY EXPERIENCE WITH NIVOLUMAB, GEMCITABINE AND LENVATINIB FOR FIBROLAMELLAR CARCINOMA IN AYA

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Background: Fibrolamellar Carcinoma (FLC) is a rare deadly form of liver cancer affecting adolescents and young adults (AYA), presenting at an advanced stage, with up to 80% relapse, and no proven systemic therapies. Effective systemic therapies could convert patients to resectable or prolong progression free survival (PFS) and overall survival. Because of reported successes with nivolumab (NIV) + lenvatanib (LEN) and of Gemcitabine (GEM) + LEN, and the potential synergy of GEM with NIV through elimination of myeloid suppresor cells in the tumor microenvironment, we offered NIV+LEN+GEN (NLG) to relapsed/refractory FLC patients ineligible for clinical trials.

Objectives: To describe our initial experience using NLG in high risk AYA FLC patients.

Design/Method: We reviewed the records of all FLC patients discussed at the FibroFighters National Tumor Board who received NLG.

Results: Twenty-four patients (9F,15 M), median age 20 (7-56), all stage IV, received a total of 285 cycles of NLG, (19 neoadjuvant, 1 adjuvant, 4 both). The median number of relapses, prior systemic therapies, and surgeries were 2(0-6), 3(0-6), and 2(0-7) respectively. The 17 patients with at least one evaluation had a mean follow up of 9 months (3-23) and 18 cyles (6-38) of NGL with the best response by RECIST 1.1 of CR(1), PR(6), SD(10), and PD(0), for an **objective response rate (PR+CR) of 41% and disease control rate (CR+PR+SD) of 100%**, and estimated best volume response median of −20% (−89%,+10%).There have not yet been any progressions. The ***PFS and Overall Survival at 6, 9, and 12 months are: 1.0/1.0, 0.82/0.82, 0.67/0.67.*** Two of 17 with carcinomatosis have no evidence of disease on PET and MRI after 10 cycles. Twenty-two of 24 are continuing NGL. Nine of 16 unresectable patients became surgical candidates. No patients have stopped therapy. Most patients had failed NIV+LEN (n = 8) or GME+LEN (n = 7) prior to starting NGL. Eleven of 16 are currently in their longest PFS since diagnosis. Sixteen patients had serial tumor-informed circulating DNA (Signatera) during therapy: Five became negative (0.0 mean tumor molecules/ml plasma), and overall mean drop was −27% (−93%,+111%). The most common toxicities were hypertension and fatigue in 25% and 20% respectively, grade 1 or 2. There have been no grade 3 or 4 toxicities to date.

Conclusion: Our retrospective experience with NGL for FLC offers another potential systemic option for patients who are not surgical candidates or with multiple relapses. NGL was well tolerated and provided excellent disease control to patients with few options. Prospective trials are needed.

POSTER # 207 | PROGNOSIS OF CHILDREN AND YOUNG ADULTS WITH BONE MARROW METASTATIC RHABDOMYOSARCOMA ON COG STUDIES

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Background: Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children. Metastatic disease occurs in 16% of all RMS cases and has a poor prognosis. There are limited studies that have examined the outcomes specific to patients with RMS metastatic to bone marrow despite an incidence of 6% at diagnosis.

Objectives: Our study aims to document the outcomes and clinical courses in children presenting with RMS metastatic to bone marrow who were treated on Children's Oncology Group (COG) cooperative trials.

Design/Method: We performed a retrospective analysis of the patients diagnosed with RMS metastatic to bone marrow between 1997 and 2013 enrolled on one of four COG RMS clinical trials of D9802, D9803, ARST0431 and ARST08P1. Bilateral bone marrow aspirate/biopsy for histologic assessment of bone marrow involvement was a required pre-study observation for all trials.

Results: We identified 179 cases with RMS metastatic to bone marrow. Patients had a mean age of 13 years, 58% were male, predominantly alveolar histology (76%), extremity was the most common primary site (32%), and 87% had metastatic disease to additional sites. 83% (n = 149) received radiation as a treatment modality. The 3- and 5-year Event-Free survival (EFS) was 9.4% and 8.2% respectively. The 3- and 5-year Overall Survival (OS) was 26.1% and 12.6% respectively. Age ≥ 10 years, alveolar histology, FOXO1 fusion presence, unfavorable primary location, higher Oberlin score, and lack of radiation were identified as poor prognostic characteristics. The 22 (12%) patients with metastatic disease only to bone marrow and no other sites had a 3-year EFS of 9.4% and a 3-year OS of 26.1%.

Conclusion: This study represents the largest analysis of RMS metastatic to bone marrow defining the poor prognostic outcome for these patients. These patients may be eligible therapy deintensification to reduce toxicity and improve quality of life or early pursuit of novel treatments/approaches. Novel therapies and approaches are desperately needed.

POSTER # 208 | PEDIATRIC AND YOUNG ADULT CHORDOMA—NCI NATURAL HISTORY STUDY OF RARE SOLID TUMORS INTERIM ANALYSIS

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Background: Chordomas are rare tumors of the spine, with approximately 20 pediatric cases in the U.S. annually. The natural history and optimal treatment of pediatric, adolescent and young adult (AYA) chordoma, especially poorly differentiated (PD) and dedifferentiated (DD) subtypes, are understudied and incompletely understood. We present an interim analysis of the first 44 pediatric (age <18 years) and AYA (age 18-39 years) chordoma patients enrolled onto a longitudinal natural history protocol (NCT03739827) with the goal of advancing knowledge of the biology, genomics, and clinical course of this rare disease and translating these findings to improved care and treatment.

Objectives: Comprehensive study of the natural history and treatment of pediatric and AYA chordoma.

Design/Method: Patients of any age with pathology confirmed chordoma are eligible for remote or in-person annual evaluation. All participants complete individual medical history, family history, and patient reported outcomes (PRO) forms. Tumors are analyzed using a 500+ gene panel (TruSight500, Illumina) and undergo comprehensive genomic and epigenomic analyses. Participants invited to NIH undergo

clinical evaluation, genetic counseling, blood collection, and imaging studies, as indicated. In a subset of patients, disease-specific PROs, volumetric image analysis, and cognitive assessment are conducted.

Results: Protocol NCT03739827 has enrolled 44 pediatric (n = 24) and AYA (n = 20) patients with chordoma, including 14 international patients. Chordoma subtypes include conventional (n = 36), PD (n = 7), and DD (n = 1). Tumor locations include the clivus (n = 35), mobile spine (n = 5), sacrum/coccyx (n = 3), and extra-axial (n = 1). Forty-three patients had surgical resection of the primary tumor and majority underwent/are undergoing radiation (n = 38). Seven patients with either PD or DD received chemotherapy. Immunotherapy or targeted therapy was administered to seven patients with recurrent disease. Majority of patients are alive with disease (n = 25) or with no evidence of disease (n = 16); a small subset have died (n = 3). Genetic testing found somatic mutations (n = 14), normal findings (n = 9), or have pending results (n = 3), but in some cases testing failed (n = 11) or tissue was unavailable (n = 3).

Conclusion: Large knowledge gaps remain for pediatric and AYA chordoma, especially how to treat less common subtypes. Protocol NCT03739827 has successfully enrolled patients with chordoma who have undergone comprehensive data collection. Further recruitment and data analysis is ongoing and will enable better clinical, immunologic, and genomic/epigenomic characterization of these tumors.

POSTER # 209 | THE LONG-TERM TREATMENT OUTCOMES OF HEPATOBLASTOMA AT A SINGLE INSTITUTION IN TAIWAN

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Background: Hepatoblastoma is the most common primary malignant liver tumor in the childhood. Fewer than 50% of the patients with HB could be resected completely at diagnosis. Most hepatoblastoma was sensitive to chemotherapy and surgical resection was the cornerstone cure for the disease. The overall HB survival rate has risen to 80% in recent decades.

Objectives: Here we report the treatment outcome of hepatoblastoma in MacKay Children's Hospital, Taipei, Taiwan.

Design/Method: From 1990 to 2022, there were 51 patients with hepatoblastoma diagnosed in MacKay Children's Hospital, Taipei, Taiwan. The first-line chemotherapy regimen was cisplatin 90 mg/m^2/day D1 and epirubicin 25 mg/m^2/day D1-3 with at most 4 courses. In view of toxicity of first-line regimen, the other regimens included carboplatin/etoposide, vincristine/cyclophosphamide/5-fluorouracil, vincristine/carboplatin/5-fluorouracil, vincristine/irinotecan, ifosfamide/carboplatin/etoposide.

From 1990 to 2022, there were 51 patients with hepatoblastoma diagnosed in MacKay Children's Hospital, Taipei, Taiwan. The first-line chemotherapy regimen was cisplatin 90 mg/m^2/day D1 and epirubicin 25 mg/m^2/day D1-3 with at most 4 courses. In view of toxicity of first-line regimen, the other regimens included carboplatin/etoposide, vincristine/cyclophosphamide/5-fluorouracil, vincristine/carboplatin/5-fluorouracil, vincristine/irinotecan, ifosfamide/carboplatin/etoposide.

Results: Based on Evans staging system, there were 8 patients with stage I, 3 with stage II, 32 with stage III and 8 with stage IV. According to PRETEXT classification, there were 3 patients with group I, 20 with group II, 19 with group III and 9 with group IV. The median age was 17-month-old. The median level of serum α-fetoprotein was 197,580 ng/ml. There were 10 patients had recurrent disease, but 8 survived after salvage therapy. The reason of death in 7 patients included 3 refractory, 2 relapse and 2 infection. For low feasibility of liver transplant, only 1 relapsed patient received liver transplant while died eventually. The median duration of follow-up for 44 survivors was 150.8 months (range 2.2∼385.4 months). The 5-year event-free and overall survival rates of 51 patients were 70.6% and 87.4%, respectively. High tone hearing impairment was the most common long-term sequalae in 51% of patients during follow-up. There was no cardiotoxicity event.

Conclusion: Patients had low AFP, PRETEXT IV, multifocal disease and refractory to treatment tend to have poor prognosis in the study.

POSTER # 210 | PROGNOSIS OF CHILDREN AND YOUNG ADULTS WITH RHABDOMYOSARCOMA METASTATIC TO BONE ON COG STUDIES

Nathan Schloemer, Wei Xue, Amira Qumseya, Leo Luo, Susan Hiniker, Timothy Lautz, Daniel Rhee, Michael Arnold, Lisa Teot, Rajkumar Venkatramani
Medical College of Wisconsin, Milwaukee, Wisconsin, United States

Background: Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children. Metastatic disease occurs in 16% of all RMS cases and has a poor prognosis. There are limited studies examining the outcomes specific to patients with RMS metastatic to bone despite an incidence of 5% at diagnosis.

Objectives: Our study aims to document the outcomes and clinical courses in children presenting with RMS metastatic to bone who were treated on Children's Oncology Group (COG) cooperative trials.

Design/Method: We performed a retrospective analysis of the patients diagnosed with RMS metastatic to bone between 1997 and 2013 enrolled on one of four COG RMS clinical trials of D9802, D9803, ARST0431 and ARST08P1. Bone positivity determined by bone scan and/or PET scan was a required pre-study observation for all trials.

Results: We identified 154 cases with RMS metastatic to bone. Patients had a mean age of 15.4 years, 58% were male, predominantly alveolar histology (74%), extremity was the most common primary site (31%), and 90% had metastatic disease to additional sites. 86% (n = 133) received radiation as a treatment modality. The 3- and 5-year Event-Free survival (EFS) was 15.4% and 14.5% respectively. The 3- and 5-year Overall Survival (OS) was 30.4% and 18.0% respectively. Alveolar histology, FOXO1 fusion presence, unfavorable primary

location, ≥ 3 metastatic sites, higher Oberlin score, and lack of radiation were identified as poor prognostic characteristics. The 15 (10%) patients with metastatic disease only to bone and no other sites had a 3-year EFS of 42.4% and a 3-year OS of 49.4%.

Conclusion: This study represents the largest analysis of RMS metastatic to bone defining the poor outcomes for these patients. These patients may be eligible therapy deintensification to reduce toxicity and improve quality of life or early pursuit of novel treatments/approaches. Novel therapies and approaches are desperately needed.

POSTER # 211 | KETAMINE USE AS AN ADJUNCT THERAPY FOR COMPLEX PAIN IN CHILDREN WITH HIGH-RISK NEUROBLASTOMA

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Background: Anti-GD2 immunotherapy has significantly improved outcomes for children with high-risk neuroblastoma. Dinutuximab promotes a complement-mediated reaction against disialoganglioside GD2, which is expressed in peripheral nerves and over-expressed in neuroblastoma tumors. Due to this mechanism of action, dinutuximab is frequently associated with>grade 3 neuropathic pain. Typically, opioids have been used for pain control. Because targeting GD2 also stimulates the NMDA receptor, ketamine has been used for pain management in children receiving the anti-GD2 antibody naxitimab. This retrospective study explores opioid use with a ketamine adjunct for pain management during dinutuximab immunotherapy.

Objectives: The objective of this study was to describe the utility of ketamine use for complex pain uncontrolled by opioids and its impact on total opioid usage for patients on dinutuximab. The primary endpoint was total IV morphine milligram equivalents (IVMME) required per cycle with and without ketamine.

Design/Method: Retrospective chart review of 40 high-risk neuroblastoma patients receiving dinutuximab immunotherapy at Nationwide Children's Hospital from 2010-2022 was conducted. Demographic data, pain scores, medication administration records, dosage information, and total daily IVMME with and without a ketamine adjunct were collected. Two-way ANOVA was used to compare IVMME used for pain management and explore the effect of ketamine on opioid sparing in subsequent cycles.

Results: A total of 189 hospitalizations for dinutuximab from 40 pediatric neuroblastoma patients were included. Patients were mostly male (65%) and age at diagnosis ranged from 1.2 to 11.4 years. Ketamine was used along with opioids during 66 infusions, whereas 123 infusions utilized only opioids. During cycle 1, the median daily IVMME was 14.2 mg per day in admissions where ketamine was used and 9.0 mg in admissions where ketamine was not used, however this was not statistically significant (adjusted p = 0.33). A similar pattern of admissions with ketamine have greater daily IVMME was observed during subsequent cycles (except for cycle 6+), but was not statistically significant (adj. p>0.05). The average daily IVMME was greater, but not significant, in admissions without ketamine (adj. p = 0.09). In both ketamine and no ketamine admissions, subsequent cycles used less daily IVMME compared to cycle 1.

Conclusion: Preliminary findings suggest ketamine may be a safe and effective adjunct for children with high-risk neuroblastoma with complex pain during anti-GD2 immunotherapy. Ketamine may also be opioid sparing in subsequent dinutuximab cycles. Additional prospective studies are needed to quantify the effect of reducing opioid side effects by including ketamine in pain management plans.

POSTER # 212 | REDUCTION IN BONE METASTASES AND CURIE SCORE IN PATIENTS TREATED WITH NAXITAMAB IN TRIAL 201

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Background: Most patients with high-risk neuroblastoma (HR-NB) present with bone (56%–65%) and/or bone marrow (BM; 70%–89%) metastases. Despite advances in treatment, ~15% of these patients have refractory disease and ~50% will relapse. Naxitamab is a humanized GD2-binding monoclonal antibody approved in the US in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), for the treatment of pediatric patients (1-year and older) and adult patients with refractory/relapsed (R/R) HR-NB in the bone or BM who have demonstrated a partial response, minor response, or stable disease to prior therapy. Curie scores (CS) are an important tool for assessing response to treatment.

Objectives: To evaluate rates of overall and complete response (ORR/CR) and CS reduction in bone compartment in patients with R/R HR-NB treated with naxitamab+GM-CSF.

Design/Method: Ongoing Trial 201 (phase II, NCT03363373) is evaluating naxitamab+GM-CSF in patients with R/R HR-NB with residual disease in bone/BM. Soft tissue and actively progressing disease were addressed prior to enrollment. Naxitamab was infused intravenously (3 mg/kg/dose) over 30-60 min on Days 1/3/5 with GM-CSF administered subcutaneously on Days −4 to 5. Cycles were repeated monthly. Efficacy was evaluated by independent radiology and BM pathology review per International Neuroblastoma Response Criteria.

Results: This planned interim analysis (data-cut-off: 31-Dec-2021) included 52 (efficacy) and 74 (safety) patients. The primary efficacy endpoint achieved ORR 50% (CR 38%). Evaluation by disease in bone compartment (n = 50) showed 58% response rate [95%CI: 43%–72%] with 40% CR [95%CI: 26%–55%]. ORR in patients with baseline CS ≤2 (n = 22) was 50% [95%CI: 28%–72%] with CR 45% [95%CI: 24%–68%] and CS ≥3 (n = 30) was 50% [95%CI: 31%- 69%] with CR 33% [95%CI: 17%–53%]. Among patients with bone disease (n = 50), baseline

median(m) CS was 3.5 (range 1-21). At end of treatment (n = 47) mean and mCS reduction were −2.7 and −1.0, and mCS percent reduction was −60%. Safety profiles were not associated with baseline CS. Overall, the most common adverse events were, as expected with GD2-binding monoclonal antibodies, pain, hypotension, urticaria, and bronchospasm.

Conclusion: Evaluation of patients with R/R HR-NB in bone treated with naxitamab+GM-CSF showed a similar ORR regardless of baseline CS (≤2 or ≥3). In patients with evaluable bone disease, naxitamab provided clinically meaningful response rates in the bone compartment and reduction in CS with an acceptable safety profile. Naxitamab+GM-CSF is an attractive therapeutic option for patients with R/R HR-NB in bone.

This study was funded by Y-mAbs Therapeutics, Inc.

POSTER # 213 | CLINICAL VALIDATION OF NOVEL URINARY MARKERS FOR NEUROBLASTOMA DIAGNOSIS

Hizuru Amano, Hiroo Uchida, Kazuharu Harada, Atsushi Narita, Shun Kumano, Mayumi Abe, Minoru Sakairi, Chiyoe Shirota, Takahisa Tainaka, Wataru Sumida, Kazuki Yokota, Satoshi Makita, Tsuyoshi Osawa, Masataka Taguri, Yoshiyuki Takahashi, Akinari Hinoki
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Background: Neuroblastomas are the most common extracranial solid tumor type in children. Because they are catecholamine-secreting tumors, the catecholamine metabolites: urinary homovanillic acid (HVA) and vanillylmandelic acid (VMA) concentrations are measured using high-performance liquid chromatography (HPLC) for neuroblastoma diagnosis. However, at least 10% of patients with neuroblastomas may be missed by screening using HVA and VMA. Therefore, more accurate diagnostic markers are needed. Mass spectrometry (MS) advancements have facilitated the detection of markers that are more accurate and reliable than conventional markers. Previously, we detected more than 2,000 metabolites using liquid chromatography-mass spectrometry (LC-MS) by comprehensively analyzing metabolites in urine samples from patients with and without neuroblastomas. We identified three potential urinary markers—3-methoxytyramine sulfate (3-MTS), vanillactic acid (VLA), and 3-methoxytyrosine (3-MTR)—using the Wilcoxon rank-sum test and random forest algorithm.

Objectives: This study aimed to evaluate the diagnostic utility of the three urinary marker candidates: 3-MTS, VLA, and 3-MTR.

Design/Method: This study was conducted at Nagoya University Graduate School of Medicine in Nagoya, Aichi, Japan.

A total of 41 pediatric participants with neuroblastomas and 155 pediatric participants with no known cancer (controls) were included. The concentrations of the three potential urinary markers—3-MTS, VLA, and 3-MTR—and those of the two conventional urinary markers—HVA and VMA—were measured using LC-MS. Age-specific cutoff values were set on the basis of the logistic regression analysis results, and sensitivities and specificities were calculated.

This study was supported by a grant from Hitachi, Ltd.

Results: The sensitivities and specificities for each marker were as follows: HVA, 90.2% and 93.5%; VMA, 90.2% and 96.8%; 3-MTS, 95.1% and 91.0%; VLA, 87.8% and 86.5%; and 3-MTR, 90.2% and 84.5%.

Conclusion: The results of this study indicate that 3-MTS, VLA, and 3-MTR may be useful urinary markers for diagnosing neuroblastomas.

POSTER # 214 | REAL-WORLD DATA FROM ADVERSE EVENTS ASSOCIATED WITH NAXITAMAB TREATMENT IN THE UNITED STATES (US)

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Background: Naxitamab is a humanized GD2-binding monoclonal antibody marketed under accelerated approval in the United States (US) in combination with granulocyte-macrophage colony-stimulating factor (GM-CSF), for the treatment of pediatric patients 1 year of age and older and adult patients with relapsed or refractory high-risk neuroblastoma in the bone or bone marrow who have demonstrated a partial response, minor response, or stable disease to prior therapy.

Objectives: To analyze naxitamab spontaneous adverse events (AE) reports (SAERs) received in the US with the events reported in clinical Trials 201 and 12-230 as presented in the current naxitamab US prescribing information (USPI).

Design/Method: The Y-mAbs global safety database was reviewed for reported spontaneous AE preferred terms (PT) associated with naxitamab from the US over the 2-year period after FDA approval (25-Nov-2020). AE PT were coded using Medical Dictionary for Regulatory Activities (MedDRA) v25.1. The spontaneous AEs were juxtaposed with the expected side-effects listed in the naxitamab USPI from Trials 201 and 12-230.

Results: At data lock point (24-Nov-2022), an estimated 185 patients had been treated with naxitamab in post-marketing in the US and 101 SAERs had been received, covering 387 AEs. From the SAERs, the patient age ranged from 2 to 40 years old (age reported in 55%); 45% were male, 35% were female, and 20% did not report patient gender. Within these SAERs, the most frequent events were pain, infusion-related reaction, hypertension, cough, vomiting, tachycardia, anxiety, headache, peripheral neuropathy, nausea, anaphylactic reaction, and positive anti-drug antibody (ADA) test; accounting for 290 (75%) AEs. There were no SAERs of transverse myelitis, cardiac arrest, or reversible posterior leukoencephalopathy syndrome. In Trials 201 and 12-230, the most commonly reported adverse reactions (≥25% in either study) were infusion-related reaction, pain, tachycardia, vomiting, cough, nausea, diarrhea, decreased appetite, hypertension, fatigue, erythema multiforme, peripheral neuropathy, urticaria, pyrexia, headache, injection site reaction, edema, anxiety, and irritability. In Trial 201, anaphylactic reactions occurred in 12% of patients. Positive ADA was reported in Trials 201 and 12-230, in 8% and 23% of patients, respectively.

Conclusion: At time of approval, the safety of naxitamab per the USPI was evaluated across 97 patients from two open-label, single arm studies (Trials 201 and 12-230). Two years after approval, with more patients receiving naxitamab in the real-world clinical setting, SAERs indicate the safety profile for naxitamab remains consistent with adverse reactions reported in the clinical trials.

Acknowledgement: This study was funded by Y-mAbs Therapeutics, Inc.

POSTER # 215 | APPROACH TO NAXITAMAB INFUSIONS AT ATRIUM HEALTH LEVINE CHILDREN'S HOSPITAL: PLAN AND BE SUCCESSFUL

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Background: Neuroblastoma is the most common extracranial pediatric solid tumor, accounting for approximately 6% of all childhood cancers in the United States and 15% of all pediatric cancer deaths. Relapsed refractory neuroblastoma remains very challenging to treat and requires an aggressive multi-modal approach including immunotherapy, which has evolved over the past few years. Naxitamab is the only FDA-approved humanized anti-disialoganglioside 2 targeted immunotherapy for relapsed or refractory high-risk neuroblastoma within the bone or bone marrow. Prior to FDA approval, Naxitamab was administered at only two sites within the United States. Infusion reaction rates of any grade occurred between 94-100% of patients receiving Naxitamab. Grade III or IV infusion related reactions, independent of pain, have been previously reported in 32-68% of patients. In addition, hypotension was reported in 89-100% of patients. Implementation of safety measures and feasibility for administration of Naxitamab is critical given reported adverse events.

Objectives: To operationalize the administration of Naxitamab through the creation of a multidisciplinary team which includes planning, preparation, and education to ensure safety and feasibility.

Design/Method: Careful planning prior to the first infusion was critical for this high acuity therapy. A multidisciplinary outpatient team of key stakeholders was established including the solid tumor provider team, pharmacist, nursing leaders, educators and navigators, administrative operations team, supportive medicine, respiratory therapy and pediatric intensive care. A Naxitamab administrative order set and roadmap, institutional pain management plan and accompanying acute supportive care plan was created. Collection and documentation of adverse events was performed to monitor safety. Dosing and timing were collected to measure feasibility.

Results: A high acuity care delivery team of providers and nurses were identified and trained through patient simulation scenarios and mock codes. To date, our high acuity team has successfully administered 110 Naxitamab infusions in 10 different patients utilizing our supportive care guidelines that can be modified for each patient's needs. Adverse event data was captured and we found there were no episodes of Grade III or IV hypotension and no patients required hospital admission to manage adverse events. Our administration technique was found to be feasible as all patients have received the full intended doses of Naxitamab without decreasing, holding, or discontinuing the medication.

Conclusion: Strategic preparation was crucial to administer a well-known, highly reactive immunotherapy drug safely without detrimental outcomes. This work has spearheaded the implementation process that is required to bring new and upcoming high acuity therapies to our institution.

POSTER # 216 | PRIMARY CUTANEOUS EXTRARENAL RHABDOID TUMOR SUCCESSFULLY TREATED WITH MODIFIED UH-1 REGIMEN

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Background: Malignant rhabdoid tumor (MRT) describes a heterogenous group of neoplasms comprising of distinct "rhabdoid" cytological features. While most frequently presenting in the kidneys and central nervous system, MRTs are reported arising from nearly every soft tissue. Extrarenal, extracranial rhabdoid tumors (EERT) are an extremely rare pediatric malignancy, with peak incidence occurring in infancy and less than 4 years of age. EERTs are characterized by aggressive behavior, metastatic spread, and low survival rates.[1]

MRTs are linked to biallelic pathogenic variants in SMARCB1/A4 genes, encoding subunits for the SWI/SNF chromatin-remodeling complex, and characterized by loss of nuclear INI-1 immunostaining. [2,3]

The use of chemotherapy regimens that use alternating courses of ifosfamide-carboplatin-etoposide (ICE) and vincristine-doxorubicin-cyclophosphamide (VDC) have been used with variable activity.[4] Survival for patients with EERTs remains poor, with 1-year survival approximately 31%.[5] Only a handful of primary cutaneous EERTs have been published.[6] Here we present a patient with primary cutaneous EERT and mosaic rhabdoid predisposition syndrome (RPS) treated with systemic chemotherapy, full excision, and radiotherapy who remains alive a year and a half from completion of therapy.

Objectives: To describe a primary cutaneous EERT in patient with mosaic RPS successfully treated on a modified UH-1 regimen of the AREN0321 study.

Design/Method: Case was reviewed and described through electronic medical records.

Results: A 3-year-old African American male presented with hemorrhage of a dermal lesion of left flank following diaper irritation. Family reported lesion had been present since birth. Initially "pimple-size," fluctuated regularly and was described to "pulsate" on occasions with a prior episode of hemorrhage at 1 year of age. Lesion was evaluated by pediatrician with diagnosis of skin-tag. Due to new episode of hemorrhage, shave excisional biopsy was obtained.

Pathology revealed a lobulated neoplasm with irregular nuclei, prominent eosinophilic nucleolus and eosinophilic cytoplasmic inclusions. Immunostaining of nuclei were INI-1 negative. Whole exome sequencing revealed an alteration in SMARCB1. Germline testing additionally with alteration in SMARCB1 in 0.78% of cells consistent with mosaic RPS.

A modified UH-1 regimen of AREN0321 (J Clin Oncol. 2020 May 10;38(14):1558-1568) was used. The patient additionally underwent full excisional biopsy and radiotherapy to the primary site. He remains with no evidence of disease 15-months following completion of therapy in addition to no disease with screening for RPS.

Conclusion: While reported, primary cutaneous lesions may be the initial presentation of EERTs, and often associated with germline SMARCB1 alterations, should be considered in differential of cutaneous lesions for early recognition and initiation of treatment.

POSTER # 217 | RARE CASE OF ROSAI-DORFMAN DISEASE LINKED TO A MIXED MALIGNANT GERM CELL TUMOR WITH PNET COMPONENTS

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Background: Rosai-Dorfman Disease (RDD) is a rare non-Langerhans cell histiocytosis. Although a few case reports have described non-Hodgkin lymphoma and Hodgkin lymphoma associated with RDD, it has not been reported with malignant ovarian tumors.

Objectives: To describe a rare case of a patient with a mixed malignant ovarian tumor associated with extra-nodal RDD.

Design/Method: Case report

Results: A 5-year-old previously healthy female presented to the Emergency Department with two weeks of abdominal pain and fatigue. CT abdomen/pelvis revealed a large 14 cm pelvic mass with hemorrhage. Labs showed profound anemia (5.8 g/dL), thrombocytopenia (36 K/UL), and elevated AFP (482 NG/ML). After resection of her right ovarian tumor, she continued to have thrombocytopenia that was refractory to blood products. Additionally, she developed neutropenia. Pathology of the ovarian tumor was best classified as in part conventional malignant mixed germ cell tumor (GCT) but with an additional morphology that was most indicative of a primitive (embryonic) neuroepithelial tumor. Given her persistent cytopenias, she had a bone marrow biopsy that showed extensive histiocytic infiltration and emperipolesis. Marrow histiocytes were positive for CD68/PGM1, focally positive for S100, and negative for CD1a, which was consistent with extra-nodal RDD. Whole body PET/MRI, CT chest, MRI brain showed no evidence of disease or lymphadenopathy. The patient was started on treatment with cisplatin, bleomycin, etoposide (per AGCT1531) to target the GCT component, alternating with cyclophosphamide and vincristine (per ACNS1422) to target the PNET component. She also started a prolonged steroid course for her RDD. After 5 cycles of chemotherapy, her most recent scans show no evidence of disease and her repeat bone marrow studies showed no evidence of histiocytic infiltration. Her counts have normalized, and she was weaned off steroids.

Conclusion: Although the etiology of RDD is unknown, RDD is likely a part of a paraneoplastic syndrome in this case. RDD has not been found simultaneously with solid tumors. In addition, the combination of PNET and GCT has been scarcely reported in the literature. There have been reports of PNET/Ewings-like sarcoma and testicular GCT in males, but not of a central PNET as described in our patient. An additional challenging aspect of this patient's care was her refractory thrombocytopenia from RDD's infiltration of the bone marrow, which is an unusual location. This case highlights the diagnostic dilemmas and intricacy of the management of both RDD with concurrent malignancy along with a rare ovarian tumor with both GCT and central PNET components.

POSTER # 218 | FETAL INTRAPERICARDIAL IMMATURE TERATOMA WITH HYDROPS FETALIS EXCISED VIA EXIT PROCEDURE

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Background: Fetal intrapericardial teratoma is a rare tumor that involves all three germ cell layers, ranging from mature to grade three immature. Immature teratomas are rare, accounting for only 1% of all teratomas. The prevalence of intrapericardial teratoma is 0.17-28/10,000, and the risk of mortality is high when diagnosed in fetal life, if there is a mass effect, or if it is associated with fetal hydrops.

Objectives: To present a patient prenatally diagnosed with fetal intrapericardial teratoma and to describe optimal management and treatment strategies.

Design/Method: We highlight a case of fetal intrapericardial immature teratoma with fetal hydrops that was removed via the Ex-Utero Intrapartum Treatment (EXIT) procedure.

Results: Pediatric Cardiology first assessed the patient at 26 weeks gestation. A prenatal echocardiogram revealed a sizable intrapericardial mass that was multicystic and attached to the base of the heart, with an associated large pericardial effusion. Mass effect was noted, with compression of the right atrium, left atrium, and right ventricle, along with displacement of the aorta and pulmonary artery. Repeat prenatal echocardiogram at 28 weeks gestation revealed enlargement of the intrapericardial mass and increase in the size of the pericardial effusion, along with interval development of ascites and pleural effusion with continued mass effect. Multiple specialists were involved, including Maternal Fetal Medicine, Pediatric Cardiothoracic Surgery, Pediatric Cardiology, and Neonatology, with extensive discussion and planning surrounding the patient's delivery, newborn resuscitation, and surgical intervention. The patient was born at 29 weeks gestation via a coordinated urgent EXIT procedure. Immediately before delivery, in-utero fetal pericardiocentesis was performed for drainage of the pericardial effusion. The patient

subsequently was delivered via cesarean section and promptly intubated, followed by immediate excision of the intrapericardial mass by Pediatric Cardiothoracic Surgery via midline sternotomy. There was no compromise of cardiac function following removal of the intrapericardial mass. The mass measured 3.1 x 2.1 centimeters, and pathology returned consistent with an immature teratoma. Serial alpha-fetoprotein levels have been expectedly down trending since the initial level of 1300 approximately two months following removal of the mass.

Conclusion: Successful management of this patient's intrapericardial teratoma at delivery was made possible through a multi-disciplinary approach from 7 different specialties. Eleven physicians were involved in providing care for the mother and the patient in the operating room on the day of delivery. Our patient spent 16 weeks in the neonatal intensive care unit before being discharged home, with no evidence of recurrence on repeat imaging.

POSTER # 219 | A RARE CASE OF A PRIMARY GERM CELL TUMOR IN THE RIGHT CORPUS CAVERNOSUM IN A PEDIATRIC PATIENT

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Background: Germ cell tumors (GCT) are neoplasms derived from primordial germ cells (PGC) that can contain both immature and mature elements differentiating into several tissue types. PGC originate from the yolk sac endoderm and migrate from the hindgut to the gonads. Primary malignant GCT commonly arise in the gonads, but may occur elsewhere. There are less than 5 known cases of yolk sac tumors that originate in the penile shaft. Here is a case of a pediatric yolk sac tumor originating from the corpus cavernosum.

Objectives: To address the prognosis and treatment of malignant GCT of the penile shaft.

Design/Method: Case Report

Results: A 36-month-old Hispanic boy with past medical history of mastocytoma presented to the Emergency Department with a painful left inguinal mass. Scrotal US revealed an enlarged 3 x 2 cm left inguinal node with normal-sized testicles. He subsequently developed sustained priapism and two weeks later physical exam showed a new ill-defined mass at the base of the penis.

Ultrasound revealed 3.8 x 3.4 x 2.5 cm mass in the perineum at the base of the penis and high flow priapism. MRI revealed a 4.7 x 4.4 x 3 cm mass arising from the right penile corpus cavernosum breaching the tunica albuginea with invasion of Buck's fascia and pelvic floor musculature into the rectal fossa fat, regional lymph node metastasis and lung metastasis. Lymph node excisional was consistent with a yolk sac tumor. Alpha fetal protein (AFP) was 10,700.

He was enrolled into AGCT1531 for Stage IV Extragonadal Malignant Germ Cell Tumors and randomized to the Carboplatin arm of Standard Risk 1 (SR1) with four cycles of Carboplatin-Bleomycin-Etoposide. Priapism resolved by day 6 of treatment.

Off therapy evaluation revealed normal AFP, resolution of pulmonary nodules, and a residual 1.5 x 1 x 0.9 cm penile mass. Surgery was considered mutilating and not attempted. He developed progressive disease 10 months later. He then received 4 cycles of Cisplatin-Ifosfamide-Paclitaxel as per AO31102. Off therapy evaluation showed normal AFP with no residual mass

Conclusion: Extragonadal GCT of the penile shaft are rare but need to be considered in penile shaft malignancies. Children <11 years old with COG Stage IV penile GCT are currently classified SR1 in the MAGIC classification for pediatric extra-cranial GCT and treated as standard risk tumors. However, the true prognosis and treatment of penile GCT is unknown because of its infrequency and inability to achieve gross total resection without mutilating surgery.

POSTER # 220 | INFLAMMATORY MYOFIBROBLASTIC TUMOR WITH METASTASIS TO THE BRAIN AND EXCELLENT RESPONSE TO LORLATINIB

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Background: Inflammatory Myofibroblastic Tumors (IMTs) are rare tumors composed of inflammatory cells and mesenchymal spindle cells accounting for 150-200 new cases per year in the US with most cases involving children and young adults. Curative therapy is complete surgical resection. Systemic therapy options such as cytotoxic chemotherapy or anti-inflammatory agents are limited for patients with unresectable, recurrent, or metastatic disease. IMT rarely present with metastatic disease and central nervous system (CNS) metastasis is also rare. Kinase fusions are found in 85% of IMTs, the majority of which involve the ALK oncogene followed by ROS1 and PDGFRb. While crizotinib, a first-generation ALK/MET/ROS1 inhibitor, is now FDA approved for unresectable IMTs, the penetration to the CNS is poor. Lorlatinib, a next-generation potent and specific *ALK/ROS1* small molecule inhibitor with robust blood-brain barrier penetration, is FDA approved for adults with non-small cell lung cancer harboring ALK or ROS1 fusions and is in clinical testing in children with *ALK*-driven neuroblastoma.

Objectives: We report the case of 6-year-old boy with metastatic Inflammatory Myofibroblastic Tumor with CNS metastasis who had excellent response to lorlatinib.

Design/Method: This is a case report. An extensive literature review was performed to review known tumor pathology, treatment, and prognosis.

Results: This pediatric patient presented after a CT head performed identified a lesion in the left frontal temporal during evaluation of minor head trauma minor. Additional imaging found a large chest mass involving the right upper and right lower lung lobes. Biopsy revealed (IMT) which was negative for the presence of an ALK fusion by FISH and immunohistochemistry. Initially he was treated with cytotoxic chemotherapy with weekly vinorelbine and methotrexate. Molecular

testing identified a TFG-ROS-1 fusion. We recommended transitioning to lorlatinib monotherapy at the pediatric recommended phase 2 dose of 115 mg/m^2 daily. Interval imaging showed reduction in both the chest and brain mass at each time point and complete resolution of the brain mass after nine months on Lorlatinib. The chest mass has slowly decreased in size with substantial decrease in metabolic activity on PET scan since diagnosis. Primary adverse events have included grade 2 weight gain, grade 2 hyperlipidemia, and grade 1 mood lability, all attributable to lorlatinib. This patient continues to receive lorlatinib therapy with excellent quality of life.

Conclusion: Lorlatinib is an ALK/ROS1 inhibitor biochemically developed to penetrate the central nervous system and can have significant anti-tumor activity in pediatric primary/multifocal or metastatic tumors of the brain that harbor target lesions.

POSTER # 221 | EXTRARENAL NEPHROBLASTOMA AND EMBRYONAL CARCINOMA ARISING FROM AN IMMATURE TESTICULAR TERATOMA

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Background: Extrarenal presentations of nephroblastoma are uncommon and inherently rare in adults. Testicular tumors are common solid tumors in young males, including teratomas, embryonal carcinoma, yolk sac tumor, seminoma, choriocarcinoma, and mixed germ cell tumors. Teratomas contain multiple embryonal tissues that have the potential to differentiate into other malignancies. We present a case of an adolescent/young adult (AYA) male with an extrarenal nephroblastoma and embryonal carcinoma arising from an immature testicular teratoma. This presentation is extremely rare, with few cases reported in the literature and limited consensus for treatment.

Objectives: Describe the rare presentation, genetic alterations, and treatment strategies for extrarenal nephroblastoma with embryonal carcinoma.

Design/Method: Case report

Results: We present the case of a 20-year-old male who presented with a large right testicular mass. He had normal AFP and B-HCG tumor markers. CT imaging of the abdomen and pelvis revealed enlarged right retroperitoneal, aortocaval, and peri- and para-caval lymph nodes. Radical orchiectomy was performed with pathology notable for small round blue cells in the teratoma, consistent with nephroblastoma. Subsequent lymph node dissection was positive for disease with the presence of small round blue cells. An additional pathologic review of the retroperitoneal lymph node dissection revealed embryonal carcinoma. The patient was started on a hybrid chemotherapy regimen, alternating treatments for both nephroblastoma and embryonal carcinoma. This regimen included alternating weeks of DD4A (vincristine, dactinomycin, and doxorubicin) along with BEP (bleomycin, etoposide, and cisplatin). Molecular testing of the primary tumor and retroperitoneal lymph nodes identified similar genetic changes, such as a RAD52 c.865+1G>A mutation. However, notable differences were identified between nephroblastoma and embryonal carcinoma components. The nephroblastoma sample from the primary tumor contained unique mutations in MAP2K2 K108N, FGF6, FGF23, and KRAS that were not found in the lymph node samples. The tumor mutation burden was higher lymph node sample compared to the primary testicular mass.

Conclusion: Molecular evidence revealed similar genetic changes in the primary tumor and metastatic lymph nodes, indicating a shared clonal origin of the nephroblastoma and embryonal carcinoma. The unique genetic changes may give some insight into the genetic pathogenesis of this rare tumor combination. The optimal treatment for testicular tumors is surgical resection with wide tumor margins and adjuvant chemotherapy. Due to the rarity of testicular extrarenal nephroblastoma with metastatic embryonal carcinoma, there are no consensus guidelines on the most effective chemotherapy regimen. These tumor types require two different approaches, and we demonstrate an effective hybrid treatment regimen.

POSTER # 222 | IMMUNOTHERAPY RESPONSE IN A PATIENT WITH XERODERMA PIGMENTOSA AND UNRESECTABLE METASTATIC MELANOMA

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Background: Xeroderma Pigmentosum (XP) is an autosomal recessive disorder resulting from abnormal DNA repair caused by ultraviolet radiation which predisposes patients to skin cancer. Melanoma turns off T-cell activation preventing the effective T-cell antitumor responses. Anti-cytotoxic T-lymphocyte antigen 4 (anti-CTLA-4) and anti-programmed death-1 (PD-1) can reverse this immune suppression and release T-cell activation. New immunotherapies, such as anti-CTLA-4 antibody ipilimumab and anti-PD-1 antibody nivolumab, are now being used for the treatment of advanced melanoma.

Objectives: Describe the clinical course of a 17-year-old female with XP, diagnosed with unresectable metastatic melanoma to the brain and treated with palliative care, who achieved complete response after immunotherapy.

Design/Method: Chart Review

Results: 17-year-old female from Costa Rica diagnosed with XP at 4 years of age, developed a mass in the right cheek, which was surgically removed, but grew back shortly thereafter. The mass kept growing, becoming unresectable, which lead to the determination her condition was terminal. Received palliative care with morphine and steroids. Six months later, family sought a second opinion. Upon arrival, patient had an exophytic 10 cm mass localized to the right preauricular region. CT head showed a large right temporal exophytic mass extending to the neck with another mass within the anterolateral right upper hemithorax overlying the right pectoralis major muscle. Brain MRI showed a mass in the right parietal region, related to metastatic disease. Biopsy showed a highly pleomorphic and ulcerated malignant spindle cell proliferation, consistent with sarcomatoid melanoma,

as well as Breslow thickness level 4, with positive margins (pT4b). Immunotherapy showed positivity for S100, p53 and Sox 10. PDL-1 expressed with a combined positive score of 60. Given the unresectable nature, underwent only debridement by plastic surgery, and started immunotherapy with Nivolumab and Ipilimumab for 3 months. Continued Nivolumab every 2 weeks for 14 cycles. Follow-up MRI one year later showed only postsurgical changes within the right temporal region with minimal increased uptake. MRI brain with stable appearance of the right parietal lesion. Patient is attending school and having regular follow-ups.

Conclusion: Xeroderma Pigmentosum (XP) is a rare genetic disorder with a poor prognosis due to high photosensitivity. Modern therapies demonstrate high rates of complete response even in unresectable and metastatic melanomas. Unfortunately, these FDA approved therapies are not widely accessible in less developed countries. This case highlights the astonishing response of new therapies on a patient, without the need for surgery. Our case also exemplifies the disparities of available treatments in different regions.

POSTER # 223 | JUVENILE GRANULOSA CELL TUMOR OF THE OVARY AND MULTIPLE ENCHONDROMATOSIS

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Background: Granulosa cell tumor (GCT) accounts for 5% of all ovarian malignancies and more than 70% of sex cord stromal tumors. GCTs are distinguished from epithelial ovarian cancer based on the nature of presentation and clinical behavior as GCTs occur in younger patients with features of hyperestrogenism. Patients may present with vaginal bleeding caused by endometrial hyperplasia or uterine cancer as a result of prolonged exposure to tumor-derived estrogen. Ollier's disease (OD) is a nonhereditary skeletal disorder causing multiple enchondromas. The most common ovarian malignant tumor associated with OD is GCT.

Objectives: To present a case of OD and juvenile GCT of the ovary.

Design/Method: Case Report

Results: A 13-year-old female with known history of enchondromatosis presented with history of iron deficiency anemia secondary to menorrhagia. Menarche occurred at the age of 12 years with cessation of vaginal bleeding after 2 months. Bleeding disorder evaluation was normal, and she was prescribed iron supplementation. Four months later, she presented with 6-week history of worsening abdominal distension and pain. An abdominal ultrasound showed a large amount of ascites. LDH and uric acid were normal. A CT showed a 19.5x 11.5x 12.4 cm right mass in direct connection to the right adnexal vasculature. Multiple osseous lesions throughout the axial and appendicular skeleton were also visualized. AFP and BHCG were normal. CA-125 was 389 U/mL. She underwent exploratory laparotomy. Six liters of serous ascites was drained. No evidence of peritoneal seeding or enlarged lymph nodes was observed. The left ovary and fallopian tube appeared normal. Right salpingo-oophorectomy was performed. Pathological examination confirmed Juvenile GCT. Ascites fluid was negative for malignant cells. FIGO stage was IC1. She received treatment with 3 cycles of BEP regimen due to the reported 25% recurrence with observation. She is currently doing well without recurrent tumor. Her menses normalized as well as the CA-125 level. She is on active surveillance for ovarian tumor and OD. None of the enchondromatous lesions appear to have malignant transformation.

Conclusion: Female patients with multiple enchondromatosis should be evaluated closely for possible ovarian tumors especially in the first or second decade of life. Young females with menorrhagia at menarche should be evaluated for hormonally active stromal cell ovarian tumors, such as juvenile GCT.

POSTER # 224 | Aggressive Systemic Infantile Myofibromatosis with Diffuse Involvement and Unique Mutation

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Background: Recent case reports in infantile myofibromatosis (IM) have shown effectiveness of tyrosine kinase inhibitors (TKI) and drugs that target platelet derived growth factor B (PDGFRB). Mutations of this gene leading to increased activation or gain of function have frequently been found in IM. IM is a rare disease in which benign, soft tissue tumors develop as solitary or multiple nodules.

Objectives: We describe a case of systemic IM with emphasis on the unique Imatinib resistant mutation PDGFRB D850V as well as the clinical challenges associated with an aggressive disease course with intestinal and pulmonary involvement requiring complex treatment.

Design/Method: Information obtained via retrospective chart review.

Results: Patient is an infant male born at 33 weeks and required immediate intubation. Flesh colored subcutaneous nodules were noted diffusely throughout the body. Bilious emesis and abdominal distention developed with concern for bowel obstruction. Abdominal surgery was performed with resection of portions of the bowel containing multiple nodules and placement of an ostomy. Biopsies of the intestinal and subcutaneous skin lesions were consistent with myofibromatosis with a somatic PDGFRB D850V mutation. He was started on weekly intravenous Methotrexate and Vinblastine per POG 9650. Imatinib was added to his treatment regimen. Bowel re-anastomosis was attempted but failed due to continued presence of numerous intestinal lesions. Treatment approach was reassessed, and it was found that the somatic PDGFRB D850V mutation was Imatinib resistant according to *in vitro* studies which also showed sensitivity to Dasatinib. Imatinib was discontinued. He began treatment with Dasatinib while continuing Methotrexate and Vinblastine. Respiratory support improved. After two months of Dasatinib treatment, bowel re-anastomosis was successful with no tumors palpated during surgery. Two weeks post-operatively, he required intubation. Echocardiogram revealed pulmonary hypertension. The reasons for crisis were multifactorial, however due to reports that Dasatinib may cause

pulmonary hypertension it was decided to discontinue Dasatinib and continue intravenous chemotherapy. His respiratory status improved, and pulmonary hypertension resolved. He was discharged home on outpatient chemotherapy and continued to grow and develop well. Chemotherapy was stopped after 1 year of treatment.

Conclusion: In conclusion, we describe a complex case of systemic IM with Imatinib resistant mutation PDGFRB D850V. This case shows the potential effectiveness of Dasatinib treatment in a patient with IM. This case also describes a rare potential side effect of Dasatinib in pulmonary hypertension, which resolved with its discontinuation. It also shows continued improvement of disease with intravenous Methotrexate and Vinblastine after Dasatinib was stopped.

POSTER # 225 | BENIGN TERATOMA MANIFESTING AS PARANEOPLASTIC JUVENILE INFLAMMATORY ARTHITIS IN A FIVE-YEAR-OLD-GIRL

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Background: Juvenile idiopathic arthritis (JIA) is an autoinflammatory disorder that is the most common type of arthritis in children under the age of 16. Benign ovarian teratomas have been associated with a variety of paraneoplastic syndromes including limbic encephalitis, opsoclonus-myoclonus syndrome, dermatomyositis, among others. There are few reports of seronegative polyarthritis associated with ovarian teratomas and sacrococcygeal teratomas in adults but none in the pediatric population.

Objectives: To report a 5-year-old female with symptoms of JIA and teratoma.

Design/Method: Case Report

Results: A 4-year-old Caucasian female presented with 6 month-history of upper and lower extremity joint pain and swelling associated with myalgias. Family history of psoriatic arthritis, rheumatoid arthritis, and lupus was reported. On examination, she had hypermobility in multiple joints associated with swelling particularly in bilateral knees, right wrist, and left elbow. Complete blood counts, BUN, creatinine, LDH, uric acid and liver enzymes were normal. Initial ESR was elevated at 15. ANA and HLA B27 markers were negative. The patient was diagnosed with oligoarticular JIA and started on scheduled non-steroidal anti-inflammatory drugs (NSAID) therapy. Due to persistent pain for 8 months despite NSAIDs, MRI of knees was ordered to look for radiological inflammation or erosive joint disease prior to starting disease modifying antirheumatic drugs. As part of routine MRI screening, the mother reported that child may have swallowed a metallic object, prompting chest X-ray, which showed a lobular mass with unusual calcifications in the epigastric area. Follow-up CT and MRI of abdomen showed an epigastric well-circumcised mass (8.8 x 8.3 x 5.5 cm) with soft tissue, fat and calcified components including numerous tooth-like structures most consistent with teratoma. The MRI of bilateral knees was negative for active inflammation. Tumor markers AFP and BHCG were negative. Tumor resection and histopathology confirmed benign mature teratoma without immature or malignant components. After tumor removal, her joint pain resolved.

Conclusion: The spontaneous resolution of an inflammatory seronegative arthritis after the excision of the tumoral mass suggests a cause-and-effect relationship between paraneoplastic manifestations and a benign teratoma. It is unclear if the early manifestations of JIA resulted from a genetic predisposition to autoimmune disorders as suggested by the family history. This case highlights the importance of thorough clinical evaluation in patients with seronegative arthritis and consideration for teratoma.

POSTER # 226 | TREATMENT OF INTRACRANIAL AND INTRASPINAL IM WITH IMATINIB

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Background: Infantile Myofibromatosis (IM) is a rare soft tissue tumor of infancy and childhood. The disease can develop as a solitary myofibroma or multicentric nodules. Familial cases have been linked to mutations in various genes including platelet-derived growth factor receptor beta (PDGFRB), which encodes a receptor tyrosine kinase. Previous treatments for these tumors have sometimes included observation, surgical resection, chemotherapy or more recently reported targeted agents are being trialed. Recent reports show these mutant PDGFR receptors are sensitive to tyrosine kinase inhibitors such as Imatinib.

Objectives: The purpose of this abstract is to report on the tolerability and efficacy of tyrosine kinase inhibitors to treat inoperable intraspinal and Central Nervous System IM.

Design/Method: Two unrelated infants diagnosed with inoperable familial multicentric IM, confirmed germline PDGFRD mutation, were prescribed 100 mg of Imatinib daily. Patients completed a diagnostic Whole Body Magnetic Resonance Imaging (WBMRI) and then WBMRI to access response to targeted agent. No patient identifiers were obtained.

Results: Results indicated significant decrease or complete resolution of multifocal lesions with no significant side effects of imatinib.

A 5-month-old male presented with over 10 lesions throughout his body and one very concerning lesion palpable left lumbar paraspinal with invasion through neural foramen and spinal cord compression. Infant had decreased strength in lower leg and presumed pain when mass compressed. Exam at 3 months on Imatinib with decrease mass and improvement in strength. After ten months on Imatinib, his WBMRI showed decrease lesion in the left paraspinal/perivertebral in the mid lumbar spine which currently measured 1.2 cm by 0.6 cm (***previously 2.5 cm x 2.7 cm***). Further improvement of other soft tissue lesions with some completely resolved; no new lesion with some completely resolved; no new lesions were identified.

Conclusion: The cases provided a brief review of the clinical manifestations and genetics of IM and summarized our recommendations

through WBMRI surveillance and the promising use of tyrosine kinase inhibitors. Further discussion is necessary to investigate length of treatment with Imatinib and when to discontinue medication.

POSTER # 227 | 11-MONTH-OLD WITH ABDOMINAL DISTENTION—CONSTIPATION OR EXTRA-GONADAL YOLK SAC TUMOR?

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Background: Liver tumors account for 1-2% of pediatric malignancies. The two most common hepatic malignancies are hepatoblastoma and hepatocellular carcinoma[1]. Germ cell tumors comprise 3% of pediatric malignancies, most arise in the gonads and sacrococcygeal area. YSTs are not common in children. They account for 30% and 15% of testicular and ovarian neoplasms respectively. YST are even more infrequent when extra-gonadal. Alpha-fetoprotein (AFP) is elevated with YST but is not specific. The therapy for YST is surgery and chemotherapy[2]. A hepatic extra-gonadal YST is a rare diagnosis.
(1. Sergi,Children, 2022. 2. Kattuoa, Yolk Sac Tumors, 2022)
Objectives: Describe a case of an 11-month-old male diagnosed with stage IV hepatic extra-gonadal YST.
Design/Method: Case report of an 11-month-old male with abdominal distention who was diagnosed with stage IV extra-gonadal YST.
Results: 11-month-old male with no significant history presented to the ED for abdominal distention, previously diagnosed with constipation. Physical exam was significant for distention with globose appearance and umibilical protusion. Abdomen was tense and dull to percusion over the right upper quadrant down to lower abdomen. Labs significant for anemia 9.9 gm/dL, elevated LDH 727 IU/L. CMP and urinalysis unremarkable. The AFP was 30,573 ng/mL. Abdominal ultrasound showed a large mass in the right upper quadrant with ascites. CT abdomen showed a large heterogeneous intraperitoneal mass, either originating from the liver or hemidiaphragm/lateral abdominal wall. CT chest showed a right upper lobe metastatic nodule as well as mediastinal and left axillary lymph nodal disease. Surgery biopsied the liver. Histopathologic findings consistent with the endodermal sinus pattern of YST with multiple fibrovascular cores rimmed by cuboidal to columnar cells, Schiller-Duval bodies and focal areas of necrosis seen. Immunohistochemical evaluation was positive for AFP and diffuse nuclear expression of sall4. HCG, CD30, and Oct3/4 were negative. Patient was diagnosed with stage IV extra-gonadal YST. Patient was started on AGCT 1531 standard risk, PEB. He has completed four cycles and AFP has nearly normalized, 13.8 ng/mL. Pulmonary metastatic disease resolved. He underwent right lateral partial hepatectomy, right diaphragmatic pleural stripping, left diaphragmatic peritoneal stripping. Pathology demonstrated liver parenchyma with extensively necrotic tumor (hepatic yolk sack tumor, s/p treatment) with fibrosis, hyalinization, histiocytic infiltrate, hemosiderin deposition, and microcalcifications, and no viable tumor present.
Conclusion: Extragonadal YST of the liver are exceedingly rare, with only four reported cases per literature review. This case recognizes the importance of early identification to avoid the high morbidity and mortality associated with these tumors.

POSTER # 228 | CARCINOMA EX PLEOMORPHIC ADENOMA OF THE EAR CANAL IN AN 8-YEAR-OLD GIRL: A CASE REPORT

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Background: Pleomorphic adenoma (PA) is the most common salivary tumor constituting up to two-thirds of all salivary gland neoplasms. PA is a benign entity with the potential for malignant transformation into carcinoma ex-pleomorphic adenoma (CXPA) over time if left untreated. PA of the external auditory canal (EAC) is extremely rare entity. We report a case of recurrent PA of the EAC that was later determined to be CXPA in a pediatric patient.
Objectives: The purpose of this report is to describe a case of pleomorphic adenoma of the external auditory canal in an 8-year-old patient that progressed to CXPA. To our knowledge this is the first case reported in this age group.
Design/Method: A retrospective chart review of the patient was conducted to investigate the patient's initial presentation, disease course, imaging, and treatment.
Results: A 5-year-old girl presented with an ear canal lesion which was excised and reported as PA. At 7 years old there was recurrence of the EAC mass, which was excised with pathology demonstrating a poorly circumscribed, multinodular mass with a dominance of myxochondroid morphology consistent with recurrent PA. At 8 years of age, she presented with persistent ear pain and imaging showed recurrence of disease now involving temporal bone. PET-CT showed no distant metastasis. She underwent left temporal bone resection, left facial nerve decompression, revision total parotidectomy; pathology was consistent with myoepithelial carcinoma ex pleomorphic adenoma. She received radiation in a total dose of 70.2 Gy by proton beam and close follow up imaging. Surveillance imaging 2 years later demonstrated local progression and diffuse pulmonary metastases with extensive pleural metastatic disease as well as iliac bone metastasis. Tumor molecular testing revealed no treatable target. At this time the option of cisplatin-based chemotherapy was discussed with understanding that it would not be a curative therapy and efficacy was unknown. Systemic therapy was deferred, and she underwent occipital craniectomy for debulking of infra- and supra-tentorial tumor after which she received 30 Gy of radiation to post-operative cavity. One year later, at 11years of age, she presented with worsening headaches, a posterior scalp mass, and metastatic lesions in her brain. Disease progression continued with worsening metastatic lung disease and death.
Conclusion: We report the first case of pediatric carcinoma ex pleomorphic adenoma of the EAC. This case highlights the importance

monitoring and follow up in patients with pleomorphic adenoma given the risk for recurrence and malignant transformation.

POSTER # 229 | PALLIATIVE CHEMOTHERAPY FOR METASTATIC COLORECTAL CARCINOMA IN AN AYA PATIENT WITH BLOOM SYNDROME

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Background: Bloom syndrome is a rare autosomal recessive condition with mutations in the *BLM* gene, resulting in increased sister chromatid exchanges and chromosomal instability, leading to an increased susceptibility to various cancers at a young age and an increased sensitivity to chemotherapy toxicity. Published data on management of colorectal cancer in Bloom syndrome is sparse.

Objectives: To provide an example of a well-tolerated palliative chemotherapy regimen with modified FOLFOX followed by FOLFIRI of widely metastatic, unresectable colonic adenocarcinoma in an adolescent with Bloom Syndrome with a BLM VUS previously undescribed in relation to Bloom Syndrome.

Design/Method: A 16-year-old female with longstanding failure-to-thrive and bronchiectasis presented with a one-month history of clinical and radiographic left lower lobe pneumonia, refractory to outpatient antibiotic treatment. Computed tomography of the chest showed widespread lymphadenopathy and left lower lobe collapse with infiltrate, representing either pneumonia or mass. CT of the abdomen and pelvis demonstrated ascites with peritoneal thickening and nodules, necrotic retroperitoneal lymph nodes, and thickening and hyperemia of the sigmoid colon. Biopsy of a peritoneal nodule was performed.

Histopathological examination revealed the presence of adenocarcinoma with mucinous and signet ring morphology. Immunohistochemistry was positive for CDX2 and CK20 while negative for CK7, p63, TTF-1, GATA-3 and calretinin, consistent with primary colorectal cancer. Evaluation for markers of Lynch syndrome was negative. Transbronchial lymph node biopsy confirmed disease above the diaphragm.

Genetic testing of the patient showed one pathogenic variant and one VUS in *BLM*, most consistent with Bloom syndrome given the clinical context.

Results: Palliative chemotherapy was started with modified FOLFOX, using a 50% dose reduction in the setting of Bloom Syndrome. The 5-FU bolus was omitted in cycle 1 and included in subsequent cycles. Although an initial favorable response to treatment was noted, imaging at 9 months revealed increased metastatic disease.

The patient was transitioned to FOLFIRI plus Bevacizumab, at 50% dose reduction. Bevacizumab was discontinued after one cycle due to stomal bleeding. Progressive metastatic disease was identified after cycle 4 of FOLFIRI. One cycle of trifluridine/tipiracil at 50% dosing was completed without response. The patient experienced mild side effects from chemotherapy, including Grade 1 thrombocytopenia and Grade 2 peripheral motor neuropathy. The patient died from respiratory failure due to progressive metastatic disease and superimposed pneumonia.

Conclusion: Palliative chemotherapy for metastatic adenocarcinoma of the colon in a patient with Bloom Syndrome can be safely administered at 50-percent dose reduction, achieving effective palliation with few toxic effects.

POSTER # 230 | FIBROLAMELLAR CARCINOMA WITH A NOVEL SQSTM1/PRKACA FUSION IN A 21-YEAR-OLD

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Background: Fibrolamellar carcinoma (FLC) is a distinct, rare primary liver carcinoma, previously thought to be a variant of hepatocellular carcinoma (HCC). FLC affects young patients, those without liver disease and has characteristic imaging, morphological features, immunohistochemistry (IHC) pattern and a pathognomonic fusion.

The DNAJB1/PRKACA fusion protein is present in all FLC cases and thought to be the driver of the disease. We report a 21-year-old man with classic radiologic, clinical, and pathologic features of FLC found to have a PRKACA rearrangement resulting in a SQSTM1/PRKACA fusion. Where DNAJB1 is a heat shock protein (HSP) thought to promote PRKACA oncogenic activity, SQSTM1 drives osteoclast activity but also interacts with HSPs in a complex, poorly understood way.

Case Presentation

A 21-year-old male presented with a large left liver mass. CBC and LFTs were normal, HIV (-), HBV (-), HCV (-), CEA (-), CA19-9 (-), and AFP <5. Triple phase imaging showed arterial enhancement without washout and no lung metastasis, both common features of FLC, but not in HCC. Biopsy showed classic FLC, with eosinophilic, large polygonal cells with abundant pink granular cytoplasm, nuclear inclusions and prominent nucleoli forming nests and aggregates with lamellar type sclerotic stroma. IHC were positive with Hepar-1, Arginase, CAM5.2, CKAE1/3, CK7, and CK8/18, CD68 and negative with CK20, CK19, AFP and Glypican-3, a typical pattern for FLC. Second opinion concurred with the diagnosis and confirmed by FISH the fusion as did two different next generation sequencing assays. The patient had an excellent response to neoadjuvant gemcitabine-lenvatinib-oxaliplatin chemotherapy (80% necrosis at surgery), typical for FLC, but not for HCC.

Objectives: Understanding the presence of a new fusion protein in Fibrolamellar Carcinoma.

Design/Method: Conducted literature review on PubMed with keywords “Fibrolamellar Carcinoma” and “SQSTM1” for English publications in the past ten years.

Results: No publications describing SQSTM1/PRKACA in FLC or in any other cancer was found.

Conclusion: PRKACA in both classic FLC and our patient with all the typical clinical, radiologic, and pathologic features of FLC, suggests

that PRKACA, but not DNAJB1, is necessary and possibly sufficient for FLC. However, further understanding of SQSTM1 and its interaction with the PRKACA pathway and HSPs is needed to understand if it is a 'bystander' or plays a role in the pathophysiology of FLC.

POSTER # 231 | RELAPSED METASTATIC NASOPHARYNGEAL CARCINOMA: CASE REPORT DESCRIBING A NOVEL TREATMENT APPROACH

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Background: Outcomes remain poor for patients who are diagnosed with relapsed metastatic nasopharyngeal carcinoma (NPC). There is no standard therapeutic strategy in this group. We describe a unique approach to therapy for a pediatric patient with this unfortunate and challenging diagnosis.

Objectives: Describe a novel approach to treatment for relapsed metastatic nasopharyngeal carcinoma.

Design/Method: Patient is an 18-year-old female first diagnosed with stage IV NPC with lung metastases in 2019. She completed standard up-front therapy per Children's Oncology Group protocol ARAR0331 stratum B. She underwent surgical resection for local control, as well as proton radiation with a boost to primary tumor for a total dose of 61.2 GyE. At the completion of her initial therapy, she had no evidence of disease by PET. She then relapsed two months after the completion with new pulmonary nodules. Gemcitabine/oxaliplatin was given for salvage therapy and she completed ten cycles. She had a stable chest CT at the end of this therapy, however there was persistent disease. Her tumor stained positive for PDL-1 and the decision was made to proceed with Nivolumab. She had an exceptional response to Nivolumab therapy and after 3 months had achieved a second complete remission. After one year of Nivolumab monotherapy, her PET scan revealed a new subcarinal lymph node with an SUV of 11. Given that she continued to have adequate disease control otherwise and a good quality of life, she was determined to have oligoprogressive disease and the decision was made to continue Nivolumab, and use personalized ultrafractionated stereotactic adaptive radiotherapy (PULSAR)for the new metastatic lesion. PULSAR is a form of SBRT or SAbR (stereotactic ablative radiotherapy) that delivers high dose of radiation per fraction but separates each fraction, or in this case, "pulse" of radiation, every 3-4 weeks to be given concurrently with Nivolumab with the goal of improved synergy.

Results: The patient was treated with PULSAR at 8 Gy/pulse x 5 pulses (40 Gy total) every 3-4 weeks with concurrent Nivolumab and had complete response noted in the oligoprogressive mediastinal lesion. She completed another year of consolidative Nivolumab monotherapy post radiation and remains in complete remission.

Conclusion: PULSAR radiation in combination with Nivolumab therapy may allow for prolonged remission in relapsed metastatic NPC. In this case, PULSAR was used in the oligoprogressive setting, but this combination could be considered upfront as a salvage treatment option as well with less toxicity from traditional cytotoxic chemotherapy and excellent quality of life.

POSTER # 232 | NOVEL USE OF TOCILIZUMAB FOR TREATMENT OF INFLAMMATION CAUSED BY RADIATION-INDUCED OSTEOSARCOMA

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Background: Radiation therapy is a common treatment modality in many solid tumor regimens. Patients who have been treated with radiation suffer an increased risk of secondary tumors, including osteosarcoma. Even with this increased risk, radiation-induced osteosarcoma continues to be a rare diagnosis. Treatment of these sarcomas has little standardization and outcomes are often poor, with the most prominent factor for survival being the ability to completely resect the tumor. We present a patient with a highly inflammatory radiation-induced osteosarcoma of the pelvis, treated with IL-6 inhibition, resulting in symptomatic relief of the inflammation.

Objectives: Our patient was 22 years old when he was first diagnosed with metastatic Ewing Sarcoma. His primary site was in the right pelvis with pulmonary and bony metastases. He was treated with chemotherapy and radiation, responding with complete remission. Three years after treatment, during his surveillance imaging, he was noted to have a new mass in the right pelvis, which was diagnosed as a radiation-induced osteosarcoma. He was treated with adjuvant chemotherapy, resection, and right pelvic reconstruction. Four months after resection, while undergoing consolidation chemotherapy, the patient began experiencing recurrent fever without a source. He subsequently developed discoloration of his right hip and persistent bony pain. During evaluation, he was found to have a relapsed mass in his right pelvis with inflammatory changes. He had elevated inflammatory markers (ESR 69 mm/hr, CRP 10.94mgdL, and IL-6 level of 42.7pg/mL), however, repeated blood cultures were negative, and procalcitonin was normal. Thus, the inflammation was determined to be secondary to tumor activity.

Design/Method: Case Report.

Results: Studies show that while elevation in IL-6 is present in osteosarcoma, it is unclear if IL-6 is a driving factor in tumor propagation. In our patient, inflammation was causing discomfort and recurrent fever. We opted to treat with tocilizumab to inhibit inflammation. The CRP dropped dramatically after the first infusion and remained suppressed for several weeks. There was an acute decrease in fever frequency and interval improvement in the overlying skin changes.

Conclusion: Inflammation may be observed in aggressive sarcomas, possibly due to the associated tissue destruction. While IL-6 inhibition is not likely to augment the response to chemotherapy, it may afford symptomatic relief. For this patient, the use of tocilizumab resulted in decreased emergency room visits, decreased fevers, decreased

inflammatory markers, and improvement in skin erythema and tissue edema.

POSTER # 233 | SIMULTANEOUS DE NOVO INTRAOSSEOUS TUMORS IN SIBLINGS

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Background: Osteosarcoma is the most common primary pediatric bone malignancy, which accounts for 2.4% of all pediatric cancers and 20% of all primary bone cancers, and its etiology is thought to be related to multiple factors such as genetics, epidemiology, or environment. The risk of osteosarcoma increases with genetic syndromes including Li-Fraumeni syndrome, hereditary retinoblastoma, and Bloom syndrome.

Objectives: We will describe the cases of two siblings with similar presentations of concurrent bone tumors.

Design/Method: Case Series

Results: Case 1: 16-year-old female presented with 2-3 months of constant right leg pain waking her from sleep. She had a noticeable 5-6 inch palpable mass on anterior right thigh. Initial x-ray showed infiltrative lytic lesion on distal diaphysis of the right femur. MRI confirmed a mass measuring 7.2 x 6.3 x 8.2 cm with a 6 mm skip lesion in the distal diaphysis. Biopsy and subsequent pathologic evaluation confirmed high grade primary osteosarcoma. Chest CT showed several pulmonary nodules measuring <2.5 mm. She was started on standard of care therapy incorporating high dose methotrexate, cisplatin, and doxorubicin. She suffered a spontaneous displaced fracture during treatment and required prompt amputation at the level of the proximal femur. In light of her brother's findings, she was enrolled in a local research study Project Inherited Cancer Risk (PICR) (eIRB 65292), which tests for germline pathogenic variants in cancer predisposition genes.

Case 2: 14-year-old male presented with a 4-month history of left leg pain, following a blunt injury to the leg. He presented approximately one month after his sister was diagnosed with osteosarcoma. His initial x-ray showed an aggressive appearing lesion in the proximal left tibial diaphysis concerning for malignancy. MRI confirmed a 1.9 x 3.2 x 6.6 cm anteromedial tibial mass with medullary component and associated T2 enhancement. Subsequent PET corroborated the MRI findings with an intensely hypermetabolic lesion in the left tibia and did not show any evidence of metastatic disease. Despite the radiographic evidence and suggestion of localized osteosarcoma, the pathology is atypical and reported as osteocartilaginous proliferation with sections of fibrous tissue and no aggregation of atypical cells. Next generation sequencing has been sent to ascertain whether or not there is a genetic fusion driver to this tumor to allow for better characterization. Chest CT showed no pulmonary nodules.

Conclusion:

Siblings with de novo presentations of intraosseous tumors simultaneously is an unfortunate and exceedingly rare circumstance. Consideration is given to underlying cancer predisposition syndromes.

POSTER # 234 | DEEP SEQUENCING OF A CASE OF MULTIFOCAL LCH THAT DEVELOPED AFTER EWING SARCOMA

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Background: We describe a case of Ewing sarcoma localized to the right femur that received chemotherapy per AEWS0031 and had surgical resection with internal fixation completed in March 2021. Approximately 6 months later, the patient was having pain of his right leg and had a new limp. MRI of the femur revealed a new hip lesion and subsequent MRI of pelvis showed an additional lesion in the right pelvis. A bone scan was obtained that revealed another lesion in the right parietal calvarium all concerning for metastatic recurrence of the Ewing sarcoma. Biopsy of the largest pelvic lesion revealed Langerhans Cell Histiocytosis (LCH) which was CD1a, Langerin, and S100 positive on immunohistochemistry. Pathology reviewed previous Ewing sarcoma biopsy sample with this new LCH lesions, and the two samples were distinctly different histologically. A PET/CT scan was performed that showed a fourth lesion in the C4 vertebrae along with these three previously described lesions. Due to these entities previously not described in the same patient, DNA and RNA sequencing was performed in both tumors to search for any common linkage.

Objectives: To obtain DNA and RNA sequencing for the Ewing sarcoma tumor and the LCH lesion to investigate for any variants to link both previously unrelated diseases.

Design/Method: DNA and RNA samples were obtained from FFPE preserved tumor samples and sequenced using NexGen techniques at the CLIA-certified lab, Caris Life Sciences. DNA variants and mRNA gene expression patterns were compared to pediatric genomic databases and clinical literature to assess for linkage of these two histologically distinct tumors.

Results: Sequencing of the Ewing sarcoma tumor revealed the characteristic EWSR1-FLI1 fusion (Exon 7 of EWSR1 (NM_005243.3) joined in-frame to exon 6 of FLI1 (NM_002017.5)). Also two STAG2 mutations were identified (p.T561fs and p.A568fs) in the Ewing sarcoma tumor sample. The LCH tumor sample harbored a BRAF p.V600E mutation and PD-L1 staining was 2+ in 25% of the tumor. Both tumors harbored a possible pathogenic mutation in MYD88, p.A6fs. A different MYD88 variant, p.L265P, is associated with development of diffuse large B-cell lymphoma (DLBCL).

Conclusion: Multi-focal LCH developing after Ewing sarcoma treatment has previously not been reported in the literature. Deep sequencing of both tumors showed biologically distinct mechanisms that led to development of Ewing sarcoma and subsequent multi-focal bone LCH. More studies need to be performed to understand if these distinct tumors are arising from common lineage progenitor cells or represent an unfortunate secondary primary tumor.

POSTER # 235 | FAVORABLE TREATMENT RESPONSE TO HIGH-GRADE SARCOMA IN NEUROFIBROMATOSIS 1

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Background: Neurofibromatosis 1 (NF1) is associated with the loss of fully functional neurofibromin GTPase activating protein causing the over activation of the RAS oncogene leading to tumor formation. Most common tumors seen in NF1 patients are optic pathway gliomas and malignant peripheral nerve sheath tumors. We present a patient with a high-grade sarcoma which is an uncommon tumor type diagnosed in NF1 patients.

Objectives: This case report demonstrates a patient with NF1 and high-grade pleomorphic sarcoma of bone who had a favorable response to the Children's Oncology Group ARST1321 regimen A as the original treatment and the St. Jude Children's Research Hospital OS99 protocol after reevaluating the diagnosis.

Design/Method: Single subject case report

Results: A sixteen-year old African American female with NF1 presented with pain and swelling of the left knee, which began one month prior to presentation. A magnetic resonance imaging (MRI) scan revealed a left distal femoral mass centered at metaphysis but extending into medial femoral condyle, with increased extra cortical extension particularly posteriorly. Subsequent imaging was negative for metastatic disease. Biopsy demonstrated a few bone fragments though no osteoid production. The tumor was classified as a high-grade pleomorphic sarcoma and was treated as per ARST1321 regimen A consisting of ifosfamide, doxorubicin, and pazopanib, with upfront local radiation therapy. After 12 weeks of neoadjuvant therapy, complete surgical resection of the tumor from the left distal femur showed an excellent pathological response to therapy with 95% tumor necrosis. Subsequently, tumor genetics showed a TP53 and ERBB2 mutation, both frequently found in osteosarcoma. Immunohistochemistry was found to be SATB2 positive, suggestive of high-grade variant of osteosarcoma. This information prompted a change of therapy to an osteosarcoma regimen, the OS99 protocol using ifosfamide, doxorubicin and carboplatin. This regimen was chosen over MAP (methotrexate, doxorubicin, cisplatin) as the patient had already received backbone therapy with ifosfamide and doxorubicin, with the above excellent response.

Conclusion: This case highlights a rare tumor in a patient with NF1 and shows the necessity of performing genetic testing on sarcomas. This patient's genetic results prompted further evaluation that ultimately changed her therapy. This patient had an optimal response with a treatment regimen not typically used as first line therapy for osteosarcoma. The addition of radiation therapy and pazopanib may have added to the efficacy of upfront doxorubicin and ifosfamide. The patient is now completing therapy per the OS99 protocol and doing well, with no evidence of disease.

POSTER # 236 | VERY LATE RECURRENCE OF TRANSLOCATION POSITIVE RHABDOMYOSARCOMA IN A PATIENT WITH LYNCH SYNDROME

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Background: Rhabdomyosarcoma (RMS) is the most common soft tissue sarcoma in children, representing 5% of all childhood cancer. Although initial responses are typically observed, 30% of children with localized disease will relapse, with 95% of all failures occurring within three years from the start of treatment[1]. Comprehensive genomic testing to identify molecular drivers and underlying cancer predisposition syndromes is performed commonly in children with newly diagnosed and recurrent RMS. Lynch syndrome is a cancer predisposition syndrome caused by mutations in DNA mismatch repair genes (*MLH1*, *MSH2*, *MSH6*, *PMS2*) or *EPCAM* that leads to increased risk of colorectal, endometrial, ovarian, gastric, urinary tract, brain and skin cancers. Association with RMS is extremely rare[2].

Objectives: We describe a case of a very late recurrence of RMS in a child with Lynch Syndrome.

Design/Method: Case report.

Results: A 14-month-old female presented with a lesion on the tip of her nose in 2007. An MRI showed a ~ 1.8 x 1.2 x 1.2 cm enhancing mass lesion involving the tip of the nose and right alar sidewall. Initial biopsy confirmed alveolar rhabdomyosarcoma with the presence of a *PAX3-FOXO1* fusion. At the conclusion of her diagnostic evaluation, the patient was determined to have Stage 1, Group III disease. Family history is notable for breast cancer in the patient's maternal grandmother and gastric cancer in a paternal second cousin. She initiated chemotherapy with vincristine, actinomycin and cyclophosphamide with 4500 cGY radiation therapy per COG ARST0531 and was disease-free at therapy completion. Fifteen years later, she presented with one month history of a left submandibular mass outside of the original radiation field, which was completely excised and unfortunately showed recurrent RMS. Whole exome sequencing of the tumor demonstrated the previously reported *PAX3-FOXO1* fusion, as well as a missense variant of uncertain significance involving *KMT2C*. Secondary findings include a truncating germline mutation of *MSH2*, associated with Lynch syndrome. There was no evidence of mismatch repair deficiency or microsatellite instability in the tumor. She is currently receiving treatment with chemotherapy and radiation therapy and will undergo surveillance for future malignancies.

Conclusion: This case suggests RMS may be a rare manifestation of Lynch syndrome and highlights the importance of long-term follow-up and germline assessment for predisposition syndromes in children with RMS.

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References:
Pappo, J Clin Oncol., 1999.
Tomida, Human Genome Variation, 2022.

POSTER # 237 | FAVORABLE RESPONSE TO IPILIMUMAB AND NIVOLUMAB IN RECURRENT SCLEROSING EPITHELIOID FIBROSARCOMA

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Background: Sclerosing Epithelioid Fibrosarcoma (SEF) is a highly aggressive and rare subtype of soft tissue sarcoma. Due to its locally infiltrative nature, radical resection is often difficult to achieve. Furthermore, there is a high incidence of both local and metastatic recurrence. Treatment options for SEF are limited, as the tumor demonstrates limited response to standard chemotherapy and radiotherapy.

Objectives: The purpose of this report is to highlight the potential utility of immune checkpoint inhibitors as a treatment option for patients with recurrent SEF.

Design/Method: This is a case report.

Results: The patient is a 13-year-old male who initially presented with progressive swelling in his right jaw. Biopsy from the affected area revealed the presence of Sclerosing Epithelioid Fibrosarcoma (SEF) with EWSR1 rearrangement and MCU-4 positivity. The patient underwent radical mandibulectomy with complete R0 tumor resection. Imaging studies after the resection did not reveal any evidence of distant metastasis. However, 9 months post-surgery, the patient was found to have multiple lung metastasis confirmed by wedge resection biopsy, as well as probable involvement of mediastinal and neck lymph nodes as per imaging studies. He was enrolled in the Pediatric MATCH (Molecular Analysis for Therapy Choice) study, but no candidate treatment was identified. The patient received treatment with doxorubicin and ifosfamide as per the ARST1321 protocol, which resulted in minimal response, and the subsequent development of enhancing masses in the right mandibular area, that were confirmed to as recurrent SEF by IR-guided biopsy. 17 months after the initial diagnosis, the patient began treatment with nivolumab and ipilimumab as per the ADVL1412 protocol. Imaging studies performed 4 months after initiation of the treatment revealed a significant interval decrease in pulmonary metastasis and a decrease in the size of the right mandibular mass. The patient continues treatment as per the ADVL1412 protocol.

Conclusion: The present case report describes a promising example of a favorable response to treatment utilizing a combination of ipilimumab and nivolumab in a patient with an aggressive and chemotherapy-resistant SEF. The data regarding treatment options for SEF is limited due to the rarity of this malignancy. However, based on the results observed in this case, providers may wish to consider the use of immune checkpoint inhibitors as a treatment option for recurrent SEF.

POSTER # 238 | CIRCULATING TUMOR DNA AS MARKER OF RESPONSE AND RELAPSE IN PEDIATRIC MALIGNANCIES: A NEW PARADIGM

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Background: The use of circulating tumor DNA (ctDNA) as a marker of treatment response and relapse represents an exciting advancement in precision oncology. A landmark study demonstrated that ctDNA-positive colorectal cancer patients were seven times more likely to relapse after surgery than ctDNA-negative patients.[1] Additionally, serial monitoring of ctDNA detected relapse a mean of 8.7 months prior to imaging in these patients.[1] Despite the increasing use of ctDNA as a minimally-invasive biomarker of relapse in adult cancer patients, few studies have examined the sensitivity of ctDNA in detecting relapse in pediatric cancer patients.[2]

Objectives: We aim to monitor levels of ctDNA during and after treatment in a small group of pediatric patients with a variety of solid tumors and use the trend in ctDNA levels to assess response to treatment and identify relapse.

Design/Method: Our institution has partnered with Natera to select a finite group of patients for assessment of molecular residual disease (MRD) via ctDNA. At the time of diagnosis and prior to the initiation of therapy, patients undergo blood draws in order to perform the Signatera assay. This is then followed by subsequent blood draws every 6 to 8 weeks during and after treatment. We expect each patient's ctDNA values to display a downward trend as disease-specific treatment is completed, with a goal of remission at a ctDNA level of 0 mtm/mL. Additionally, we anticipate that the ctDNA level will rise prior to other signs of relapse, allowing us to quickly identify and treat disease recurrences.

Results: There are currently five patients enrolled in the program. Ewing sarcoma, histiocytic sarcoma, and rhabdomyosarcoma comprise the diagnoses. Patient 1 (Ewing sarcoma, age 15) and Patient 2 (histiocytic sarcoma, age 15) joined the study at the conclusion of treatment, and their ctDNA levels have remained stable at 0 mtm/mL over the last 7 to 8 months. Patient 3 (Ewing sarcoma, age 17) demonstrated an initial ctDNA level of 19.39 mtm/mL, but all subsequent levels have remained stable at 0 mtm/mL. Patient 4 (Ewing sarcoma, age 15) demonstrated an initial ctDNA level of 3,041.89 mtm/mL, and patient 5 (rhabdomyosarcoma, age 7) demonstrated an initial ctDNA level of 431.13 mtm/mL.

Conclusion: We continue to monitor the ctDNA levels of five pediatric patients with three different types of sarcoma/solid tumor and aim to enroll additional patients in our study, with a goal of demonstrating the efficacy, safety, and swiftness of using ctDNA to monitor for relapse after treatment.

POSTER # 239 | RECOGNIZING THE CENTRAL NERVOUS SYSTEM AS A SITE OF PEDIATRIC SARCOMA RELAPSE: A 3-PATIENT SERIES

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Background: Sarcomas are diverse malignancies derived from primitive mesenchymal cells that are difficult to diagnose and treat. Advances in local control techniques, chemotherapy regimens, and imaging modalities have led to improvements in both morbidity and mortality in pediatric patients. However, one-third of patients develop disease relapse. Previously, intracranial metastasis was thought to be rare. The incidence of sarcoma brain metastasis is thought to have increased and is associated with grim outcomes.

Objectives: The objective was to illustrate the central nervous system as a potential site for pediatric sarcoma relapse, investigate the patterns of such relapses, and suggest a screening tool for early detection.

Design/Method: This was a retrospective study of 3 deidentified patient charts.

Results: Case 1 – A male Asian infant was born with a mass involving lower left extremity requiring through-the-knee amputation shortly after birth. Pathology confirmed infantile fibrosarcoma (IF). He was started an IF-based regimen after pulmonary biopsy confirmed metastatic disease. Two months after chemotherapy completion, 5.6 x 7.2 x 6.3 cm intracranial tumor was found with pathology confirming metastatic IF. Despite salvage chemotherapy and entrectinib, he continued to have increased neurological symptoms and died.

Case 2 - Ten-year-old Caucasian female presented with 8-month history of progressively enlarging right foot mass measuring 6.2 x 4.5 x 4.2 cm, consistent with Ewing Sarcoma upon biopsy. PET scan showed bilateral pulmonary metastatic disease with lymph node involvement. Chemotherapy and radiation therapy (XRT) were started. After completion of cycle 6, she had increased neurological symptoms and imaging showed 5 x 6 cm temporal mass with hemorrhage. Brain XRT, palliative chemotherapy, and Ruxolitnib were started; however, the patient subsequently died.

Case 3 – Six-year-old Hispanic female with large mass arising from right proximal humeral metaphysis with evidence of bilateral pulmonary metastasis. Biopsy confirmed metastatic osteosarcoma and chemotherapy was started. Although the patient was treated further with methotrexate, salvage chemotherapy, palliative XRT, and Pazopanib, she began to develop neurological symptoms over several weeks before passing.

Conclusion: We note this is the only report of IF brain metastasis, a rare report of sarcoma lymph node metastasis, and each patient was treated with an immunotherapy agent. Caregivers in cases 2 and 3 reported new-onset neurological manifestations prior to identification of new brain metastasis, indicating a lag in detection of new intracranial relapse in asymptomatic sarcoma patients. We suggest implementing a brief review of systems screening tool focused on concerning neurological manifestations to screen for brain metastasis.

POSTER # 240 | SMALL DESMOPLASTIC ROUND CELL TUMOR OF THE KIDNEY FOLLOWING HODGKIN'S LYMPHOMA: CASE REPORT

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Background: Desmoplastic small round cell tumor (DSRCT) is a rare and aggressive sarcoma that typically presents in males with abdominal and peritoneal invasion. There are curative therapeutic options, but survival remains dismal. Occasionally DSRCT can present as a solid tumor such as in the salivary glands, cervical lymph nodes, lungs, heart, stomach, etc. To this day, there have only been 19 reported cases of primary renal DSRCT in the literature.

Objectives: We describe a case of primary renal DSRCT following Hodgkin's Lymphoma (HL).

Design/Method: This is a case report describing the first presentation of DSRCT of the kidney following HL.

Results: We report a 13-y.o. female, 5 years in remission from stage IIA HL nodular lymphocyte predominant subtype, treated with 3 cycles of doxorubicin, vincristine, prednisone, and cyclophosphamide. She then presented with a left kidney mass (2.5 cm^3) on surveillance imaging. Biopsy of the mass was notable for sheets of malignant epithelial cells, positive for desmin, CD57, and PLAP by immunohistochemistry, no desmoplasia was identified. Tumor cytogenetics showed chromosomal losses, and FISH and RT-PCR identified the pathognomonic EWSR1-WT1 t(11;22(p13;q12), confirming the diagnosis of DSRCT. PET scan was negative for metastatic disease. Whole genome sequencing did not identify any actionable mutations for targeted therapy nor germline mutations (truncated TP53 was present). She underwent radical nephrectomy and received 14 cycles of vincristine, doxorubicin, cyclophosphamide alternating every 2 weeks with ifosfamide etoposide (VDC/IE). Her lifetime dose of doxorubicin was limited to 400 mg/m2 to avoid cardiac toxicity. Dexrazoxane was provided as a cardioprotective agent. Laparoscopic exploration with peritoneal biopsies was negative for disease after 6 cycles and at the end of chemotherapy. Six months later, surveillance imagery and subsequent PET showed new hilar lymphadenopathy and lung nodules with pleural involvement. Pathology and molecular studies from the hilar lymph node confirmed DRSCT relapse. Through shared decision-making, we elected to treat with pazopanib in conjunction with 3-weeks cycle of palliative chemotherapy (vincristine, irinotecan, and temozolomide). The disease progressed after 2 cycles of chemotherapy. The patient elected to stop all intensive therapies and died 4 months later.

Conclusion: We present the first case of renal DSRCT following HL. This case was also unique as whole genome sequencing was performed without actionable/germline mutations; suggesting EWSR1-WT1 translocation fusion mutation alone is sufficient to cause DSRCT. Outcomes remain poor despite aggressive conventional therapies and

new targeted therapies, such as pazopanib. An international registry could therefore allow for improved surveillance and monitoring of therapeutic response.

POSTER # 241 | TWO RARE PARATESTICULAR MALIGNANCIES

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Background: Rhabdomyosarcomas are rare malignant tumors that originate from mesenchymal tissue that form skeletal muscle. Clinical features include head and neck involvement, the genitourinary tract, and extremities. Less than 25% of patients present with distant metastasis. Malignant ectomesenchymomas are soft tissue tumors with heterologous rhabdomyoblastic components arising from neural crest cells. Approximately 50 cases have been published worldwide.

Objectives: We aim to highlight two rare metastatic paratesticular tumor cases and discuss the importance of detailed history-taking and physical examination (H&P) for early diagnosis, treatment, and outcome.

Design/Method: Two patients with rare paratesticular tumors diagnosed between 2020-2021 at our hospital were included. Diagnoses were confirmed with biopsy, and treatment per expertise protocols and guidelines were followed. Outcome is ongoing.

Results: **Case #1**: A previously healthy 16-year-old male presented with left-sided testicular swelling and pain with left inguinal lymph node involvement. Imaging revealed multiple retroperitoneal lymph nodes and pulmonary nodules with pericardial and pleural effusions. Biopsy showed stage IV embryonal rhabdomyosarcoma. Patient started chemotherapy per ARST 0431 and completed therapy 14 months later, followed by proton beam radiation (PBR). Six months later, scans were negative for relapse. Shortly thereafter, patient developed treatment-related myelodysplastic syndrome. He was bridged with Azacitidine prior to bone marrow transplant (BMT). Course was complicated by Cryptococcus infection and thrombus. After resolution, BMT was successful but died from septic shock complications.

Case #2: A previously healthy 15-year-old male presented with pleural effusions and left-sided testicular pain. Imaging and biopsies confirmed metastatic stage IV malignant left paratesticular ectomesenchymoma with pulmonary nodules and bone involvement. Patient received multimodal therapy consisting of surgery (left-sided orchiectomy, hemiscrotectomy, and retroperitoneal lymph node dissection), PBR for metastasis, and active chemotherapy. Due to no established protocols for ectomesenchymoma treatment, expertise guidance recommended treating similarly to rhabdomyosarcoma. Patient was enrolled per ARST 0431 but switched to D9803 due to Etoposide anaphylaxis. Overall, patient is responding well to chemotherapy and recent scans show no evidence of disease.

Conclusion: Both paratesticular masses highlight the importance of obtaining detailed H&P, especially in the adolescent population in hopes of earlier detection. Both patients were initially successful while receiving rhabdomyosarcoma therapy. However, more studies are needed to determine which treatment is optimal for paratesticular ectomesenchymoma and if outcomes are similar. Additionally, secondary malignancies can unfortunately result in childhood and better exploratory treatments should be investigated. With improved technology and medicine in oncological research, it is vital to continue maximizing opportunities for novel therapies and minimizing childhood deaths.

POSTER # 242 | EPITHELIOID SARCOMA IN TWO PEDIATRIC MALES- CHALLENGING DIAGNOSIS OF A RARE SOFT TISSUE SARCOMA

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Background: Epithelioid Sarcoma (ES) is a rare mesenchymal soft tissue tumor, accounting for <1 % of all sarcomas. ES is an aggressive tumor with a propensity for local recurrence and metastasis, most commonly to the lungs. The median age of presentation is 26 years. Spontaneous pneumothoraces and hemoptysis in ES have been described in adults but have not been reported in children.

Objectives: We report two cases of young males aged 10 and 11-years with ES who developed pneumothoraces and hemoptysis during their disease course.

Design/Method: Case Series

Results: A 10-year-old male presented with a firm mass to the left side of his neck for 4-6 months. MRI demonstrated a mass in the paraspinal musculature. Biopsy was concerning for Primitive Neuro-Ectodermal Tumor but after expert review the patient was diagnosed with ES, Proximal-Type. Radical neck dissection removed the mass and positive local nodes, followed by chemotherapy with ifosfamide and doxorubicin, and radiation therapy. He developed metastases to chest wall, lung, and bone with paraspinous and epidural extension. Hemoptysis occurred and he was trialed on pazopanib but developed a pneumothorax and exudative pleural effusions. Tazometostat was given on APEC1621C with good clinical response.

An 11-year-old male presented with hemoptysis for several weeks. CT imaging showed multiple <4 mm cavitary pulmonary nodules with ground-glass opacities throughout his lungs. Infectious, autoimmune and immunodeficiency evaluations were unremarkable. He subsequently developed serial bilateral pneumothoraces. Transbronchial biopsy showed organizing lung inflammation with patchy, mixed histiocyte-rich inflammation and areas of perivascular accentuation, raising the possibility of vasculitis; cytology was negative for neoplasia, fungi and AFB. Further review of the biopsy was concerning for a metastatic INI1 deficient malignant epithelioid neoplasm. Transthoracic wedge biopsy was consistent with ES, Classical-Type. MRI and PET-CT scans demonstrated a mass posterior to the proximal humerus. Needle biopsy was consistent with ES, identifying it as the primary site. Tazemetostat treatment was initiated.

Conclusion: ES is a rare, aggressive tumor with clinical and histopathological features mimicking more commonly encountered benign and malignant conditions, often resulting in delays in diagnosis and institution of therapy. Its rarity in children makes diagnosis in pediatrics even more challenging. Owing to its aggressiveness, ES frequently recurs locally and can undergo metastasis. Due to its indolent course, symptoms from distant metastases may precede that of the primary lesion. A high degree of clinical suspicion supported by histopathologic evaluation is required for its diagnosis.

POSTER # 243 | HYPERCALCEMIA AS A PRESENTATION OF DIFFUSE BONY METASTATIC RHABDOMYOSARCOMA

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Background: Hypercalcemia is a commonly associated complication of some adult malignancies, but occurs far less frequently in pediatric malignancies, with greater prevalence in patients with leukemia than in those with solid tumors. Presentations of hypercalcemia in children may include variable and non-specific symptoms.

Objectives: We describe two pediatric patients with rhabdomyosarcoma who presented with significant hypercalcemia secondary to widespread osseous involvement: one occurring at the time of diagnosis and one during progression of relapsed disease.

Design/Method: Case report

Results: Case 1: A previously healthy 4-year-old male initially presented with an isolated lumbar compression fracture. Over a 4-6 week period he developed fatigue, irritability and vomiting as a result of hypercalcemia (serum calcium 13.8 mg/dL). He also had hyperuricemia and mild acute kidney injury (AKI). Positron emission tomography with computed tomography (PET-CT) imaging revealed extensive multifocal lytic bone lesions throughout the axial and appendicular skeleton as well as multiple pathologic fractures. Biopsy demonstrated fusion-negative rhabdomyosarcoma with spindle cell morphology. No primary tumor was identified by clinical or radiologic examination. The patient's hypercalcemia was effectively treated with 3 days of hyperhydration. Endocrinology workup revealed a low parathyroid hormone (PTH) and a minimally elevated parathyroid hormone-related peptide (PTHrP) consistent with osteolytic metastasis and bone absorption.

Case 2: A 13-year-old male with extremity alveolar rhabdomyosarcoma relapsed with brain metastasis during maintenance therapy and was treated with palliative chemotherapy and radiation. During palliative treatment he presented with worsening back and leg pain as well as nausea and was found to have hypercalcemia (serum calcium 12.7 mg/dL), AKI and Magnetic resonance imaging (MRI) demonstrated multiple osseous metastatic lesions of the vertebral column and bilateral lower extremities as well as a pathologic tibia fracture. Hyperhydration alone did not improve his hypercalcemia. A single dose of Denosumab (120 mg) resulted in complete resolution of his hypercalcemia within two days. Endocrinology workup revealed normal PTH and PTHrP, suggesting that hypercalcemia and AKI were a result of rapid disseminated osteolytic metastases.

Conclusion: Symptomatic hypercalcemia is a rare presentation for metastatic rhabdomyosarcoma. Evaluation of children with hypercalcemia and pain should include thorough radiologic workup for malignancy with bone involvement. Symptomatic or significantly elevated hypercalcemia may require intervention beyond simple hydration for resolution.

POSTER # 244 | A CASE OF PHARYNGEAL SYNOVIAL SARCOMA IN AN ADOLESCENT MALE PRESENTING AS PROLONGED TONSILITIS

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Background: Synovial sarcoma is a malignant mesenchymal neoplasm that represents approximately 5-10% of all pediatric soft tissue tumors with head and neck accounting for only 3-10% of all cases. Treatment typically involves wide-local excision with or without radiation therapy and chemotherapy. The 5-year overall survival rate has a wide range, from 95% for fully resected and smaller tumors to about 10% for patients with metastatic disease.

Objectives: This case highlights the challenge of swiftly differentiating highly malignant lesions from more benign diagnoses and the importance of maintaining a broad differential in patients who present with a rather common complaint.

Design/Method: Case Report

Results: A 14-year-old boy presented to the ED with progressively worsening sore throat and difficulty swallowing for one month leading to voice hoarseness, dysphagia, and a 12-pound weight loss. The month prior to presentation, he was prescribed cephalexin followed by a course of oral corticosteroids for suspected bacterial pharyngitis with no improvement. He had been scheduled for a tonsillectomy.

On presentation, he was in mild distress with tachycardia, tachypnea, pooling of secretions, and pain. He spoke with a hoarse, "hot potato" voice. He was afebrile and maintained normal saturations on room air. His throat exam revealed copious pooling of phlegm and saliva, bilaterally enlarged tonsils without exudate or uvular deviation, and no pharyngeal erythema. His WBC count was elevated to 18.6 x 10^3/mcL with a negative infectious work-up. CT of the neck with contrast demonstrated a 4.6 x 4.2 x 7.6 cm heterogenous, highly-vascular, and mixed cystic-necrotic lesion anterior to the prevertebral soft tissues, with significant narrowing of the airway extending just below the level of the epiglottis. No neck lymphadenopathy was appreciated, but there was a 1 cm spiculated noncalcified solid nodule in the left upper lung lobe. Tracheostomy established a definitive airway during excisional biopsy. Pathology determined the mass to be a pharyngeal synovial sarcoma. Staging evaluation revealed no other possible sites of disease outside of the lung. With the extensive morbidity associated with gross total resection and the presence of a possible metastatic lesion in the lung, the patient was started on neoadjuvant

chemotherapy with doxorubicin and ifosfamide. He completed 6 cycles of therapy and underwent local control via proton beam irradiation alone to the primary site with no further evidence of active disease.

Conclusion: Maintaining a certain level of suspicion for rarer possible diagnoses of common pediatric complaints can impact the morbidity of complicated and life-threatening diagnoses.

POSTER # 245 | ALVEOLAR RHABDOMYOSARCOMA PRESENTING AS CARDIAC ACHALASIA IN A 7-YEAR-OLD PATIENT

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Background: Dysphagia in pediatric populations is becoming more common with an estimated incidence of 0.9%, and is a presenting complaint with an extremely broad differential.

Objectives: Here, we examine a pediatric patient who presented to medical attention with the chief complaint of dysphagia and was ultimately diagnosed with thoracoabdominal rhabdomyosarcoma (RMS).

Design/Method: The electronic medical record of one patient was accessed through a secure network to conduct a thorough review. No patient identifiers were collected.

Results: A 7-year-old female with no significant past medical history presented to the emergency department with a two-week history of dysphagia mainly to solids. She experienced intermittent abdominal pain in the preceding weeks and had the sensation of "something stuck in her throat." Her dysphagia progressively worsened over several days, and she began vomiting each time she ate or drank, which prompted her presentation. On presentation, she was afebrile with stable vital signs, and her physical examination was benign except for mild epigastric tenderness.

An esophogram showed findings suggestive of achalasia with high grade obstruction near the level of the gastroesophageal junction without filling defect. Gastroenterology was consulted and put forth initial differential diagnoses as eosinophilic esophagitis, achalasia, and severe gastroesophageal reflux. An esophagogastroduodenoscopy (EGD) with biopsy and esophageal dilation demonstrated thickening and furrowing of the mid and distal esophagus and gastric fundus, with increased pressure in the lower esophageal sphincter (LES), suggestive of LES obstruction. A CT chest was obtained to evaluate the source of the external esophageal compression, and revealed a large thoracoabdominal mass, measuring 6.2 x 8.9 cm, and extending over at least 12 cm cephalocaudally. The mass was located primarily in the abdomen and involved the lower mediastinum.

Laboratory studies demonstrated a CBC, LDH, alpha-fetoprotein, β-hcg, urine vanillylmandelic acid and homovanillic acid all within normal limits. Workup including an IR-guided biopsy and staging scans demonstrated stage III group 3 rhabdomyosarcoma alveolar subtype, Foxo1 mutation positive. The patient was started on chemotherapy protocol for high-risk RMS and had significant clinical improvement of her dysphagia.

Conclusion: Although malignancy is quite low on the differential diagnosis of pediatric dysphagia, this case shows it should not be discounted, particularly when the early diagnostic workup fails to yield a diagnosis. This case also highlights that RMS presentation depends on the anatomical site involved and its function.

POSTER # 246 | LOCALIZED PRIMARY SKULL OSTEOSARCOMA IN AN ADOLESCENT

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Background: Osteosarcoma is the most common bone malignancy in pediatric patients. Itis an aggressive neoplasm that primarily affect long bones, however approximately 6-7% present in the head and neck, and they comprise 1-2% of all cranial tumors. Primary osteosarcoma of the head and neck is rare in children and can be associated with genetic predisposing cancer syndromes, but most of them occur without familial predisposition or prior history of radiation.

Objectives: To report a case of sporadic primary skull osteosarcoma that has progression while on treatment.

Design/Method: Review of the electronic medical record and consultation with treating physician.

Results: 16 year old female, previously healthy who presented to ED after an episode of fainting and right side facial droop followed by a tonic-clonic seizure that lasted approximately 2 minutes while at an amusement park when event occurred. CT head revealed a large, aggressive, ill-defined, blastic lesion on the left frontal bone 3.5 x 2.0 x 2.9 cm. The Brain MRI showed mass with extensive parenchymal edema in the left frontal lobe and left lateral ventricle compression. She had surgery two days later (craniectomy). After surgery patient found to have residual right sided weakness improved and loss of expressive speech, both improved with rehabilitation. Disease evaluation with chest CT scan reveal bilateral densely calcified pulmonary nodules in the expected pattern of prior granulomatous disease, however metastatic disease could have a similar appearance. Bone scan without additional metastatic lesions. Pathology report confirmed high grade osteosarcoma. Pre-chemotherapy echocardiogram and audiogram within normal limits. Chemotherapy per AOST0331 started three weeks after initial presentation. Completed Neo-Adjuvant phase of treatment and imaging at that time showed concern for disease progression. Decision made to change to systemic therapy with Ifosfamide and Etoposide. She also began XRT for local control (70 Gy 35 fractions. She is currently tolerating chemotherapy well. Genetic test done and negative, demonstrating this is a sporadic case.

Conclusion: As of today, the exact cause of osteosarcoma remains unknown, but a number of risk factors has been described. Some of

them include bone dysplasia, Li-Fraumeni syndrome (TP53 mutation), retinoblastoma gene mutation, and prior history of radiation exposure. Presentation of skull osteosarcomas are often painless, which is a distinct difference from the presentation of long bone osteosarcomas. Best survival is related to complete surgical excision with negative margins and chemotherapy does increase survival for localized disease.

POSTER # 247 | NOVEL USE OF BLAND TRANSARTERIAL EMBOLIZATION FOR HEPATOBLASTOMA: A CASE REPORT

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Background: Hepatoblastoma is the most common primary pediatric liver malignancy. Standard treatment involves the use of chemotherapy with surgical resection or transplantation. Due to the limited availability of donor organs, some patients receive additional cycles of chemotherapy while awaiting transplantation which may increase risks of toxicities.

Angioembolization is a technique for elective obstruction of arterial flow using coils or gelatin microspheres to induce tumor necrosis. The use of transarterial chemoembolization, transarterial radioembolization, and bland transarterial embolization (TAE) are well described modalities for adults with hepatocellular carcinoma, including use as bridging therapy to transplantation. TAE has not been described routinely as a bridging therapy for pediatric hepatoblastoma.

Objectives: This case report describes TAE used as bridging therapy for hepatoblastoma while awaiting liver transplantation.

Design/Method: Case Report

Results: A 12-month-old boy, born prematurely at 25-weeks gestation, was incidentally found to have a large right upper quadrant mass. Initial alpha fetoprotein (AFP) was 2,140,000 ng/mL. Diagnostic evaluation was consistent with pretext III, intermediate-risk, non-metastatic, unresectable hepatoblastoma. Systemic chemotherapy was initiated with cisplatin, 5-fluorouracil, vincristine, and doxorubicin, and escalated to carboplatin and etoposide (CE) given concerns for chemotherapy resistance. His poor response to chemotherapy made him ineligible for liver transplantation. After multidisciplinary discussion, Yttrium-90 (Y90) radioembolization was performed to improve his chances of resection as an alternative to transplantation. His AFP initially declined, his tumor size decreased, but his disease remained unresectable. To capitalize on his response to Y90 but avoid additional radiation, TAE of the four branches of the right hepatic artery supplying the tumor was performed using 70-150 micron LC beads and 100-300 micron embospheres until stasis in all vessels. This was followed by a cycle of CE chemotherapy to minimize risk of metastatic spread. Repeat evaluation showed reduction in liver mass, increased necrosis on imaging, and marked reduction in AFP, deeming him eligible for transplantation. Due to history of prolonged myelosuppression following chemotherapy, a second course of TAE was pursued as a bridge to transplantation. Following TAE, scans showed continued response with reduced AFP, allowing for postponement of further chemotherapy and avoidance of additional systemic toxicity.

Conclusion: This case represents the novel use of TAE for chemo resistant hepatoblastoma as a bridging therapy while awaiting liver transplantation. While bland embolization of hepatoblastoma is not considered standard management, this case demonstrates its efficacy for local disease control. This case presents an important report in successful use of TAE in the pediatric population.

POSTER # 248 | A CASE OF RARE NESTED STROMAL EPITHELIAL TUMOR OF THE LIVER WITH METASTATIC RECURRENCE

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Background: Calcifying Nested Stromal Epithelial Tumor (CNSET) is a rare hepatic malignancy characterized by nests of epithelial cells within a mesenchymal stroma, typically found in female pediatric to young adult patients with an indolent course well treated by resection, however metastatic potential has been described, typically to the lungs. Adjuvant chemotherapy has been attempted in several patients, but with little improvement in outcomes.

Objectives: To report a case of CNSET that has undergone a metastatic recurrence, outlining the pathologic findings in this tumor and potential of targeted therapy for this entity.

Design/Method: Review of the electronic medical record and consultation with the treating physician

Results: We present a 15 year old male with multiple year complaint of progressive abdominal distention who underwent abdominal CT scan as part of a trauma workup. An incidental finding of a 22.2x13x12.3 cm heterogenous mass with central scar in the left lobe of the liver, with multiple smaller lesions within the right lobe of the liver was identified. All lesions avidly uptook radiotracer on PET CT Scan and were also visualized on MRI with contrast. Laboratory testing at that time revealed normal chemistry, liver function tests, inflammatory markers, and tumor markers including CEA, AFP, LDH, CA-19-9. Patient underwent left sided liver lobectomy and resection of the larger right lobe lesions, with radio frequency ablation of the smaller lesions resulting in complete resolution on follow up scans for a year thereafter. Initial tumor stained positive for keratin, CD10, Beta-catenin, WT1 C-Terminus and WT1 Terminus, and negative for HepPar, arginine, S100, Chromogranin, synaptophysin, p40, GATA3, ACTH, NUT, and SMA. Genetic analysis demonstrated characteristic mutations in CNSET of CTNNB1 and the TERT promotor region.

Unfortunately, follow up scans about one year post ablation found metastatic recurrence with multiple small hepatic lesions as well as pelvic and lymphatic masses. These pelvic and lymphatic inguinal masses were resected, and on evaluation once again consistent with

CNSET, though interestingly now demonstrating a new PTEN mutation. Complete evaluation is underway and we plan to repeat RFA to liver lesions and begin targeted therapy for systemic treatment.

Conclusion: This case demonstrates the metastatic recurrent potential of CSNET which typically follows a more indolent course. Tumors described in the literature have demonstrated resistance to chemotherapy including regimens typical to sarcoma and hepatoblastoma, thus leading to the ongoing consideration of targeted chemotherapy against the WNT, B-Catenin, mTOR, or PTEN pathways.

POSTER # 249 | HEPATOBLASTOMA TREATMENT IN A COMPLEX CARDIAC PATIENT

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Background: Hepatoblastoma is the most common primary malignant hepatic neoplasm in children, comprising two-thirds of primary liver tumors, and is most commonly seen under the age of five years [1][2]. Treatment of hepatoblastoma in most cases requires a combination of chemotherapy and surgery, however only about 33% of tumors are resectable at diagnosis. Commonly used chemotherapeutic agents include cisplatin, fluorouracil, and vincristine, with the addition of doxorubicin in higher risk populations [3].

Objectives: The objective of this study was to discuss the treatment of hepatoblastoma in a complex cardiac patient, including the usefulness of contrast-enhanced ultrasound when cross-sectional imaging cannot be obtained and the utility of vincristine and irinotecan when other agents cannot be used.

Design/Method: In this case, we discuss an ex 35 week, now 3-month-old female with prenatally diagnosed Ebstein's anomaly who was incidentally found to have hepatoblastoma on routine imaging. Ultrasound-guided biopsy confirmed epithelial type hepatoblastoma with embryonal pattern and AFP at diagnosis was 17,890. A CT scan demonstrated disease in her right lobe (PRETEXT 2), however there was significant artifact due to the location of her pacemaker that made it difficult to fully interpret. She subsequently proceeded with contrast-enhanced ultrasound, which identified several additional lesions in the left lobe that were biopsy-proven hepatoblastoma, making her PRETEXT 3. Due to the extent of disease and high risk for cardiac decompensation, she was not a surgical candidate. Additionally, due to her poor cardiac and performance status, she was not eligible to enroll on study AHEP1531 or receive doxorubicin. As such, she proceeded with neoadjuvant chemotherapy using cisplatin with modified hyperhydration. Unfortunately, this was not well-tolerated, with development of fluid overload and acute kidney injury. Additionally, she developed fungemia with Candida parapsilosis, requiring treatment with three antifungals. Her chemotherapy regimen was switched to vincristine and irinotecan.

Results: Altering her chemotherapy regimen was well-tolerated and effective, based on a robust response in her AFP and on contrast-enhanced ultrasound. To date, she has received four cycles of vincristine and irinotecan, with plans to undergo surgical resection of her remaining disease.

Conclusion: This case supports the use of contrast-enhanced ultrasound when cross-sectional imaging cannot be obtained and the utility of vincristine and irinotecan as active agents in hepatoblastoma, and raises the need to develop guidelines for hepatoblastoma in complex cardiac patients.

References

[1] Darbari A et al, Hepatology, 2003.
[2] Fiaschetti V et al, Case Rep Med, 2010.
[3] Katzenstein HM et al, Lancet Oncol, 2019.

POSTER # 250 | SOME UNKNOWNS STILL REMAIN: MULTIGENERATIONAL WILMS TUMOR FAMILY WITHOUT A GENETIC DIAGNOSIS

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Background: Approximately 10-15% of Wilms tumor is hereditary. Pathogenic variants in *WT1* account for the up to 5% of non-syndromic Wilms tumor, and other genes have been described to less frequently cause Wilms tumor such as *REST* or *TRIM28*. Despite advances in genetic testing methodology and new gene discoveries, some families still lack a genetic explanation for multigenerational Wilms tumor.

Objectives: Describe a family with multigenerational Wilms tumor without a genetic diagnosis.

Design/Method: Medical chart review of the family's demographic information, clinical presentations, disease courses, and genetic results.

Results: A family with multigenerational Wilms tumor presented to the Family Cancer Assessment Clinic at Huntsman Cancer Institute for surveillance of unaffected, at-risk children. In total, there are eleven family members diagnosed with unilateral Wilms tumor across five generations. Ages of diagnosis ranged from age 3 to age 12, and three family members passed away in childhood due to Wilms tumor. Genetic testing has been completed in stages as technology improved. Testing included *WT1* single gene analysis, 28 gene next generation sequencing panel of Wilms tumor predisposition genes, research whole exome sequencing (WES), and clinical WES. All testing has failed to identify a pathogenic variant causing Wilms tumor. A likely pathogenic in the *TTN* gene associated with hereditary cardiomyopathy was identified through clinical WES. Therefore, risk assessment for Wilms tumor has been based on family history. The pattern of cancer in the family is most consistent with autosomal dominant inheritance with incomplete penetrance. Surveillance with abdominal US every 4 to 6 months until age 9 has been recommended for individuals who are first- or second-degree relatives to an affected family member. Between 2020-2022, 18 at-risk children were evaluated in our high-risk clinic. Of those 18, 9 (50%) pursued screening with ultrasound. One at-risk child was

diagnosed with Wilms tumor at age 3 through screening. Reasons for not being screened were cost (67%), older age (11%), and being more than two degrees of relation from an affected person (22%).

Conclusion: Improvements in genetic sequencing and novel gene discoveries have been hailed as the solution to long diagnostic journeys for families with obvious hereditary risks. Unfortunately, despite these advances, some families are still missing a genetic diagnosis. Cancer screening based on empiric cancer risk assessment is still important for families. Continued follow-up with families with unknown genetic etiologies is also needed to offer them updated genetic testing overtime.

POSTER # 251 | HEPATOBLASTOMA IN A PATIENT WITH CONGENITAL NEPHROTIC SYNDROME

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Background: Congenital nephrotic syndrome and hepatoblastoma are rare in pediatric patients. Hepatoblastoma is the most common primary liver tumor in children less than three years of age, however in the setting of congenital nephrotic syndrome is incredibly unusual. Risk factors of hepatoblastoma include preterm infants with low birth weight, Beckwidth-Weidemann syndrome, Trisomy 18, Li-Fraumeni syndrome and fetal alcohol syndrome. Previous reports have also suggested an association between polycystic kidney diseases and hepatoblastoma.

Objectives: We describe a case of pediatric hepatoblastoma complicated by congenital nephrotic syndrome.

Design/Method: Retrospective chart review.

Results: A fourteen-month-old male with history congenital nephrotic syndrome, stage 3 chronic kidney disease and hypothyroidism presented with fever and concern for sepsis. Blood cultures were obtained and broad-spectrum antibiotics started. During the initial evaluation there was concern for peritonitis and an abdominal ultrasound was obtained. Imaging demonstrated a 8 cm lesion in the right lobe of the liver with concern for abscess versus solid mass. MRI, obtained for better characterization, confirmed the mass in segments VII and VIII and an appearance highly suggestive of hepatoblastoma (PRETEXT2 with negative annotation findings). Alfa-fetoprotein (AFP) was elevated to 187,191 ng/mL. Hepatoblastoma was histologically confirmed after right hepatic lobectomy. The tumor had predominant embryonal epithelial pattern and lymphovascular invasion was present. Surgical margins were negative. There was no evidence of lung involvement at diagnosis. He tolerated 2 cycles of dose reduced cisplatin monotherapy with no impact on his renal function. There is no evidence of disease at the end of therapy with normal AFP levels. He continues on supportive care measures for nephrotic syndrome without current need for dialysis.

Conclusion: There is limited literature regarding hepatoblastoma in with congenital nephrotic syndrome, as both conditions are rare in pediatrics. There is some evidence to suggest an association with other congenital kidney conditions with hepatoblastoma, such as polycystic kidney disease. Surgical treatment is the definitive treatment for hepatoblastoma, however preoperative chemotherapy with cisplatin is used as a neoadjuvant agent in unresectable tumors. This may present a challenge in patients with compromised renal function. This case is the second reported case of hepatoblastoma in congenital nephrotic syndrome, highlighting the importance of understanding a potential association of these two conditions.

1. Ranganathan, S., et. al,. Pediatric and Developmental Pathology, 2019
2. Chan, R, et. al. , Pediatric Blood and Cancer, 2014
3. McGuire M.M., et. al., Pediatric Transplantation, 2010.

POSTER # 252 | NOVEL COMBINATION OF CYCLOPHOSPHAMIDE, TOPOTECAN AND NAXITIMAB FOR RELAPSED REFRACTORY NEUROBLASTOMA

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Background: Approximately 50% of patients with neuroblastoma are categorized as high-risk (HR) and, despite treatment advances, HR disease remains challenging to treat with 40% of patients experiencing relapse. In recent years, immunotherapy with anti-disialoganglioside 2 (anti-GD2) antibodies (dinutuximab and naxitamab) has become available for patients with HR neuroblastoma. Many consider the combination of irinotecan, temozolomide and dinutuximab as standard of care treatment in patients with neuroblastoma in first relapse. Naxitamab monotherapy has been FDA approved for relapsed/refractory disease in the bone and bone marrow, and is now being studied in combination with upfront chemotherapy modalities.

Objectives: This is a case series evaluating the safety profile of the novel combination of cyclophosphamide, topotecan and naxitamab in patients with relapsed/refractory neuroblastoma. Four patients have been treated at our institution with this combination therapy.

Design/Method: A treatment plan was created with the help of a clinical pharmacist and dosing was as follows: cyclophosphamide 400 mg/m2/dose IV on Days 1-5; topotecan 1.2 mg/m2/dose IV on Days 1-5; naxitamab 3 mg/kg/dose IV on Days 1, 3, 5; GM-CSF 250 μg/m2/dose subcutaneous on Days −4 to 0; and GM-CSF 500 μg/m2/dose subcutaneous on days 6-10. We followed each patient for adverse events (AEs) as well as disease response.

Results: The novel combination of agents was overall well tolerated. The most common infusion related AEs included: pain, hypotension, and hypertension, all of which are known side effects of naxitamab. The most common non-infusion related AEs were admissions for fever and neutropenia, per institution standard, after which the dosing of cyclophosphamide and topotecan was reduced. Disease response

based on MIBG, PET and bone marrow studies were evaluated and were as follows: complete response in one patient; partial response in two patients; and stable disease in one patient.

Conclusion: The novel combination of chemotherapy and naxitamab was well tolerated in these heavily pre-treated patients with relapsed/refractory neuroblastoma. Experienced AEs were no more severe than would have been expected based on the individual agent's side effect profiles.

POSTER # 253 | ATYPICAL PRESENTATION OF NEUROBLASTOMA IN THE CERVICAL LYMPH NODE

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Background: Neuroblastoma develops from immature nerve cells and accounts for 97% of neuroblastic tumors and 8-10% of all childhood cancers. The most common primary site for these tumors is the adrenal galnd (40%), followed by abdominal (25%), thoracic (15%), cervical (5%) and pelvic sympathetic ganglia (5%). In most cases, the presentation is often seen as a primary tumor in the abdomen with or without abdominal pain. However, few cases in the literature have been reported on Neuroblastoma presenting in a lymph node wiith no primary tumor site.

Objectives: To report a rare case of Neuroblastoma presenting as Right Cervical Adenopathy with no primary mass affect.

Design/Method: Case Report

Results: A previously healthy 8-month-old male, born full term via C-section, presented with a 2 month history of persistent Right Cervical Lmphadenopathy refractory to antibiotics. On presentation, he was afebrile with no mass affect and no other symptoms. Ultrasound of the Thyroid showed a hypoechoic nodule measuring 2.2x1.5x2.3 cm with calcifications concerning for malignancy. Surgical excision of the lymph node was done and pathology results showed poorly differentiated Neuroblastoma without N-myc amplification. Ploidy was 1 and MKI index was low. Further evuluation with CT scan of chest, abdomen and pelvis, PET/CT whole-body and MIBG scan were negative for residual or metastatic disease. No primary site for Neuroblastoma was identified. In addition, bilateral bone marrow aspirate biopsies were obtained and were also negative. After completion of chemotherapy, he was monitored clinically and with Ultrasound of Neck. There has not been any evidence of recurrence 1.5 years since diagnosis.

Conclusion: This case highlights the importance of recognizing the possibility of Metastatic Neuroblastoma presenting soley as right lymphadenopathy with no primary tumor site.

POSTER # 254 | METASTATIC NEUROBLASTOMA TO THE JAW WITH SPONTANEOUS HISTOLOGICAL MATURATION

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Background: Peripheral neuroblastic tumors (PNT) arise from neural crest cells and include both malignant and benign tumors. PNTs represent a variety of tumors where neuroblastomas (NB) are made of immature cells and behave as malignant variants while ganglioneuromas (GN) and ganglioneuroblastomas (GNB) are made of mature cells and therefore, have a benign behavior. GNs usually present in the posterior mediastinum or retroperitoneum making the jaw an unusual location.

Objectives: Describe the case of a 5-year-old girl diagnosed with a concomitant right adrenal ganglioneuroblastoma intermixed and a mandibular neuroblastoma with ganglioneuromatous differentiation.

Design/Method: Chart review / Literature review

Results: A 5-year-old female, previously healthy, presented with a 1.5-year history of a slowly growing, painless, left jaw mass. No associated fevers, night sweats or weight loss. Initial ultrasound was concerning for a lytic lesion and CT was suggestive of an odontogenic myxoma. CBC, Lactate dehydrogenase, uric acid and ferritin were within normal limits. Whole body imaging revealed an additional 4.3 cm diameter right adrenal lesion with an associated small periportal lymph node measuring up to 1.2 cm in the short axis. Subsequent MIBG scan showed focal uptake only in the right adrenal tumor but not in the jaw lesion. Urine VMA slightly elevated (10.1 [1.7-6.5]), but urine HVA was normal. She underwent laparoscopic right adrenalectomy as well as biopsy of the jaw lesion. Adrenal mass pathology was consistent with a ganglioneuroblastoma intermixed and the left mandibular mass with a metastatic neuroblastoma with ganglioneuromatous differentiation, no MYC or ALK amplification and a diploid cell population. She then underwent radical resection of the mandibular lesion with a costochondral graft reconstruction. No further treatment was needed. No chemotherapy or radiation given. Patient is being followed every 3 months. She is doing well and is already free-of disease for more than 6 months.

Conclusion: A rare feature of the highly malignant NBs is that they can undergo histological maturation after metastasizing behaving as a benign ganglioneuroma. Above we highlighted the unusual case of a patient who presented with multifocal GNs on the jaw and adrenal gland. Primary ganglioneuromas within the jaw are extremely rare. Given the finding of an adrenal GNB, this suggests the possibility that the jaw lesion is the result of a metastatic NB, which after metastasizing underwent spontaneous maturation of their neuroblastic elements in both locations. Although initially malignant, surgery and surveillance are sufficient treatment for these tumors, which are now benign.

POSTER # 255 | Association between Sanjad Sakati syndrome and congenital neuroblastoma in children

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Background: Hypoparathyroidism-retardation-dysmorphism (HRD) syndrome, also known as Sanjad-Sakati Syndrome (SSS), is a rare

genetic disorder that is characterized by facial dysmorphism, generalized convulsions, hypocalcemic tetany, low parathyroid hormone, and low insulin-like growth factor 1 (IGF-1). It is caused by a 12-bp deletion in the tubulin-specific chaperone E (TBCE) gene. The association between HRD and malignancies is very rare, and only one study reported data regarding this association.

Objectives: We aimed to present a case of a 2-year-old child with HRD syndrome who was diagnosed with abdominal neuroblastoma stage 4.

Design/Method: A case report of a single case that was admitted on pediatric oncology ward in King faisal specialist hospital and research center, Jeddah, Saudi Arabia. We described the clinical course of the case and the consequences of the current management protocols.

Results: A 2-year-old boy presented to our department with developmental delay, failure to thrive, and hypoparathyroidism. Physical examination revealed dysmorphic features, including a long narrow face, deep-set eyes, beaked nose, floppy and large ears, long philtrum, thin lips, and micrognathia. The Whole Exome Sequencing (WES) showed homozygous for the TBCE gene. Clinical examination revealed an abdominal mass, which was subjected to a biopsy. Histological assessment and immune-histochemical findings were consistent with neuroblastoma, a poorly differentiated type with multiple calcifications. Bone marrow biopsy showed positive metastasis. N-myc expression was negative. Cumulatively, given these findings, the patient has been diagnosed with Stage 4 neuroblastoma. The patient was assigned to a tumor resection (LT supra-renal), stem cell collection, and six cycles of induction chemotherapy as per the ANBL0532 protocol. After the sixth cycle, He had stormy course, He was admitted to the intensive care unit due to septic shock, so he was intubated, he covered with broad spectrum antibiotic and antifungal after stabilization and discharged from picu he had delayed platelet recovery. He received two tandem of transplant with no major sequel apart from some delay of platelet recovery. The patient was subjected to radiotherapy as per protocol. However, during the first session, he passed away due to unexpected cardiopulmonary arrest and eventually, he died.

Conclusion: HRD is a very rare condition that is caused by a mutation in the TBCE gene. This is the second case reporting the association between HRD and neuroblastoma and the first case discussing the management of neuroblastoma in patients with HRD. The presence of neuroblastoma with HRD makes treatment difficult and reduces the patient's ability to tolerate treatment.

POSTER # 256 | GONADOTOXIC RISK STRATIFICATION IN CNS PHASE III TREATMENT PROTOCOLS IN THE COG FROM 2000-2022

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Background: As various specialists do fertility preservation counseling with varied training, it is essential that information provided on gonadotoxic risk of oncologic therapy be uniform. The Pediatric Initiative Network (PIN) of the Oncofertility Consortium published recommendations that satisfy treatment-related risk for future infertility that can be used to counsel patients. However, these recommendations are not integrated into upfront protocols, hindering timely risk counseling and referral for fertility services.

Objectives: Provide a comprehensive guide in gonadotoxic risk categorization for patients with CNS cancer and treated on current era COG protocols.

Design/Method: CNS phase III treatment protocols from the COG were identified from 2000-2022. Protocols were evaluated for gonadotoxic therapies (alkylating agents, heavy metals, or hypothalamic or gonadal radiation). Cumulative alkylating agent dose was determined for each arm and converted to cyclophosphamide equivalent dosing (CED). Patients were grouped as pre-pubertal female, pubertal female, and male. The level of risk (minimal, significant, or high) for gonadal dysfunction/infertility was then determined using the PIN Risk Stratification System. Patients not receiving gonadotoxic therapies were considered unlikely to be at risk. A second reviewer confirmed dose calculations and risk stratifications.

Results: In total, 11 protocols were reviewed: medulloblastoma, 4 protocols; low grade glioma, 3 protocols; ependymoma, 1 protocol; germ cell tumors (GCT), 1 protocol; atypical teratoid rhabdoid tumors (ATRT), 1 protocol, and high grade glioma, 1 protocol. Overall, 64% of CNS protocols placed patients at a high level of risk in at least one patient group and treatment arm. The percent of protocol arms by disease that placed a patient at high risk in at least one group was 100% for medulloblastoma, ependymoma, GCT and ATRT and 0% for low grade glioma and high grade glioma. The risk assignments within protocols placed 7/11 (64%) of males and 6/11 (54%) prepubertal and pubertal females at high risk while minimal or unlikely to be at risk was assigned for 18% of prepubertal females and 9% of pubertal females and males. When the hypothalamus or ovaries are exposed through direct tumor or craniospinal irradiation the risk level will be higher.

Conclusion: This comprehensive list provides gonadotoxic risk stratification that can be used to guide fertility preservation counseling for patients treated on COG CNS protocols. The majority of protocols evaluated place patients at high risk for gonadal dysfunction/infertility which warrants pre-treatment counseling regarding fertility preservation interventions.

POSTER # 257 | ROLE OF DNA METHYLATION PROFILING IN PEDIATRIC BRAIN TUMORS: A SINGLE INSTITUTIONAL SERIES

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Background: The role of molecular testing of central nervous system (CNS) tumors has come to the forefront as it provides information regarding subgroups and potential targeted treatments beyond just the histological diagnosis. DNA methylation profiling has now been

integrated into the WHO classification of CNS tumors and has shown to be a confirmatory means to diagnose CNS tumors that were previously considered as being homogeneous. The role of methylation in diagnosis is clearly understood, however the clinical implications are not clearly identified.

Objectives: Our goal is to review cases with methylation analysis and identify how frequently this testing aided clinical practice and the great utility it holds.

Design/Method: Methylation analyses was performed in 20 cases, including both new and retrospective cases, in 2022 at Children's Hospital of Orange County. We performed retrospective chart review to identify cases in which methylation analysis was beneficial in diagnosis and treatment of pediatric CNS tumors. Standard histological diagnosis, molecular analysis, and next generation sequences were also performed. We identified cases that confirmed rare diagnosis, subclassification and or clarified histological grade with methylation assay.

Results: Of the 20 cases, 18 were prospectively analyzed and 2 were retrospectively analyzed. Fifty percent of the cases were re-identified new diagnosis or subclassified using methylation analysis. One example is a diagnosis of dysembryonic neuroepithelial tumor (DNET), which was originally diagnosed as diffuse astrocytoma histologically. Another example is a patient with initial diagnosis of hemisphere glioma, which was further subclassified as diffuse pediatric-type high grade glioma RTK2 subtype A by methylation analysis. Management in both cases was impacted by the result of methylation analysis. DNA methylation testing served as a means for providing a clarified diagnosis or subgroups, and aided in directing management.

Conclusion: In our limited institutional case series, we identified that in 50 percent of the cases diagnosis was either changed or subclassified by methylation analysis. Methylation analysis is not currently a standard practice; however it plays a significant role for patients with rare tumors or ones with an indeterminant diagnosis. Methylation analysis is an important adjuvant diagnostic tool that should be considered in the workup of newly diagnosed CNS tumors. Additionally, it provides information about the molecular profile of CNS tumors allowing for the incorporation of potential targeted therapies to improve patient outcomes.

POSTER # 258 | PLGG DISEASE BURDEN AND HEALTH CARE UTILIZATION: LINKED CLAIMS AND EHR DATA STUDY

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Background: Pediatric low-grade glioma (pLGG), the most common brain tumor in children, is an indolent disease with insidious symptoms that progress over months to years. Despite excellent long-term survival, pLGGs cause significant tumor- and treatment-associated morbidities that persist throughout life.

Objectives: To gain insights into the disease burden and healthcare utilization of patients with pLGG.

Design/Method: We performed a retrospective study using the Optum® de-identified Market Clarity Dataset linked claims (commercial, Medicare advantage and Managed Medicaid beneficiaries) and electronic health records (EHRs) of cases ≤18 years of age, with ICD-10 code for brain neoplasm and ≥1 physician notes between January 2017 and June 2018. Index date was first claim or EHR with ICD-10 code for brain neoplasm. Natural language processing was used to identify pLGG-relevant data from physician notes. The observation period included 3 months prior to index date and 6-month segments from index date for 36 months. Cases had either continuous insurance coverage or continuous EHR activity in this period.

Results: A total of 154 patients with pLGG were identified. Median age was 11 years (range 2—18), 49% were female, 75% non-Hispanic white, 13% Hispanic, 5% African American, 1% Asian and 6% other/unknown. Of benefits, 56% had commercial and 44% Medicaid. Only EMR was used for reporting clinical presentations. An unspecified tumor (44%), headache/migraine (34%) and seizures (32%) were the most common clinical features prior to the index date. Study results are reported with ranges over a three-year follow-up period. Nausea and vomiting were seen in a third of patients in the immediate post-index period and again 2 years after index date. Seizures (22—38%) and tiredness/weakness (16—29%) were reported over the entire course of the study. The most common provider specialties consulted for pLGG care were oncologists (36—55%), pediatricians (32—51%), and radiologists (24—39%). Ninety-five—98% of patients visited an office or outpatient facility, 38—50% a diagnostic lab, 18—28% an emergency room, and 9—27% an inpatient facility in each of the 6-month segments. Throughout the 3-year follow-up period, more than 50% of patients regularly utilized laboratory services.

Conclusion: Despite the low-grade classification, patients with pLGG experience significant symptomatology and have complex health care needs that require high utilization of health care services, that persist over years. Further studies using integrated data sources are warranted to help us better understand the disease burden of pLGG.

This study was supported by Day One Biopharmaceuticals.

POSTER # 259 | THE IMPACT OF RACE AND SOCIOECONOMIC STATUS ON MORTALITY IN PEDIATRIC PATIENTS WITH CNS TUMORS

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Background: Pediatric patients with central nervous system (CNS) tumors are a niche group, requiring a multidisciplinary approach to mitigate sequelae from the tumor and subsequent treatment. Several investigations, in both adult and pediatric literature, describe inferior outcomes in minority and socially disadvantaged populations with oncologic diagnoses. While it is known that CNS tumor grade and location affect overall survival, it is also prudent to evaluate the effect

of socioeconomic status on mortality to mitigate disparities where possible.

Objectives: The effects of race and socioeconomic status (SES) on the 5-year overall survival (OS) and 5-year event free survival (EFS) of pediatric patients with primary CNS tumors diagnosed and treated at Akron Children's Hospital (ACH) were analyzed.

Design/Method: All patients, identified via retrospective chart review, were less than 22 years of age at the time of diagnosis and diagnosed between 2009-2017 (n = 184). Race was determined through self-designation in the patient chart. SES was determined utilizing an index-based county economic classification system from the Appalachian Regional Commission. This system is based on a county's three-year average unemployment rate, per capita market income, and poverty rate compared to national averages. Kaplan-Meier Survival Analyses (overall and risk stratified) were performed for both OS and EFS. Cox Proportional Hazards models assessed the effect of race, SES, WHO classification of tumor (glioma versus non-glioma), WHO grade of tumor (high or low), and location of the tumor, both individually and in combination, on OS and EFS.

Results: As expected, high grade tumors had worse OS and EFS (p-values of <0.001). Primary tumor location also had a significant impact on OS and EFS (p-values of ≤0.001). Specifically, tumors located in the midbrain had worse OS compared to spinal and supratentorial tumors (p-values 0.001 and 0.047 respectively). Race and SES did not impact OS (p-values 0.522 and 0.212) or EFS (p-values 0.459 and 0.863) individually. When combination models were developed to best estimate OS and EFS, race and SES were less important than grade of tumor, location of tumor and classification of tumor, which is consistent with their known impact on survival.

Conclusion: The 5-year OS and 5-year EFS were not impacted by race or SES, but rather a combination of tumor classification, grade, and location, in pediatric patients with CNS tumors at ACH. Therefore, we do not demonstrate the same disparity previously reported in the literature.

POSTER # 260 | CLINICAL REVIEW OF FACTORS LEADING TO BRAIN STEM TOXICITY AFTER RADIATION THERAPY FOR DIPG PATIENTS

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Background: Children with diffuse intrinsic pontine glioma (DIPG) have a uniformly dismal prognosis. Currently, standard radiation therapy (RT) administered at cumulative doses of approximately 54 Gy with daily fractionation is the mainstay of treatment. Radiation-induced imaging changes can be associated with serious signs and symptoms in DIPG patients that are very similar to the previous brain stem symptoms. Distinguishing disease progression versus reversible acute or subacute radiation toxicity versus irreversible radiation necrosis is important in manageing clinical course of DIPG.

Objectives: 1: Understand incidence of radiation necrosis versus reversible radiation toxicity in patients with DIPG in our institution. 2: Retrospective review of clinical course and treatment of brainstem symptoms after radiation. 3: Analysis of predictive values for radiation-associated brainstem toxicity in DIPG patients.

Design/Method: Retrospective chart review of patients with DIPG who were diagnosed 2017-2022 at our institutions, all received photon radiation therapy. Information about the clinical course, brain stem symptoms, imaging studies, management of symptoms and surgical interventions were reviewed. Radiation planning parameters were analyzed for dose-volume histogram (DVH) values associated with CTCAE grade 3 or 4 brainstem symptoms.

Results: There were 8 cases of DIPG treated to 54 Gy in 30 fractions. Photon radiation therapy was started between 2 to 57 days after diagnosis. All cases developed progressive brainstem symptoms after radiation therapy without progressive disease. Among them, ventriculoperitoneal shunt (VPS) was needed for obstructive hydrocephalous in 4 patients between 19-43 days after the end of radiation therapy. All brainstem symptoms as well as radiological findings were improved with steroid and/or bevacizumab. Staying below the DVH constraints of D10% <56 Gy and D0.1cc <58.8 Gy (per COG ACNS1721) was associated with no cases of acute grade 3 or 4 brainstem toxicity.

Conclusion: Progression of brainstem symptoms was commonly seen after radiation therapy and responded well to steroid and or bevacizumab. Though, numbers studied were small, our case series may suggest that meeting strict radiation planning DVH parameters is important for preventing severe toxicity and protecting quality of life.

POSTER # 261 | CHART AUDIT IN PEDIATRIC LOW-GRADE GLIOMA: MOLECULAR TESTING AND TREATMENT PATTERNS

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Background: Molecular studies have identified genomic alterations of components of the mitogen-activated protein kinase (MAPK) pathway as common oncogenic drivers in pLGG, leading to the investigation of MAPK pathway-targeted agents in this setting. Although pLGGs tend to be less aggressive than high-grade tumors and associated with significant long-term survival, disease progression after initial treatment means that approximately half of patients may require additional lines of therapy.

Objectives: This market research chart audit was conducted to understand molecular testing and treatment patterns for pLGG.

Design/Method: US-based physicians with a primary or secondary medical specialty in pediatric oncology, who have been in practice for 3–30 years and had treated ≥3 patients with relapsed/refractory pLGG in the previous 24 months were recruited. Participants completed an online survey in May 2022 and provided information from medical charts for 3–10 patients with relapsed/refractory pLGG representative of their typical treatment patterns. Patients included in

the chart audit were <15 years of age at diagnosis and had received their most recent dose of systemic treatment on or after April 1, 2020 (within the past 2 years).

Results: Information about 163 patients was collected from 27 pediatric oncologists. Tumors had been biopsied and/or resected in 138 (85%) patients and had been genomically tested at first procedure in 93 (67%) patients, not tested in 29 (21%), and testing status was unknown in 16 (12%). The most common reasons for not conducting genomic testing were prohibitive cost of biopsy/tissue testing or no insurance coverage (31%), testing felt not relevant for initial treatment (21%), and tissue being poor quality (21%) or insufficient (17%). Chemotherapy (119, 73%) was the most common first-line treatment, with 45 (28%) of patients receiving targeted therapy [32 (20%) received MAPK pathway-targeted agents] and 31 (19%), radiation therapy. In the second-line setting, a greater proportion of patients were treated with targeted therapy (91, 56%; MAPK pathway-targeted agents 66, 40%) and 65 (40%) with chemotherapy.

Conclusion: Although genomic testing of tumors is common in patients with relapsed/refractory pLGG, cost and insurance coverage are perceived as barriers. While chemotherapy is the most common first-line treatment in patients with pLGG, targeted therapies are used more frequently in the second-line setting.

This study was supported by Day One Biopharmaceuticals.

POSTER # 262 | A NOVEL PD-1 SWITCH RECEPTOR CAR T-CELL THERAPY TARGETS DIFFUSE INTRINSIC PONTINE GLIOMA

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Background: Among pediatric brain tumors, Diffuse Intrinsic Pontine Glioma (DIPG), now renamed H3K27 mutant diffuse midline glioma, is one of the largest contributors to cancer related deaths in children. This locally aggressive tumor remains uniformly fatal with patients having a mean survival of 9-11 months and 5-year overall survival of 2%. Immunotherapy has emerged as a recent therapeutic modality in many adult and pediatric brain tumors including DIPG with limited success, likely due to multiple variables including tumor heterogeneity, inability to cross the blood brain barrier or immunosuppressive tumor microenvironment.

Objectives: Our objective is to evaluate cytotoxicity of a newly developed PD-1 switch receptor Chimeric Antigen Receptor (CAR) T cell therapy, MC9324, targeting PD-L1 on DIPG patient derived cell lines. This novel CAR construct uses the interaction of the extracellular domain of PD-1 on CAR-T cells to PD-L1 on tumor cells taking advantage of this usually inhibitory pathway to activate and promote CAR-T cell-mediated, antigen-specific killing.

Design/Method: MC9324 CAR-T cells were generated from naïve T cells isolated from healthy donors, following lentiviral infection to deliver the CAR-encoding gene, and *in vitro* expansion for 14 days. To identify the suitable model, we evaluated the PD-L1 expression on a panel of primary DIPG cell lines using flow cytometry. Antigen-specific activation and cytotoxicity of the CAR-T cells against DIPG tumor cells were measured by CD107a expression on the surface of T cells with flow cytometry and Granzyme B release with MSD-ELISA.

Results: High PD-L1 expression was detected on a panel of patient-derived DIPG cell lines. MC9324 CAR-T cells were activated by DIPG tumor cells leading to significantly increased CD107a expression on CD8 CAR-T cells. Antigen-specific cytotoxicity against tumor cells was evidenced by the release of cytotoxic granules (Granzyme B).

Conclusion: PD-1 CAR-T cell therapy targeting the PD-L1 axis can be beneficial in DIPG patients with high PD-L1 expressing tumors. We plan to further evaluate this innovative CAR-T therapy using *in-vivo* models, complete pre-clinical studies, and develop a Phase 1 clinical trial.

POSTER # 263 | CNS TUMOR WITH BCOR INTERNAL TANDEM DUPLICATION: TREATMENT COURSE OF A LONG TERM SURVIVOR

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Background: Central Nervous System (CNS) tumor with BCL6 co-repressor (BCOR) internal tandem duplication (ITD) is a newly described CNS tumor, characterized by in-frame internal tandem duplications of the BCOR gene. There is no standard practice regarding the management of this tumor.

Objectives: To review a unique treatment course of a patient with CNS tumor with BCOR alteration which was treated with focal radiation only following gross total resection.

Design/Method: Case report

Results: A six-year-old male with a history of congential sensorineural hearing loss, autism spectrum disorder, and ADHD presented to the hospital with persistent headaches. CT scan showed a large right-sided parietal supratentorial mass and brain MRI confirmed a 6 x 8 x 6.7 cm lobulated, solid but heterogeneous mass in right parieto-occipital region. While initial pathology suggested a WHO grade 3 anaplastic meningioma, additional investigation with molecular analysis confirmed the diagnosis of high-grade neuroepithelial tumor (HGNET) with BCL6 corepressor (BCOR) exon 15 internal tandem duplication (ITD). This diagnosis was renamed CNS tumor with BCOR ITD in the 2021 WHO CNS tumor classification. The patient received 54 Gy of focal radiation and has no evidence of disease recurrence after 48 months from the end of treatment.

Conclusion: CNS tumor with BCOR ITD is a newly identified distinct entity and further investigation is necessary to determine optimal treatment approach. This report provides a unique treatment course for a patient with a CNS tumor with BCOR alteration which was

treated with focal radiation only following gross total resection. Longer follow-up and further investigation are warranted to determine the optimal approach to treatment, including the role of radiation and chemotherapy.

POSTER # 264 | ROMIPLOSTIM FOR TEMOZOLOMIDE-INDUCED APLASTIC ANEMIA: SUCCESSFUL TREATMENT OF A RARE COMPLICATION

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Background: Temozolomide has rarely been associated with fatal hematologic toxicities, such as secondary malignancies and marrow failure (temozolomide-induced aplastic anemia; TIAA). TIAA affects <1% of patients receiving Temozolomide for CNS malignancies and frequently fatal in patients who do not achieve hematological recovery. We present a pediatric case of TIAA treated successfully with thrombopoietin receptor agonist (TPO-RA) romiplostim.

Objectives: To describe the successful use of a TPO-RA in a child with TIAA, along with a focused literature review.

Design/Method: Clinical and laboratory data were extracted from the electronic medical record. PubMed was searched for reports of TIAA, and bibliographies of relevant articles were reviewed to identify additional relevant publications.

Results: The patient was a 7-year-old female with a high-grade glial phenotype CNS lesion harboring a rare PATZ1 fusion. She received focal radiation with concurrent temozolomide 90 mg/m2/day administered for 28 days. Four days after cessation of temozolomide, thrombocytopenia (6 x109/L) and anemia (9.8 g/dL) were noted. Shortly thereafter, pancytopenia developed with nadir hemoglobin 6.6 g/dL, platelets 6 x109/L, and ANC 110/μL. After nearly two months of profound cytopenias, and a total 9 platelet and red blood cell transfusions, she was noted to meet diagnostic criteria for TIAA (ANC <500 and platelet count <20 + no hematologic recovery for at least 4 weeks).[1] Bone marrow biopsy is not required for the diagnosis as the etiology of cytopenia is apparent. At diagnosis of TIAA, romiplostim 10 mcg/kg/week was promptly initiated to stimulate trilineage hematopoiesis. After three doses of romiplostim, she required no further transfusions. All cell counts normalized after the sixth dose. After four weeks of complete trilineage recovery, romiplostim was decreased weekly in 2.5 mcg/kg/week decrements until off. No side effects were attributed to romiplostim, and she remains in complete hematologic remission. She received no further temozolomide.

Literature review identified a single publication of TIAA in the pediatric population describing an adolescent who ultimately required allogeneic stem cell transplant (alloHCT) to re-establish hematopoiesis. Therapies employed to address TIAA include alloHCT and various immunosuppression approaches. TPO-RAs have recently been reported for TIAA in adults, with favorable hematologic responses.

Conclusion: In conclusion, we describe the successful management of TIAA with romiplostim in a young child. Prompt identification of this rare complication and initiation of treatment could prevent a potentially fatal outcome or escalation to a high-risk procedure such as alloHCT.

POSTER # 265 | CHEMOTHERAPY RESPONSE IN CLIVAL CHORDOMA PATIENTS: A SINGLE CENTER RETROSPECTIVE OBSERVATIONAL STUDY

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Background: Clival chordomas are rare, locally aggressive tumors arising from the base of the skull, which are thought to develop from remnants of the notochord. Chordomas primarily affect adults, with less than 5% of chordomas occurring in children. Those that do occur in children often involve the skull base, including the clivus. The World Health Organization recently classified chordomas into multiple histological subtypes: conventional, dedifferentiated, and poorly differentiated. Traditionally, chordomas have been treated with surgical resection and radiation therapy, as they have been thought to be largely resistant to chemotherapy. However, there is emerging evidence that poorly differentiated chordomas (PDC) are responsive to chemotherapy. We performed a retrospective analysis of poorly differentiated clival chordomas treated with chemotherapy at our institution.

Objectives: To evaluate whether progression free survival (PFS) and overall survival (OS) are prolonged with the addition of chemotherapy in the treatment of poorly differentiated clival chordoma in children and adolescents.

Design/Method: Three subjects with a diagnosis of poorly differentiated clival chordomas who received chemotherapy at our institution between 2007 and 2019 were retrospectively studied. All subjects received chemotherapy following Children's Oncology Group Protocol ARST 0431.

Results: After initial surgical intervention, all three patients treated with chemotherapy showed favorable responses demonstrated by significant reduction in tumor burden. Of the three patients, one is alive with no evidence of recurrent disease 15 months after diagnosis and has not received radiation therapy. The remaining two patients had PFS of 22 months and 33 months, with OS of 42 months and 47 months, respectively. Neither of these two patients underwent radiation until tumor recurrence.

Conclusion: PDC is known to be an aggressive tumor associated with poor outcomes, despite traditional treatment with surgery and/or radiation therapy. All three patients at our institution with PDC showed a significant response to chemotherapy, demonstrated by reduced tumor burden and avoidance of radiation therapy/subsequent surgeries. While survival rates remain poor, chemotherapy may play a significant role in improving rates of PFS and OS for poorly differentiated clival chordomas.

POSTER # 266 | A RARE CASE OF CARBOPLATIN-INDUCED SEVERE HEMOLYTIC ANEMIA IN A CHILD WITH LOW GRADE GLIOMA

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Background: The combination of vincristine/carboplatin is the most widely accepted chemotherapy for childhood low grade glioma (LGG). Carboplatin hypersensitivity reactions are frequent. Drug-induced immune hemolytic anemia (DIIHA) is an uncommon but life-threatening complication of carboplatin therapy without an established standard plan of action.

Objectives: We report a case of carboplatin-induced DIIHA in a patient with LGG.

Design/Method: Case Report.

Results: A 3-year-old girl with neurofibromatosis 1 was receiving treatment with carboplatin (175 mg/m2/dose) and vincristine (1.5 mg/m2/dose) for an optic chiasm glioma. She had received 30 doses of carboplatin prior to presentation for maintenance cycle 6, day 14 chemotherapy.

A complete blood count (CBC) 1 week prior to presentation showed white blood cell (WBC) count 6820/dL, hemoglobin level 8.6 gm/dL (mean corpuscular value (MCV) 77.1), and platelet count 100000/dL. CBC on presentation showed WBC count 4200/dL, hemoglobin level 6.5 gm/dL (MCV 77.6), and platelet count 240000/dL. She did not have any associated symptoms and her exam was unchanged from previous visits. A packed red blood cell (pRBC) transfusion was ordered, and the chemotherapy infusion commenced while crossmatch was in progress. After carboplatin began infusing, the patient had new-onset seizure activity, severe pallor, and altered mental status. She was not responsive to questions or stimuli. She had tachycardia and tachypnea but normal oxygen saturation. CBC showed WBC count 24360/dL, hemoglobin level 1.4 gm/dL (MCV 104.8), and platelet count 175000/dL. Reticulocyte count was elevated at 9%. Bilirubin was elevated to 1.5 (all unconjugated, baseline 0.3), lactate dehydrogenase was elevated to 7722, and haptoglobin was normal. Previously obtained type and screen demonstrated the presence of antibodies. Initial direct antiglobulin test was positive (polyspecific and IgG; complement initially negative but positive on reflex testing). Alloantibodies to common red blood cell antigens were not detected.

The carboplatin infusion was discontinued; pRBC transfusion and intravenous methylprednisolone (2 mg/kg to be given every 12 hours) were immediately initiated. A total of 30 mL/kg pRBC was well-tolerated and she recovered with a hemoglobin level of 11 gm/dL. A computed tomography scan of the head was negative for hemorrhage. Chemistries were negative for electrolyte imbalances. Blood cultures remained negative. Steroids were gradually weaned.

Conclusion: The patient likely had prior sensitization to carboplatin (indicated by positive antibody screen on type and screen) and an acute hemolytic crisis precipitated by the carboplatin infusion. This case highlights the value of quick recognition of DIIHA as a rare complication of carboplatin and prompt initiation of supportive cares.

POSTER # 267 | EVEROLIMUS AND BEVACIZUMAB AS A TREATMENT FOR TRAF-7 MENINGIOMATOSIS SYNDROME

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Background: Although meningiomas account for 35.8% of all brain tumors they are rare primary brain tumors in the pediatric population, associated with multiple genetic mutations. Recent descriptions of mutations in the TRAF7gene, a pro-apoptotic E3 ubiquitin ligase, have been found in up to one-quarter of non-NF-2 tumors. TRAF is downregulated in human keratinocytes after inhibition of the PI3K/AKT/mTOR signaling. Germ-line mutations in this gene are associated with facial, and cardiac malformations, variable intellectual deficiency, and musculoskeletal abnormalities. Inhibition of mTORC1 signaling has been shown to diminish the growth of meningiomas in clinical trials.

Objectives: We report a case of meningiomatosis in an adolescent with TRAF 7 mutation managed with Everolimus and Bevacizumab.

Design/Method: Literature and chart review.

Results: A 17 yo female with complex medical history that includes syndactyly of the left foot, small hands and digits, congenital heart disease, overgrowth of the right lower extremity with lipomatous subcutaneous tumors, conductive hearing loss developed meningiomas of both optic nerves requiring decompression and unroofing on two separate occasions, with associated blindness. Repeat MRI brain showed bilateral optic nerve sheath enhancement, dysplasia of the corpus callosum, mild hemimegalencephaly, inter-hemispheric fissure 1.5 cm meningioma, bilateral enhancement of internal auditory canals as well as trigeminal and glossopharyngeal nerve, consistent with meningiomatosis. Pathology showed a grade I meningioma with a TRAF7 p.G536S detected by performing a 500 genomic panel (UCSF500). She was started on Everolimus 4.5 mg/m2/day orally, and Bevacizumab 10 mg/kg IV every 2 weeks, after 6 months, weaned to every 4 weeks showing radiographically and clinically stable disease for over one year after starting treatment.

Conclusion: Recurrent multiple meningiomas represent a treatment challenge for neuro-oncologists. The evolving understanding of the genetics of these tumors has improved our understanding of their pathogenesis as well as treatment. TRAF 7 mutations are associated with non-NF-2 meningiomas, and in this case, inhibition of the mTOR signaling pathway in combination with a VEGF-A inhibitor such as Bevacizumab showed clinical benefits given no new presence of meningiomas or growth of the pre-existing tumors. Management of meningiomatosis continues to be a medical enigma, evaluation of germline mutations and combination of therapies such as tumor angiogenesis, cytokines, and antibody inhibitors could represent the next first line of treatment.

POSTER # 268 | CHRONIC INFLAMMATION AS A PRESENTATION OF A RARE LOW GRADE CENTRAL NERVOUS SYSTEM TUMOR

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Background: Intracranial mesenchymal tumor FET-CREB fusion-positive (IMT) is a newly designated provisional diagnosis in the current WHO Classification of CNS Tumors. Fewer than 30 cases have been reported. It is a pediatric-predominant tumor occurring most often in adolescents, but patients range from 4 years to 70 years of age. It is predominantly localized with a propensity toward local recurrence. Metastatic disease is uncommon. Characteristics include various histomorphology and fusion of a FET RNA-binding protein gene (*EWSR1*, *FUS*) with a CREB family transcription factor gene (*CREB1*, *ATF1*, or *CREM*). Another tumor harboring FET-CREB fusions, angiomatoid fibrous histiocytoma (AFH), is associated with a hyperinflammatory state (elevated CRP and interleukin-6). This inflammatory association has not been reported in IMT.

Objectives: Review a pediatric case of IMT with associated hyperinflammatory state.

Design/Method: Case report

Results: A 13-year-old previously healthy male presented with 6 months of fatigue, abdominal pain, anorexia, weight loss, joint pain, and night sweats. He was seen by gastroenterology and was found to have microcytic anemia, thrombocytosis, elevated ESR (46-78 mm/hr), CRP (5.7-8.4 mg/dL), and ferritin (146-186 ng/mL). An extensive GI workup was performed and was felt to be suggestive of mild Crohn's. He was treated with infliximab without improvement. Follow-up capsule endoscopy was inconsistent with Crohn's. Shortly after, he developed migratory arthralgias and was referred to rheumatology. Workup showed ongoing anemia and worsening inflammatory markers. A PET-CT was performed and was unremarkable. Two months later, GI symptoms severely worsened prompting admission for further evaluation. He had ongoing microcytic anemia and increased inflammatory markers: ESR (107 mm/hr), CRP (12.4 mg/dL), ferritin (255 ng/mL), interleukin-6 (13.8 pg/mL), and interleukin-10 (3.9 pg/mL). Infectious workup, bone marrow aspirate and biopsy, and lumbar puncture were unremarkable. Full-body MRI revealed a 1.5 cm enhancing mass in the brain. A dedicated MRI brain showed a lobulated T2 heterogeneous, T1 hypointense, homogenously enhancing non-diffusion-restricting mass measuring 1.4 x 2.6 x 1.7 cm involving the foramen ovale and right middle cranial fossa. The final pathologic diagnosis was IMT. RNA sequencing confirmed a FET-CREM fusion. Shortly after resection, he had no constitutional symptoms, normal inflammatory markers, and nearly resolved anemia. No additional treatment was given, and an MRI brain showed no disease recurrence.

Conclusion: IMT is an uncommon low-grade CNS tumor; no reported cases have been associated with systemic inflammation. Like AFH, a similar yet distinct low-grade tumor known to cause a hyperinflammatory state, IMT may be associated with a hyperinflammatory state.

POSTER # 269 | SUCCESSFUL SYSTEMIC TREATMENT OF PROGRESSIVE PAPILLARY GLIONEURONAL TUMOR IN AN INFANT

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Background: Papillary glioneuronal tumor (PGNT) is typically considered a low grade tumor, though sometimes can have a more aggressive phenotype. Patients with this diagnosis usually are young adults.

Objectives: To describe a rare histologic tumor type in a difficult location in the infant/young toddler age group and describe a radiation-avoiding systemic treatment approach when complete surgical resection is not possible.

Design/Method: A 13-month old male presented with several month history of progressive macrocephaly (56.4 cm,>99th percentile) and developmental delay. Brain magnetic resonance imaging (MRI) revealed a large, lobulated, heterogeneously enhancing intraventricular mass arising from the corpus callosum, with effacement of the majority of the lateral ventricles. He underwent craniotomy and tumor debulking, with approximately 30% tumor resected. Surgical pathology showed proliferation of cells with rounded nuclei, that stained positive for synaptophysin, OLIG2, and GFAP, A Ki-67 labeling index of ~10% was noted focally, less than 10% of cells stained for P53. Findings were considered consistent with PGNT. Next generation sequencing revealed a BRAF fusion alteration (KIAA1549-BRAF) and PTEN pathogenic variant (p.K125N, c.375A>C). Germline analysis also revealed a PTEN VUS: c.375A>C (p.Lys125Asn) in exon 6 – the first such reported variant of its kind. Repeat imaging one month later revealed significant tumor growth one-month post-partial resection.

Results: The patient received a total of 8 cycles of chemotherapy as per the CNS14 regimen with cyclophosphamide, etoposide, and carboplatin. A very significant reduction in tumor burden was seen with this therapy (measurements decreased from 7.6 x 10.1 x 7.9 cm to 2.5 x 1.9 x 3.0 cm). Some expected toxicities did occur (febrile neutropenia, cytopenias requiring transfusions). As he was still responding to chemotherapy, decision was made to defer surgical resection and continue single agent carboplatin x 4 cycles. The tumor continued to decrease to a negligible measurement, obviating the need for any surgical resection. The patient has reached many developmental milestones now 15 months after diagnosis. Mitogen-activated Extracellular signal-regulated Kinase (MEK) inhibition as a maintenance therapy is planned. He will undergo lifetime surveillance for presumed pathogenic PTEN variant.

Conclusion: This is the youngest reported patient with a diagnosis of PGNT; additionally, a germline variant in PTEN exists that is the first reported of its kind. This potentially aggressive tumor type, in a location impossible to completely resect, can be successfully treated with systemic chemotherapy, with such excellent responses that adjuvant surgical resection may not be needed.

POSTER # 270 | BIALLELIC BRCA2 AND BLM GENE MUTATION IN A SHH MEDULLOSBLASTOMA WITH SEVERE CHEMOTHERAPY TOXICITY

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Background: Fanconi Anemia and Bloom Syndrome are two chromosomal instability disorders in genes that encode DNA helicases, which are responsible for DNA replication, repair, and recombination functions. We present a case of a patient with a medulloblastoma who experienced severe toxicity from chemotherapy, which led to the identification of a FANCD2 mutation on DNA molecular testing.
Objectives: Single-case presentation highlighting the combination of mutations found on a patient with SHH medulloblastoma and extreme chemosensitivity.
Design/Method: Chart review / Literature review
Results: A previously healthy 4-year-old female presented with headaches and intermittent vomiting. Imaging demonstrated a heterogeneously enhancing right-sided posterior fossa mass with local mass effect on the fourth ventricle, which demonstrated restricted diffusion. MRI Spine was negative for metastasis. An EVD was placed and then she underwent suboccipital craniotomy for gross total resection of a posterior fossa tumor. Pathology showed a large cell, anaplastic medulloblastoma, SHH subtype. Tumor sequencing demonstrated high-risk somatic alterations including GLI2/MYCN amplification and TP53 mutation. Germline sequencing showed two different BRCA2 mutations, diagnostic for Fanconi Anemia and a heterozygous truncating mutation in the BLM gene, suggesting the patient is a Bloom Syndrome carrier. The patient started on ACNS 0334 chemotherapy receiving one dose of vincristine and high dose methotrexate. She developed severe nephrotoxicity, hepatotoxicity, and bone marrow suppression. Treatment was recommended with focal proton radiation to the tumor bed to avoid toxicity of craniospinal radiation in patient with Fanconi anemia followed by adjuvant bevacizumab, everolimus and posaconazole to avoid toxicities from conventional chemotherapy.
Conclusion: Germline testing and tumor sequencing is essential in all patients diagnosed with medulloblastoma. This may prompt the early diagnosis of patients with genetic predisposition syndromes that may affect the clinical course and genetic counseling of the patients and families. Moreover, different mutations can affect long term survival rates and relate to a poor prognosis. Further research could potentially discover target therapy or new combined therapies for specific mutations.

POSTER # 271 | SEVERE GASTROINTESTINAL BLEEDING SECONDARY TO TRAMETINIB IN PEDIATRIC LOW-GRADE GLIOMA

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Background: Trametinib is an oral, reversible, and highly selective inhibitor of MEK1 and MEK2, the final kinase in the MAPK signaling pathway. It is approved for use in BRAF-mutant tumors in adults. Nearly 20% of pediatric patients diagnosed with Neurofibromatosis type I (NF1) develop pilocytic astrocytomas due to dysregulation of the RAS-MAPK pathway. The MAPK pathway plays a vital role in regulating cell proliferation and differentiation in epithelial cells, including those in the gastrointestinal tract. Trametinib is generally well-tolerated in children, but is associated with rare, serious side effects.
Objectives: We herein present a case of a pediatric patient who developed severe gastrointestinal bleeding after using trametinib as a salvage regimen for an NF1-associated pilocytic astrocytoma.
Design/Method: Clinical history was obtained through retrospective chart review from electronic medical records.
Results: The patient is a 17-year-old male with NF1 who was treated with trametinib for disease progression of a right cerebellar pilocytic astrocytoma. He had previously received initial therapy with vincristine and carboplatin for a tectal/optic glioma, which was switched to bevacizumab and irinotecan due to carboplatin hypersensitivity. He then underwent salvage treatment regimens with imatinib, vinblastine, and trametinib for disease recurrence. Twenty months into treatment with trametinib, the patient presented with hematemesis and melena. Complete blood count (CBC) showed moderate anemia with a hemoglobin of 9 g/dL. Esophagogastroduodenoscopy (EGD) was performed and confirmed a bleeding duodenal ulcer with several gastric antral erosions, which were treated with carafate and omeprazole. Trametinib was discontinued at that time. The patient is now 20 months progression-free and has had no repeat gastrointestinal bleeding episodes.
Conclusion: Clinical trials are underway to investigate MEK inhibitors for the treatment of NF1-associated pediatric low-grade gliomas. However, there is need for close vigilance in monitoring for rare on-target, off-tumor adverse side effects with the use of newer, targeted cancer drugs in children.

POSTER # 272 | A RARE PRESENTATION OF CENTRAL NERVOUS SYSTEM DIFFUSE LARGE B-CELL LYMPHOMA

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Background: Central nervous system (CNS) tumors are the most common solid tumors in pediatrics. Some CNS neoplasms primarily arise in the sellar/suprasellar regions such as pituitary adenoma, craniopharyngioma and germ cell tumors (GCT) while others can be present in other intracranial sites. Though suggestive of etiology, location and radiographic characteristics cannot reliably differentiate tumors so analysis of tumor markers can assist in diagnosis. In GCTs, if tumor markers such as Alpha-fetoprotein (AFP) and beta subunit human chorionic gonadotropin (beta-HCG) are elevated, histological confirmation with biopsy is not needed for diagnosis.

Objectives: Review a rare presentation of CNS diffuse large B-cell lymphoma (CNS-DLBCL).

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

Results: A 6-year-old previously healthy female presented to the emergency department with one month of progressive headache, nausea, weight loss and fatigue. Initial neurologic exam was unremarkable. Serum studies revealed elevated LDH and prolactin. Imaging revealed enhancing masses involving the suprasellar and pineal regions. Serum AFP and beta-HCG were negative. Following admission patient was found to have pan-hypopituitary with severe diabetes insipidus. Lumbar puncture revealed negative AFP and beta-HCG. CSF cytology was positive for atypical cells. Given negative GCT markers, decision was made to proceed with endoscopic biopsy prior to initiation of chemotherapy.

Pathology revealed negative GCT markers including SALL4, PLAP, OCT3/4, CD117, CD30, AFP, and beta-HCG. Synaptophysin, chromogranin, AE1/AE3, and myogenin were also negative. Atypical cells were B cells, positive for CD20, CD45, CD79a, and PAX5, which further express monotypic kappa light chain. The morphologic and immunohistochemical findings were diagnostic of diffuse aggressive B-cell non-Hodgkin lymphoma.

Conclusion: Imaging with a bifocal process in the suprasellar and pineal region was suggestive of bifocal germinoma. However, our patient's age and gender were not consistent with the typical age seen for bifocal germinoma. Additionally, serum and CSF tumor markers were negative. Decision was made to biopsy lesion before initiation of chemotherapy. Histology confirmed a diagnosis of CNS-DLBCL. PET revealed no other sites of disease.

CNS-DLBCL, is an extra-nodal lymphoma in the brain, spinal cord, leptomeninges or eye and represents the majority of CNS-lymphomas. CNS-DLBCL is more common in the adult population, with onset generally after the fifth decade of life. Due to the absence of a typical clinical presentation, multiple neuroimaging appearances, heterogeneity of the pathological morphology and no specific laboratory examination, the immunohistochemistry and molecular biology are of vital importance in accurate diagnosis. Although rare in the pediatric population, CNS DLBCL must remain on the differential.

POSTER # 273 | A NOVEL PATHOGENIC VARIANT OF THE KRAS GENE FOUND IN A PATIENT WITH PILOCYTIC ASTROCYTOMA

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Background: Pilocytic astrocytomas are relatively common low-grade gliomas with a generally favorable prognosis. These tumors typically have solitary genetic alterations that result in activation of the MAPK signaling pathway, most commonly as KIAA1549::BRAF fusions. Approximately 2% of cases of pilocytic astrocytoma have been found to have a KRAS mutation. Activating mutations in KRAS can lead to increased cellular proliferation through the MAPK pathway and have the highest incidence rates in pancreatic, colon, and lung carcinomas.

Objectives: Describe a case of a pediatric patient with a pilocytic astrocytoma with a novel KRAS gene mutation.

Design/Method: Case Report

Results: A 12-year-old male presented with intermittent vomiting associated with episodes of dizziness and headaches. He had difficulty with tandem stance, tandem gait, and difficulty with upward gaze. An MRI of brain demonstrated a large cystic mass within the cerebellar vermis with associated mass-effect and mild surrounding edema. He underwent a posterior fossa craniotomy with near total resection of the mass. Pathology was consistent with a WHO grade I pilocytic astrocytoma. A tumor-only next generation gene sequencing panel was completed. Sequencing of the pilocytic astrocytoma demonstrated a small complex insertion (c.193_198delAGTGCAinsCTTGACCAGTAC) in the *KRAS* oncogene affecting codons 65 and 66 (p.S65_A66delinsLDQY). While this exact variant has not been described, similar in-frame insertion pathogenic changes in *KRAS* have been functionally demonstrated to be oncogenic. The patient did not undergo additional treatment and is followed with serial exams and MRIs. On post-operative imaging there was a small focus noted concerning for possible residual tumor that will continue to be monitored closely.

Conclusion: This is a case of a patient with a pilocytic astrocytoma with a novel pathogenic mutation in the KRAS gene. Further studies are needed to understand the diagnostic and therapeutic consequences of this previously unidentified gene mutation.

POSTER # 274 | PEDIATRIC GERMINOMA PRESENTING WITH A NORMAL MRI

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Background: Precocious puberty is classified as the development of secondary sexual characteristics before eight years of age in females and nine years of age in males. Signs of precocious puberty warrant urgent evaluation, especially in males who are more likely to have an underlying pathologic diagnosis. Malignancy should be considered in the differential diagnosis when evaluating children with precocious puberty.

Objectives: We describe the case of a six-year-old boy with rapid onset precocious puberty associated with elevated serum beta human chorionic gonadotropin (b-HCG) and testosterone.

Design/Method: Case presentation

Results: A six-year-old boy initially presented to pediatric endocrinology clinic with polyuria and polydipsia. He was diagnosed with central diabetes insipidus (DI) and started vasopressin treatment. In three to four weeks, he was evaluated for facial hair growth and pubarche. X-ray imaging of the hand/wrist showed an advanced bone age. Due to concern for rapid onset precocious puberty, an MRI of the brain and spine

were performed, which was unremarkable. Laboratory workup was significant for elevated serum B-HCG (22 IU/L) and serum testosterone (665 ng/dl). A testicular ultrasound, CT chest/abdomen/pelvis, and PET scan were obtained to evaluate for an extracranial hormone-secreting tumor and were found to be normal. His presentation, despite a normal MRI brain, remained concerning for an intracranial process. CSF was obtained via lumbar puncture and showed normal AFP (<1 ng/mL), elevated B-HCG (75 IU/L), and elevated WBC (10/mcl), suggestive of a possible intracranial germinoma. A repeat MRI brain was performed two months later which showed a thickened pituitary infundibulum (4 mm in largest dimension) with new enhancement and absence of the pituitary bright spot. A diagnosis of CNS germinoma was rendered. Chemotherapy (carboplatin, etoposide) was initiated for a planned four cycles. Following two cycles of chemotherapy, serum B-HCG normalized (CSF evaluation was deferred at this time point), and his pituitary infundibulum returned to a normal size with decreased enhancement.

Conclusion: A diagnosis of germ cell tumor should be considered when evaluating children with precocious puberty and/or DI, especially in the setting of elevated serum and/CSF B-HCG. Prompt evaluation is warranted to decrease the potential of metastatic spread. Elevated B-HCG in the setting of DI and/or precocious puberty warrants prompt evaluation for neoplasm, including germ cell tumors, even in individuals with normal imaging. The presence of endocrinologic abnormalities and elevated tumor markers may precede detectable MRI findings; serial imaging and close follow-up are warranted in these cases.

POSTER # 301 | HEALTH INEQUITIES AND THE USE OF HEMATOLOGIC TESTING IN CASES OF SUSPECTED CHILD ABUSE

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Background: The presenting symptoms of suspected non-accidental trauma (NAT) can also be features of an underlying bleeding disorder. The American Academy of Pediatrics urges a thoughtful approach to bleeding evaluation in children with suspected NAT to avoid unnecessary testing and limit the false attribution of traumatic injuries to medical causes.

Objectives: To evaluate hematologic testing in suspected NAT, to determine frequency and factors associated with expanded hematologic testing (EHT).

Design/Method: We analyzed data from the Pediatric Health Information System, an administrative database of US children's hospitals. We included inpatient pediatric patients (<18 years old) with primary or secondary ICD-9 or ICD-10 codes for child physical abuse, shaken infant syndrome, unspecified child maltreatment or child neglect or abandonment from 2007 through 2017. Only the first encounter per patient was included, patients with known bleeding disorders were excluded. We evaluated demographics, use of hematologic testing, hematology consultation and incidence of subsequent diagnoses of bleeding disorders through descriptive and statistical analysis. We utilized multivariate regression to evaluate factors associated with EHT and hematology consultation.

Results: There were 15,530 patients meeting inclusion criteria with mean age 1.56 years, 61% of patients non-white race and 14% of patients Hispanic ethnicity. Laboratory data was available for 14,823 patients. Fracture, bruising, ICH and retinal hemorrhages were documented in 50%, 14%, 1.8% and 19% of patients respectively. Hematology testing was sent in majority of the patients (91%). EHT (testing beyond CBC, PT, PTT, INR, Factor VIII, Factor XI, Ristocetin cofactor and von Willebrand antigen) was obtained in 4,655 encounters (31.4%). Hematology consultation was obtained in 294 cases (1.98%), consultation was associated with increased odds of EHT (OR 15.51, p <0.001). On multivariate analysis, EHT was significantly associated with younger age, presenting symptom, hematology consultation, Hispanic ethnicity, geographic region, private insurance and increased injury severity and mortality risk scores (p <0.001 for all). Non-white race was not associated with EHT. A bleeding disorder was later identified in 76 patients (0.5%), of whom 9.21% presented with fracture, 38.16% with retinal hemorrhage and 26.32% with multiple injuries suspicious for NAT. EHT was associated with a significant increase in laboratory associated charges (median $6495 vs $1826, p <0.001).

Conclusion: Our data show a low incidence of bleeding disorders diagnosed in children with suspected NAT despite EHT. This leads to significant expense. Health inequities may contribute to the selection of patient groups for EHT. Further studies are needed to address thehealth inequities and develop guidelines for judicious use of testing.

POSTER # 302 | COUGH PEDS—CLINICAL OUTCOMES OF A COMBINED GENETICS AND HEMATOLOGY PEDIATRIC CLINIC

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Background: Multidisciplinary clinics (combined clinics) are becoming more visible and have been shown to have multiple benefits. There are many goals of multidisciplinary clinics including increasing access to subspecialty care, offering a standard model of care and testing, and increasing patient engagement with the medical team. A large benefit of multidisciplinary clinics is the ability for a patient to see multiple specialists in one place and for those specialists to be able to communicate in real time.

Objectives: The combined pediatric hematology/genetics clinic at the University of Maryland Children's Hospital began in 2013 and offers services to a wide variety of patients. This study aimed to highlight some benefits of this combined clinic. We hypothesized that a combined clinic would shorten time to access of specialized care and provide comprehensive management for certain conditions such as Ehlers-Danlos syndrome (EDS).

Design/Method: A database was created in 2013 consisting of patients who were seen in the combined pediatric hematology/genetics clinic.

The database was used to select all patients who were seen for concerns for connective tissue disorders including EDS. Chart review was completed for each patient and data was collected from 2013 to present.

Results: Fifteen patients were seen in the combined pediatric hematology/genetics clinic due to concerns for EDS. The average time between making a referral to the clinic and clinic appointment was five months. Nine patients received a diagnosis of EDS, and five patients had family members who received a new likely diagnosis of EDS. Other needs identified during these visits included recommendations for follow up, referral to other specialists, imaging studies, and further genetic testing. During each visit, a thorough medical and family history was obtained and discussed, previous lab results were reviewed if applicable, and anticipatory guidance was provided.

Conclusion: Our unique combined pediatric hematology/genetics clinic has provided multiple benefits for patients and families. Geneticists are in high demand, and the average wait time for a new pediatric patient to see a geneticist at this institution is seven to twelve months. Patients who were referred to the combined clinic were able to see a geneticist on average within five months, with the shortest wait time being one month after referral. Similar to other multidisciplinary clinics, this clinic has been able to increase access to subspecialty care and tailor testing and treatment with the goal of improving patient knowledge, care, and outcomes.

POSTER # 303 | STANDARDIZING PREMEDICATION FOR BLOOD PRODUCT TRANSFUSIONS: A PROSPECTIVE QI INITIATIVE

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Background: Blood product transfusions are common in pediatric oncology. Transfusion-related reactions, though uncommon, range in severity from mild allergy to severe anaphylaxis. Despite lacking clear benefit, many patients receive premedication (such as with acetaminophen, antihistamines, and/or hydrocortisone) to prevent transfusion reactions, resulting in practice variability, unnecessary treatments, and additional costs.

Objectives: To develop and implement an evidence-based algorithm for blood product premedication for pediatric oncology patients at MSK Kids.

Design/Method: We developed an evidence-based algorithm for premedication prior to red blood cell (RBC) and platelet transfusions at MSK Kids. Premedication was recommended only in patients with a history of transfusion reaction and guidance was provided regarding which medication(s) to administer based on severity of previous transfusion reaction. Patients with a history of complex transfusion reactions were excluded. Descriptive statistics were used for analysis.

Results: Between January and April 2022, 127 patients met inclusion criteria, comprising 858 total transfusions (52.2% platelets, 47.8% RBCs). Median age at transfusion was 9.1 years (range 0.4 – 18.7), and 52% (n = 66) of patients were female. Each patient received a median of 3 transfusions (range 1-52). Guidelines for premedication per our algorithm were followed in 73% (626/858) of transfusions. Premedication was administered in 28.6% of total transfusions (245/858) following algorithm introduction, compared to 72.0% (434/603) of total transfusions prior. Patients with a previous history of transfusion reaction received 287 transfusions, of which 71.4% (205/287) were premedicated. Patients without a history of previous transfusion reactions received 565 transfusions, of which 6.7% (38/565) were premedicated; this is markedly lower compared with the 57.5% (222/386) of patients with no history of transfusion reaction who received premedication prior to guideline implementation.

Transfusion reactions occurred in 1.5% (13/858) of transfusions compared to 3.2% prior to guideline implementation. Reactions included: rash/pruritus (n = 9), fever (n = 6), and/or respiratory symptoms (n = 1). There was no significant difference in the incidence of transfusion reactions between those that were premedicated (0.8%) versus those that were not (1.8%; p = 0.45 by Chi-squared test). No transfusions led to severe sequelae, including anaphylaxis, sepsis, acute hemolysis, or TRALI, and no patient required admission to the intensive care unit due to transfusion reaction.

Conclusion: Standardization of an evidence-based algorithm and provider education resulted in decreased premedication for blood product transfusions without an increase in frequency or severity of transfusion reactions. Based on this analysis, we will expand education to improve adherence to our algorithm and implement broader institution-wide guidelines based on our results to standardize practice throughout the institution.

POSTER # 304 | A 5-YEAR QUALITY ASSESSMENT OF OUTPATIENT BLOOD PRODUCT TRANSFUSIONS IN PEDIATRIC PATIENTS:2014-2018

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Background: Transfusion involves the practice of replacing blood components to treat symptoms or replacing deficient blood components.[1] Transfusion guidelines with blood typing and strict infectious controls have all been developed to decrease transfusion-related adverse events (AE). Pediatric transfusion reactions have been reported at 0.538% (538/100,000).[2] A cohort study among 35 academic children's hospitals from 2001 to 2003 analyzed 51,720 pediatric patients who received transfusions and found that 492 (0.95%) of patients who received 793 blood product transfusions experienced complications from the administered blood product.[3] Each blood product transfusion has its own risk of AE. The American Association of Blood Banks found that the approximate per unit risk for platelet

transfusions was 7% for fevers, 2% for allergic reaction, and 0.0013% for bacterial sepsis.[4]

Objectives: A five-year retrospective, single-institution review of pediatric outpatient blood product transfusions to evaluate clinical safety.

Design/Method: With IRB approval, a retrospective single-institution analysis of pediatric blood product transfusions completed between January 2014 and December 2018 was performed. Transfusions were performed in the outpatient hematotherapy suite at Westchester Medical Center. Blood products were provided by the hospital blood bank and verified by three people or two people and a computer-based system. Products were transfused using an IV pump over one to three hours.

Results: From January 2014 to December 2018, there were 1067 total transfusions in pediatric patients. Blood product transfusions consisted of red blood cells (RBCs) (51%), platelets (plts) (32%), factor products (14%) followed by plasma (2.34%). No patient had a life-threatening event related to the transfusion. There were 5 moderate AEs (0.46%) that included fever (80%) and rash (20%). In the patients that spiked a fever, 1 patient received plts, 1 patient received RBCs, 1 patient received both RBCs and plts, and 1 patient received factor in the form of WinRho. Transient adverse events included nausea and mild allergic reaction.

Conclusion: The AE review demonstrates that outpatient blood product transfusion is safe and AE incidence of 0.46% is comparable to previously published benchmarks. Of note, the AE rate in pediatric patients is observed after all patients were pre-medicated. Although the AE percentage of 0.46% is low, it would be interesting to study platelet product characteristics such as the source, dose, duration of storage of platelets, and ABO matching status that might contribute to transfusion-related adverse events.

1. Connell, Primary Care, 2016
2. Vossoughi S, Transfusion, 2018
3. Wong, Journal of Clinical Apheresis, 2012
4. Kaufman, Annals of Internal Medicine, 2015

POSTER # 305 | T-LARGE GRANULAR LYMPHOCYTE FREQUENCIES AND CORRELATES IN DISEASE STATES DETECTED BY FLOW CYTOMETRY

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Background: T large granular lymphocytes (T-LGL), though not completely understood, have identified unique roles in cellular immune system. They are characterized by dim CD5 staining and frequently express CD8 and T cell receptor alpha/beta chain. Increased presence in peripheral blood (PB) clonal T-LGL populations has been associated with various entities including aplastic anemia, myelodysplastic syndrome, dasatinib use, solid organ recipients, and lymphomas in adults. We have previously demonstrated clonal PB T-LGL proliferations in pediatric immunodysregulation conditions. However, presence of T-LGL populations has not been studied in broad spectrum pediatric pathologies.

Objectives: To investigate frequencies and correlates of T-LGL populations in the pediatric and young adult populations with various disease states.

Design/Method: Lymphocyte subsets including T-LGL are investigated retrospectively by reviewing PB multiparameter flow cytometric analysis using two different protocols (leukemia immunophenotyping and immune profile) in samples submitted to our laboratory with various indications over a four-year period. Associations with clinical and laboratory findings with T-LGL populations sizes are sought.

Results: Five hundred eighteen cases were reviewed with a mean age of 9 (0-33), 238 female and 280 males. Mean T-LGL was 14 $\pm$ 10% (1-67%) of the T cell population in the entire group. Top five most common indications, in order, are thrombocytopenia/idiopathic thrombocytopenic purpura (12.8%), visualization of suspicious cells on PB slide review (12.6%), leukopenia/neutropenia (8.6%), lymphadenopathy (7.1%) and pancytopenia (6.9%) constituting 48% of all cases. The T-LGL percentages correlated with absolute T-LGL values ($R = 0.459$; $P < 0.01$). There was a positive correlation between T-LGL and CD8+/DR+ ($R = 0.570$; $P < 0.01$), and CD8+/CD11b+ ($R = 0.597$; $P < 0.01$) expression pointing at an activated cytotoxic phenotype. The highest T-LGL populations were seen in the following indication categories: 1. Bone marrow transplant recipients with or without graft versus host disease (T-LGL of 23.7%); 2. Evans syndrome (23.7%); 3. Lymphoma (20.6%) and 4. EBV infection (20.4%), all with underlying immunodysregulation pathology. T-LGL content was higher in these four groups of cases associated with immunodysregulation ($N = 46$) when compared with the 'visualization of suspicious cells on PB slide review' as the indication group ($N = 66$) (22.6% vs. 13.9%; $P < 0.01$).

Conclusion: We show that PB T-LGL subset constitutes an average of 14% of the T cells in pediatric and young adult patients with several different disease states. These cells typically have an activated cytotoxic T cell phenotype and a higher relative presence in cases with immunodysregulation background. The results of this study may serve as a reference for enigmatic T-LGL research efforts.

POSTER # 306 | SURVEY-BASED ASSESSMENT OF QUALITY OF LIFE AND UNMET NEEDS OF PEOPLE LIVING WITH CHRONIC NEUTROPENIA

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Background: Chronic neutropenia encompasses multiple blood disorders with different etiologies resulting in absolute neutrophil count $<1500/\mu L$ for >3 months. Granulocyte colony-stimulating factor (G-CSF) treatment can improve clinical outcomes, but chronic use is associated with side effects.

Objectives: Survey and assess perspectives of patients/caregivers (P/C) and health care professionals (HCP) on unmet needs, treatment

experiences, impact of disease on daily life, and quality of life (QoL) of people living with chronic neutropenic (CN) disorders.

Design/Method: Respondents were recruited via direct emails and outreach to chronic neutropenia Facebook and patient advocacy groups. Patients with chemotherapy-induced neutropenia were ineligible. P/C (n = 100) and HCP (n = 10) completed ≤29 and ≤13 survey questions, respectively.

Results: P/C aged ≥2 years were included. Neutropenic etiologies included idiopathic (29%), congenital (18%), cyclic (20%), autoimmune (19%), and unknown (14%). When asked about symptoms that most impacted the health of a person with a CN disorder, P/C listed fatigue (61%) and frequent infections (37%), while HCP listed mouth sores (70%) and frequent/recurrent infections (70%). HCP and P/C identified G-CSF as the most frequently prescribed (80%) and taken medication (51%), respectively. Thirty-five percent of P/C reported not taking any medication currently. G-CSF was also the most common medication taken irrespective of the neutropenia etiology (idiopathic, 15%; congenital, 15%; cyclic, 12%). Top patient-reported issues with G-CSF treatment were bone pain (76%) and muscle pain/cramps (75%); 51% reported adjusting/stopping G-CSF (43% due to side effects such as bone pain). Additionally, 50% of HCP noted G-CSF as having the most difficult to manage side effects. When asked what treatment improvements were needed, P/C listed fewer/less frequent severe infections (50%) and less fatigue (48%), while HCP listed how medication is administered (60%) and fewer/less frequent severe infections (60%). Additionally, while P/C ranked less fatigue (20%) as the priority treatment need, HCP ranked fewer and/or less frequent severe infections as the priority treatment need.

Conclusion: Results showed differing perspectives between P/C and HCP on the impact of chronic neutropenia and treatment on QoL. Although both groups reported similar symptom prevalence and improvement needs, perceptions of patient experience with current treatment differed. P/C cited fatigue as the most impactful symptom and fatigue reduction as a priority treatment need, while HCP ranked fatigue at the bottom or not at all. Additional studies are needed to understand unmet needs of people living with CN disorders and reasons for differing perspectives.

Legassie, ASH, 2022

Funded by X4 Pharmaceuticals, Inc.

POSTER # 307 | RETROSPECTIVE CLAIMS DATABASE ANALYSIS TO EXPLORE THE PREVALENCE OF CHRONIC NEUTROPENIA IN THE US

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Background: Chronic neutropenia encompasses different blood disorders characterized by low levels of peripheral blood neutrophils, with absolute neutrophil count ≤1500/uL for>3 months. The common causes of chronic neutropenic (CN) disorders include congenital, cyclic, and idiopathic neutropenia. Moderate and severe CN disorders are associated with increased risk of recurrent and/or severe infections and deterioration of quality of life in affected individuals. There are limited data available regarding the prevalence of CN disorders in the US.

Objectives: Examine prevalence of CN disorders in the US using retrospective analysis of a large US claims database.

Design/Method: This retrospective analysis of US claims data for people diagnosed with neutropenia was designed to project the prevalence of CN disorders during calendar years 2018, 2019, and 2021. The analysis used longitudinal prescription and office-based claims data with a 2-year lookback period. The year 2020 was excluded from this analysis owing to anticipated reduced claims during the COVID-19 pandemic. People diagnosed with congenital, cyclic, and idiopathic neutropenia were identified using the earliest relevant diagnosis claim based on *International Statistical Classification of Diseases, Tenth Revision (ICD-10)* codes in the calendar year of interest as the index date with a 13- to 24-month lookback period to confirm chronicity. For people who had multiple *ICD-10* codes, a hierarchical order (cyclic>congenital>idiopathic) was established to avoid double counting. People with neutropenia resulting from secondary causes were excluded.

Results: The projected prevalence of congenital (D70.0), cyclic (D70.4), and idiopathic neutropenia (D70.8, D70.9) were 1787, 4991, and 33,965, respectively, in 2018 (N = 40,743); 2081, 5426, and 39,257 in 2019 (N = 46,764); and 2102, 4839, and 40,636 in 2021 (N = 47,576). People with CN disorders were more likely to be female (65%), and <50% see hematologists or immunologists. Across all 3 neutropenia types, most people were aged ≥18 years (≈91%), while a lower proportion were aged 12-17 years (≈3%) and <12 years (≈6%). Among people aged <12 years, diagnoses of congenital neutropenia were more common (13%–20%) than cyclic (5%–8%) or idiopathic neutropenia (5%–6%).

Conclusion: Results establish a projected prevalence of CN disorders close to 50,000 in the US. Idiopathic neutropenia was the most common CN disorder, cyclic was second, and most people were aged ≥18 years. Additional studies are needed to evaluate severity and number of infections and the impact on quality of life of people living with CN disorders in the US.

Tollefsen, ASH, 2022.

Funded by X4 Pharmaceuticals, Inc.

POSTER # 308 | A PHASE 1B, OPEN-LABEL STUDY OF MAVORIXAFOR IN PATIENTS WITH CHRONIC NEUTROPENIC DISORDERS

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Background: Chronic neutropenia encompasses multiple blood disorders with different etiologies resulting in absolute neutrophil count (ANC) <1500/μL for>3 months. Mavorixafor is an investigational oral

antagonist of CXCR4 in clinical development for treatment of chronic neutropenic (CN) disorders.

Objectives: To report results of a phase 1b, open-label, multicenter trial (NCT04154488) evaluating the safety and tolerability of mavorixafor alone or with concurrent granulocyte colony-stimulating factor (G-CSF) across several CN disorders.

Design/Method: Participants aged ≥12 years with diagnosis of chronic idiopathic neutropenia (CIN), congenital neutropenia, or cyclic neutropenia (CYN) ≥6 months prior and ANC ≤1000/μL at screening visit or on G-CSF with ANC <10,000/μL were included. Participants received 1 dose of mavorixafor (> 50 kg, 400 mg; ≤50 kg, 200 mg) alone or with concurrent G-CSF on day 1. ANC levels were assessed over 6 to 8 hours on day −1 (baseline) and day 1 (treatment day). Primary end points were change in ANC levels from day −1 to day 1 and safety and tolerability at day 30.

Results: As of July 2022, 25 participants (CIN, n = 16; congenital neutropenia, n = 6; CYN, n = 3) completed post-dose assessments. An at least 2-fold mean average increase in ANC levels from day −1 to day 1 was observed in most participants after 1 dose of mavorixafor regardless of type of CN disorder studied (93.8%, 66.7%, and 66.7% of participants with CIN, congenital neutropenia, and CYN, respectively) or G-CSF use (not on G-CSF, 100.0% [n = 8/8]; on G-CSF, 76.5% [n = 13/17]). In a subgroup analysis of participants not on G-CSF, mean peak ANC levels increased by 2.4×10^3 cells/μL on day 1 vs day −1. Similar trends were observed in participants dosed with G-CSF in the morning; the mean peak ANC levels increased by 4.1×10^3 cells/μL on day 1 vs day −1. Most (98.5%) treatment-emergent adverse events (AEs) were mild (81.5%) or moderate (16.9%). No treatment-related serious AEs were reported.

Conclusion: Meaningful increases in ANC were observed on day 1 in all participants treated with 1 dose of mavorixafor. Responses were observed regardless of G-CSF use or type of CN disorder. Mavorixafor was well tolerated; most AEs were mild or moderate. Based on these results, the phase 1b trial has been expanded to continue to a phase 2 trial to assess safety and tolerability of mavorixafor alone or with concurrent G-CSF for up to 6 months and to enroll ≤25 additional participants with CN disorders.

Warren, ASH, 2022

Funded by X4 Pharmaceuticals, Inc.

POSTER # 309 | SUSTAINED RESPONSE AMONG PEDIATRIC PATIENTS WITH ITP TREATED WITH THROMBOPOIETIN RECEPTOR AGONISTS

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Background: Immune thrombocytopenia (ITP) is the most common acquired bleeding disorder in children, and patients developing persistent or chronic disease, particularly after failing standard front-line therapies, require alternative treatment approaches. The thrombopoietin receptor agonists (TPO-RAs) eltrombopag and romiplostim are increasingly used in this population of patients, with consideration recommended prior to rituximab or splenectomy in the most recent American Society of Hematology (ASH) guidelines for ITP (1). Furthermore, there is evidence of sustained response in up to 1/3 of adults with ITP following discontinuation of TPO-RA therapy. Despite this, there is scarce data reporting long-term outcomes or sustained response with TPO-RA therapy in pediatric ITP.

Objectives: To describe clinical outcomes related to TPO-RA use among pediatric ITP, and chiefly, to define the incidence of sustained response at 6 months following TPO-RA discontinuation in children with persistent or chronic ITP who achieved early response to TPO-RA therapy.

Design/Method: We completed a retrospective chart review of pediatric patients (ages 0-21) diagnosed with ITP and treated with eltrombopag or romiplostim for at least 3 months' duration throughout a 10-year period (2012 – 2022) at a large pediatric tertiary care center. Treatment outcomes were evaluated utilizing platelet response criteria (platelet count $\geq 30 \times 10^9$/L and at least doubling of the baseline count in accordance with ASH ITP guidelines) at baseline, 4 weeks, 12 weeks, and 24 weeks.

Results: Seventy-five patients initiated TPO-RA therapy during the persistent (n = 28) or chronic (n = 47) phase of ITP, at a median age of 11.5 years. Twenty-nine (39%) received eltrombopag alone, 22 (29%) received romiplostim alone, and 24 (32%) received both. Median time from ITP diagnosis to initiation of TPO-RA therapy was 8.5 months, and median duration of TPO-RA therapy was 28 months. Excluding those who received rituximab therapy or splenectomy within 1 year of TPO-RA discontinuation (n = 7) and those who never demonstrated TPO-RA response throughout a minimum 12 weeks of therapy (n = 6), 34% (n = 21) demonstrated sustained response 6 months following discontinuation of TPO-RA therapy. Among the remaining patients, 56% (n = 35) were still receiving TPO-RA therapy at the time of analysis and 10% (n = 6) had insufficient follow-up data to determine sustained response following TPO-RA discontinuation.

Conclusion: The incidence of sustained response following TPO-RA therapy in an institutional pediatric ITP cohort (34%), previously unreported, appears consistent with that reported in adult ITP. This merits further study in the future, and could better guide the clinical management of children with ITP.

(1) Neunert, *Blood Adv*, 2019.

POSTER # 310 | EXPERIENCES WITH FATIGUE AMONG CHILDREN AND ADOLESCENTS WITH ITP: DATA FROM THE ITP STUDY REGISTRY

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Background: Immune thrombocytopenia (ITP) is an autoimmune bleeding condition associated with poor quality of life and fatigue. Limited information exists on how different pediatric age groups experience fatigue. Understanding this difference between children and adolescents may help individualize approaches to management.

Objectives: Prospective registry data were utilized to report and compare 28 children (age 1-12) and 16 adolescents (13-18) with ITP in how they experience factors that influence fatigue.

Design/Method: The ITP Natural History Study is a prospective patient-consented web-based registry that collects data on ITP diagnosis, treatment, management, quality of life, and clinician reporting. Forty-four participants (£18 years) were enrolled through November 2022. Survey responses were based on experiences within the prior seven days. Data were analyzed using Pearson Chi-square and Fisher exact tests.

Results: Most participants were male (27; 61%) from the United States (38; 86%). International participants (6; 14%) were from Canada, India, Mexico, and Australia. Of thirty-three participants who reported the date of diagnosis, all (33/33) had chronic ITP with 73% (24/33) reporting they had ITP for more than two years.

Fatigue: Both children and adolescents reported feeling 'tired easily' (71.4% (20/28) vs. 75% (12/16), respectively). More adolescents (62.5% (10/16)) felt 'too tired for sports/exercise' compared to children (48.1% (13/27)), and 'too tired for things they usually enjoyed' (56.3% (9/16) vs. 39.3% (11/28)). More adolescents (56.3% (9/16)) felt 'too tired to pay attention' during the day than children (38.5% (10/26)). Children felt 'too tired to do schoolwork' significantly less frequently (44% (11/25) vs. 81.3% (13/16), $p = 0.025$).

Potential fatigue influencers: A greater number of adolescents (50% (8/16) vs. 22.2% (6/27) in children) reported worry when going to bed ($X^2 = 3.53$ p (<0.10) = 0.06). A greater proportion of adolescents also reported they 'could not stop feeling sad' (25% (4/16) vs. 11.5% (3/36)) and felt pain at bedtime (42.9% (6/14) vs. 22.2% (4/18)), though the source of pain was not assessed.

Conclusion: Most children and adolescents with ITP reported fatigue, underscoring that fatigue is a symptom associated with pediatric ITP. While there were marked differences between children and adolescents, many differences were not statistically significant likely due to the small sample size. Adolescents struggled more frequently than children with 'schoolwork completion' suggesting they may have a reduced capacity to handle an increased workload, perhaps due to fatigue. Adolescents may have unique needs compared to younger patients with ITP. Future investigations will evaluate how treatment impacts fatigue in this cohort.

POSTER # 311 | SERUM CYTOKINE EXPRESSION IN PEDIATRIC PATIENTS WITH IMMUNE THROMBOCYTOPENIA (ITP)

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Background: Despite significant advances in the understanding of immune thrombocytopenia (ITP) pathogenesis, including an abundance of evidence for T cell dysregulation, studies have not yielded definitive or reproducible evidence for the use of particular serum biomarkers for clinical prognostication in ITP. Predicting clinical outcomes such as treatment response or spontaneous resolution with a readily obtainable serum assay would be invaluable in the management of ITP.

Objectives: To characterize cytokine expression in children with different phases of ITP.

Design/Method: This prospective pilot study evaluated 13 serum cytokines by quantitative multiplex bead assay at a single time point in children with ITP at our center between July—November 2022. This included Interleukin-1beta, Interleukin-2, soluble Interleukin-2 Receptor (sIL-2R), Interleukin-4, Interleukin-5, Interleukin-6, Interleukin-8, Interleukin-10, Interleukin-12, Interleukin-13, Interleukin-17, TNF-alpha, and IFN-gamma.

Results: Nineteen children were included (8 patients with newly diagnosed ITP, 4 patients with persistent ITP, and 7 patients with chronic ITP). At the time of cytokine analysis, patients with newly diagnosed ITP were significantly younger (newly diagnosed vs persistent vs chronic: median age 4 vs 11 vs 14 years old, $p < 0.01$) with significantly lower platelet counts (7 vs 196 vs 104 K/uL, $p = 0.05$) and tended to have higher Buchanan and Adix bleeding scores (Grade 1 or higher: 88% vs 50% vs 14%, $p = 0.09$). Soluble Interleukin-2 Receptor (sIL-2R) was elevated in 50% of patients with newly diagnosed ITP ($n = 4$) and 14% of patients with chronic ITP ($n = 1$). Patients with newly diagnosed ITP had a higher continuous sIL-2R which did not meet significance (median level 888 vs 681 vs 584 pg/mL, $p = 0.09$). Interleukin-10 was elevated in 50% of patients with newly diagnosed ITP ($n = 4$), 25% of patients with persistent ITP ($n = 1$) and 71% of patients with chronic ITP ($n = 5$). Interleukin-13 was elevated in 50% of patients with persistent ITP ($n = 2$) and no other patients ($p = 0.04$). There were no significant differences between patients with the other cytokines tested. There was a significant difference in the distribution of bleeding scores based on sIL-2R level ($p = 0.03$). There were no identified correlations with cytokine level and age at or platelet count at diagnosis.

Conclusion: Our data provide further evidence of T cell involvement in ITP pathogenesis given elevation of sIL-2R, Interleukin-10 and Interleukin-13 in patients with ITP. There were notable differences in cytokine expression between patients with newly diagnosed, persistent, and chronic ITP. These results support larger studies to assess clinical utility of these biomarkers in ITP prognostication and management.

POSTER # 312 | INTRAVENOUS IRON INFUSIONS IN PEDIATRICS PATIENTS: A RETROSPECTIVE REVIEW OF EFFICACY AND SAFETY

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Background: Iron deficiency is the most common nutritional deficiency and the leading cause of iron deficiency anemia (IDA) in children worldwide. IDA is treatable with iron supplementation, commonly oral therapy. However, adherence is poor due to gastrointestinal side effects. In adult patients, IV iron is frequently used for patients who were unable to tolerate oral iron side effects. IV iron therapy is less commonly utilized in pediatric patients due to limited safety and efficacy data.

Objectives: This single-institution retrospective chart review of pediatric patients analyzed the safety, efficacy, and compliance of IV iron infusions compared to oral iron therapy.

Design/Method: We reviewed medical records of patients aged 1-21 with various etiologies of IDA who received at least one IV iron infusion at Cooper University Hospital between 2016 and 202. A paired t-test compared lab values for hemoglobin (Hgb), mean corpuscular volume (MCV), red blood cell (RBC), red cell distribution width (RDW), ferritin, total iron binding capacity (TIBC), iron stores, and iron saturation (% saturation). These values were also compared across age groups (<6, 6-12, 13-17, ≥18 years of age), races, and etiologies of IDA. We analyzed adherence and adverse effects to both oral iron and IV infusions.

Results: Our study had 107 subjects with an average age of 12.7 years (± 4.91), of which 81.3% were female and 18.7% were male. Hgb and iron parameters (ferritin, iron, and iron saturation) between pre-infusion one and post-final infusion showed significant improvement. In each age group, only Hgb significantly improved. When comparing improvement by race and etiology, white race and menorrhagia demonstrated significant improvement across all lab values ($p < 0.05$). Of the 107 patients, at least 70.1% were adherent to IV iron infusions and three experienced adverse reactions including rash, IV infiltration, and thrombophlebitis. Among the 86 patients initially prescribed oral iron therapy, 43.5% were adherent but 77.9% had adverse effects, of which 91% were GI-related.

Conclusion: Our study demonstrated that IV iron infusions administered to pediatric patients with IDA were safe and effective. Several hematologic parameters for IDA significantly improved, including adherence, when compared to oral iron. As a single institution study, the results are limited to a regional patient population. Another limitation is that laboratory values were not collected at the third infusion for every patient due to difficult IV access. Future studies could compare patient adherence with multiple doses of IV infusions versus other single-dosing IV iron formulations.

POSTER # 313 | ALGORITHM FOR MANAGEMENT OF ANEMIA DUE TO HEAVY MENSTRUAL BLEEDING IN THE EMERGENCY DEPARTMENT

Luisanna Sanchez, Sarah Kappa, Chelsea Daignault, Josaura Fernandez-Sanchez, Cecile Karsenty, Madeleine O'Keefe, Meghan Shekar, Leander Timothy, Gladstone Airewele, YoungNa Lee-Kim, Mehmet Okcu, Clay Cohen, Jacquelyn Powers

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Background: Iron deficiency anemia (IDA) secondary to heavy menstrual bleeding (HMB) is estimated to affect approximately 60% of post-menarchal women worldwide. Many patients initially present to the Emergency Department (ED) due to symptomatic anemia and ongoing blood loss. Despite readily available hormone, anti-fibrinolytic, and iron therapies, no consensus guidelines exist for these patients.

Objectives: As part of a multidisciplinary quality improvement (QI) project, we developed an algorithm to standardize the care of post-menarchal patients less than 21 years of age presenting to the ED with anemia due to HMB.

Design/Method: A literature review was performed to identify existing guidelines or clinical algorithms for the management of IDA in post-menarchal patients presenting to the ED. To obtain baseline data, a retrospective chart review of ED encounters for post-menarchal patients diagnosed with IDA secondary to HMB at Texas Children's Hospital in Houston, Texas from January to December 2021 was conducted. A 14-question survey regarding laboratory assessment, treatment, and follow-up recommendations was sent to Hematology and Gynecology providers involved in the management of such patients.

Using this formative data, a draft algorithm was created. The algorithm was presented to Hematology, Gynecology, Emergency Department, and Hospital Medicine to obtain feedback with revisions incorporated in an iterative manner. The final version was incorporated into an existing institutional Heavy Menstrual Bleeding Practice Standard and approved by the Division of Hematology/Oncology's Practice Standard Committee. Implementation began in November 2022.

Results: Baseline data of 20 patients (median age 15 years, 60% White, 55% Latinx, median hemoglobin 5.4 (g/dL), median ferritin 3 (ng/ml)) revealed that 9/20 (45%) had incomplete laboratory assessment, 5/20 (25%) did not have appropriate hematology or gynecology consultation, and 45% (9/20) received inadequate iron therapy.

A total of 39 survey evaluations were completed by 66% (32/48) of Hematology and 70% (7/10) Gynecology providers, respectively. Majority consensus was achieved regarding recommendation for hematology consult (90%), transfusion threshold (50%, when hemoglobin is ≤6 g/dL or symptomatic) and initiation of IDA treatment (100%). Aspects of the algorithm for which consensus was not identified via surveys were adjudicated via group discussion and consensus.

Conclusion: Stakeholder input identified key drivers and informed the creation of a multi-disciplinary ED-based algorithm for evaluation and treatment of adolescent patients presenting with anemia due to HMB. Model for Improvement Methodology will be utilized to assess algorithm utilization and adherence, including laboratory assessment and therapy choice (outcome measures), provider documentation of the algorithm (process measure), and ED length-of-stay (balancing measure).

POSTER # 314 | HEALTH-RELATED QUALITY OF LIFE, FATIGUE, AND PICA: DATA FROM THE IRON DEFICIENCY ANEMIA COHORT STUDY

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Background: Iron deficiency anemia (IDA) is associated with poor neurocognitive outcomes in young children, and fatigue and decreased concentration in adolescents. Despite these associations, characterization of the impact of IDA on health-related quality of life (HR-QoL) in children and adolescents is limited.

Objectives: To characterize HR-QoL, fatigue, and pica in infants, young children, and adolescent females with IDA utilizing established patient-reported outcome (PRO) measures, and to evaluate the association between hematologic response and change in PRO measures.

Design/Method: A prospective study was conducted of three patient cohorts: infants (age>12 to <24 months), young children (age>24 to <48 months), and adolescent females (age>13 to <18 years) at the Texas Children's Hematology Center in Houston. Eligible patients had microcytic anemia and clinical diagnosis of nutritional IDA (cohorts 1 and 2) or IDA due to menstrual blood loss (cohort 3) and were enrolled at their initial Hematology outpatient visit.

PRO measures included established Pediatric Quality of Life Inventory (PedsQL) and NIH Patient Reported Outcomes Measurement Information System (PROMIS) surveys and a novel pica survey. Surveys were administered via tablet or computer at standard-of-care visits (baseline, 1 month, and 3 months). IDA management was at the discretion of the primary provider. Demographic, clinical, laboratory, and treatment information were collected via a REDCap database. Within-subject changes in PROs scores were analyzed using repeated-measures ANOVA and 2-tailed Pearson correlation test.

Results: From 2018 to 2022, 102 subjects were enrolled; 66 had at least one follow-up visit and were included in the analysis. Median ages were 13.9 months (Cohort 1, n = 24), 25.5 months (Cohort 2, n = 17), and 14.5 years (Cohort 3, n = 25). Median baseline hemoglobin was 8.6 g/dL, 7.5 g/dL, and 8.6 g/dL respectively. Within each cohort, hemoglobin had a significant increase at each time point.

The infant cohort had a positive correlation between PedsQL scores and changes in hemoglobin over time ($r = 0.29$, $p = 0.04$). Cohorts 2 and 3 had aspects of PRO measures improve over time, but these did not significantly correlate with hemoglobin response. Parental fatigue assessment in adolescents correlated with change in hemoglobin ($r = 0.357$, $p = 0.033$). Pica was reported in 29%, 65%, and 40% of cohorts 1-3, respectively.

Conclusion: Established PRO measures demonstrated variable changes in infants, children, and adolescents with IDA over their treatment course. Such data may support the incorporation of appropriate PRO measures in future therapeutic iron trials for pediatric patients with IDA.

POSTER # 315 | THERAPEUTIC EFFECTS OF PARENTERAL IRON AFTER ORAL IRON IN TREATMENT OF FEMALES WITH IRON DEFICIENCY

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Background: Iron deficiency is the most common vitamin deficiency with a prevalence of 20% in adolescent females. Iron deficiency may be asymptomatic or present with pallor, syncope, and fatigue. Prolonged iron deficiency results in anemia and cognitive and behavioral changes. Oral iron is the first line of treatment. There is a high incidence of treatment failure with poor absorption and tolerance. Parenteral (IV) iron administration in symptomatic, non-anemic, iron deficient adolescent females has been shown to alleviate fatigue and improve ferritin (Sharma et al, American Journal of Hematology, 2016).

Objectives: To describe the tolerability and efficacy of oral versus IV iron in teen girls with low iron with or without anemia.

Design/Method: IRB approval was obtained from SIUSOM for a prospective study of adolescent females with low iron. Patients who weighed > 50 kg or with chronic illnesses were excluded. Patients with low hemoglobin (<12 g/dl) or low ferritin (<20 ng/ml) were included. The Pediatric QL Multidimensional Fatigue Scale was administered. Oral iron was given until demonstrated failure, defined as suboptimal improvement in symptoms and/or laboratory values after 1-2 months. Next, IV ferrous dextran (1 g) was administered. The treatment groups were re-evaluated 1, 2, and 6 months following IV iron. Results were analyzed using averages.

Results: Fifteen patients were enrolled from 2018 to 2020: 8 received oral iron only and 3 received IV iron and 4 were lost to follow up. Age ranged from 12-17 years. At enrollment, fatigue scores ranged from 26-54, average ferritin: 8, and average hemoglobin:10.5. Two month follow up fatigue scores ranged from 5-54, average ferritin: 21.9 and average hemoglobin: 12.6. Thirty-three percent of patients were lost to follow up after the 2-month mark. At 6 months, the oral iron group fatigue scores ranged: 2-57, average ferritin: 23.3, average hemoglobin:13.3. Due to treatment failure, 3 patients proceeded to IV iron with average ferritin: 147.9,139.3,112.3 and hemoglobin: 12.9, 13, 13.9 at 1, 2 and 6 months respectively. Due to poor response rate fatigue scores for IV iron arm could not be analyzed.

Conclusion: Given the small sample size, statistical significance was not reached. However, results trended in a positive direction with treatment using both forms of iron. This study was closed to accrual in 2022 as many patients with iron deficiency had previously been started on oral iron, not meeting eligibility. Loss to follow up was common. Treatment of iron deficiency in adolescent females remains a clinically important question and further studies are needed.

POSTER # 316 | DELETIONAL ALPHA GLOBIN GENE MUTATION TESTING YIELDS IN A PEDIATRIC POPULATION

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Background: Alpha thalassemia trait (ATT), an inherited mild microcytic anemia, and silent carrier, sometimes with microcytosis, affects up to 5% of the world's population and is often confused with iron deficiency anemia. Common deletional alpha globin gene (AGG) mutation analysis is a widely available PCR testing up to 95% of ATT due to deletion of 1 or both AGGs. The proportion of diagnoses confirmed by, and laboratory characteristics correlating with testing results for deletional AGG mutations are currently unknown.

Objectives: To determine factors which may help influence deletional AGG mutation testing, we compared characteristics of subjects with negative results (no gene deletion) to those with positive results (gene deletion).

Design/Method: Our descriptive, retrospective, electronic medical record review included subjects, aged 0-25 years treated at Yale New Haven Health, Connecticut, who had common deletional AGG mutation testing obtained between 1/1/2017 – 12/31/2022. Frequency of silent carrier and alpha thalassemia trait was calculated. Characteristics at the time of AGG testing included age, sex, pregnant vs non-pregnant females, and within 6 months of AGG testing included low ferritin, low hemoglobin, low mean corpuscular volume (MCV), abnormal hemoglobin electrophoresis, and elevated CRP or ESR.

Results: The 1436 subjects tested consisted of 157 (11%) males, 987 (69%) pregnant females and 292 (20%) non-pregnant females, with a median age of 23 yrs. We identified 480 (33%) subjects with positive results, of which 296 (62%) were silent carrier. The highest percentage of positive results was in males (69%) and lowest in pregnant females (21%). Although low MCV (62%) was more common in those with positive results compared to negative results (33%), abnormal hemoglobin electrophoresis (26%) was also more common among those with positive results compared to the negative group (6%). Overall low ferritin (43%) was found in both groups equally, as was elevated CRP (3 %) and ESR (36%). In both groups, low hemoglobin was similar in pregnant females (90% and 94%) yet lower in males (68% and 60%).

Conclusion: Common deletional AGG mutation testing identified one third of subjects with either ATT or silent carrier status. More pregnant females were tested compared to males/non-pregnant females with a lower percentage of positive results, perhaps due to the need to screen for at-risk pregnancies. Low MCV was more frequent among individuals with positive test results compared to negative. Deletional AGG testing is worthwhile in individuals with microcytosis.

POSTER # 318 | LENTIVIRAL-MEDIATED GENE THERAPY FOR SEVERE PYRUVATE KINASE DEFICIENCY: GLOBAL PHASE 1 STUDY RESULTS

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Background: Pyruvate kinase deficiency (PKD) is a rare inherited hemolytic anemia caused by mutations in the PKLR gene. Manifestations include anemia, splenomegaly and iron overload, which may be life-threatening. Currently available treatments are limited to a recently-approved enzyme activator or palliative therapies such as chronic blood transfusions, iron chelation therapy and splenectomy which are associated with significant side effects. A global Phase 1 clinical trial RP-L301-0119 (NCT04105166) is underway to evaluate lentiviral mediated hematopoietic stem and progenitor cell (HSPC)-targeted gene therapy for adults and children with severe PKD.

Objectives: To assess the safety and efficacy of RP-L301 for the treatment of patients with severe PKD.

Design/Method: Splenectomized patients with severe PKD (severe and/or transfusion-dependent anemia) are eligible. Following apheresis, HSPCs are transduced with lentiviral vector and cryopreserved. Myeloablative therapeutic drug monitoring-guided busulfan is administered and the gene therapy product (RP-L301) is thawed and infused. Patients are followed for safety assessments (including insertion site analysis [ISA]), and efficacy (genetic correction, decrease in transfusion requirements, significant improvement in anemia and reduction of hemolysis) for 2 years post-infusion.

Results: As of October 2022, 2 patients (age 31 and 47 years at enrollment) with severe anemia have received RP-L301. Patient 1 received 3.9x106 CD34+ cells/kg with mean vector copy number (VCN) of 2.73. Patient 2 received 2.4x106 CD34+ cells/kg with mean VCN of 2.08. Despite baseline hemoglobin (Hb) levels in the 7.0-7.5 g/dL range, at 24 months post-infusion both patients have normal-range hemoglobin (13.2 g/dL and 14.7 g/dL, respectively), and no red blood cell transfusion requirements post-engraftment. Other parameters of hemolysis and anemia (LDH, bilirubin, erythropoietin) are improved. Peripheral blood mononuclear cell (PBMC) vector copy numbers (VCNs) were 1.75 and 1.65 at 24- and 18-months, respectively. Both patients reported improved quality of life (QOL), also demonstrated by increases in both FACT-An and SF-36 scores, with marked improvement in SF-36 energy/fatigue, physical functioning, and general health components. No serious adverse events (SAEs) have been attributed to RP-L301. Hematopoietic reconstitution occurred within 2 weeks of administration. ISAs in PB and BM for both patients up to 12 months following therapy indicate highly polyclonal patterns.

Conclusion: Clinical efficacy and safety data indicate that RP-L301 is a potential treatment for patients with severe PKD, including those who did not derive benefit from available therapies. Robust and sustained efficacy in both patients at 24 months post-treatment was demonstrated by normalized hemoglobin, improved hemolysis parameters, and transfusion independence.

Supported by Rocket Pharmaceuticals, Inc.

POSTER # 319 | PEDIATRIC ERYTHROCYTOSIS: ETIOLOGIES AND CLINICAL CHARACTERISTICS

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Background: Erythrocytosis is defined as an increase in hemoglobin, hematocrit, or erythrocyte count above ranges adjusted for age, gender and altitude and may be the presenting sign of a serious underlying condition. Polycythemia vera (PV) is the most well-known primary cause of erythrocytosis due to its predilection for malignant transformation. Secondary causes can include underlying hypoxia or autonomous erythropoietin synthesis. However, data on the clinical risk factors and spectrum of underlying etiologies of erythrocytosis in children is limited. Such information could inform the development of a standard diagnostic approach in such children.

Objectives: To identify the underlying etiology and clinical characteristics associated with pediatric erythrocytosis.

Design/Method: We performed a retrospective chart review of all patients age 1 to 21 who were referred to the Texas Children's Hematology Center in Houston for elevated hemoglobin over a six-year period (January 2016 thru December 2021). Demographic and clinical information were extracted from the electronic medical records. Descriptive statistics and two sample t-tests were performed.

Results: One hundred eighty-seven subjects met inclusion criteria and were included in the study (80% male, median age 15.6 years). Males ≥12 years comprised 70% of the study population and were compared to all females and males <12 years. The most common comorbidities were asthma (n = 27, 14%), obstructive sleep apnea (n = 16, 9%), and other pulmonary diseases (n = 18, 10%). The average referral hemoglobin was higher in the ≥12-year-old male population compared to the remaining subjects (17.3 vs 16.3 g/dL, respectively, $p < 0.005$).

In addition to CBC and reticulocyte count, additional evaluations included erythropoietin (n = 124), basic metabolic panel (n = 102), pulse oximetry (n = 97), hemoglobin electrophoresis (n = 58), JAK2 mutation (n = 38), uric acid (n = 19), oxygen dissociation curve (n = 16), bone marrow aspirate/biopsy (n = 10), pulmonary function tests (n = 4), and testosterone (n = 3). Seventy-three patients (X%) had genetic testing.

No pathogenic mutations in the JAK2 gene were identified. Secondary erythrocytosis was diagnosed in 185 patients (99%). Primary erythrocytosis was diagnosed in 2 patients: Hemoglobin New Mexico (n = 1) and pathogenic von Hippel-Lindau variant (n = 1). Significant additional findings included patient report of smoking/vaping (n = 18), elevated erythropoietin (n = 3), hypoxia (n = 2), and exogenous testosterone (n = 1). Seven patients received phlebotomy and 1 patient initiated aspirin for erythrocytosis.

Conclusion: Our findings align with previous literature of children with erythrocytosis having a low incidence of primary erythrocytosis and highlight the importance of evaluating for secondary causes prior to pursuing specialized testing. Further studies on its incidence in the adolescent male population are warranted.

POSTER # 320 | CLINICAL OUTCOMES OF CHILDREN AND ADOLESCENTS WITH PAROXYSMAL NOCTURNAL HEMOGLOBINURIA

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Background: Paroxysmal Nocturnal Hemoglobinuria (PNH) is a rare, acquired disorder of the bone marrow causing intravascular hemolysis (IVH). PNH exists as a spectrum, ranging from asymptomatic small PNH clone size (subclinical PNH), to moderate clone size in patients with another bone marrow disorder (BMD-PNH), to large clone size leading to significant IVH (classic-PNH). The safety and use of complement inhibition in pediatric PNH is underreported. We conducted a retrospective-prospective cohort study of PNH patients from one of the largest pediatric hematology centers in the United States.

Objectives: We aim to describe the clinical features, laboratory trends, and treatment regimens of pediatric patients with classic-PNH and BMD-PNH.

Design/Method: Retrospective-prospective chart review between 2001 and 2023.

Results: Eighteen patients with PNH were identified in our cohort, of which 50% were males. Median age at diagnosis was 14.66 years. Time from symptom onset to diagnosis ranged from 0 to 46.93 months (Median = 1.45 months). Five patients had classic-PNH (28%) and 13 had BMD-PNH (72%). Ten patients had concurrent severe aplastic anemia (SAA) throughout the course of their disease, one had moderate aplastic anemia, and one had myelodysplastic syndrome. Four patients developed clinically significant IVH after immunosuppressive therapy for SAA due to increasing PNH clone size. Of 5 patients with classic-PNH, 100% were treated with complement inhibitor therapy (C3, n = 1 or C5, n = 4). Thromboses of the hepatic veins (Budd-Chiari syndrome) were noted in 2 of our patients with classic-PNH. Of the 13 patients with BMD-PNH, 6 received immunosuppressive therapy, 8 received complement inhibition, and 7 underwent bone marrow transplant. One patient with BMD-PNH died. All patients with classic-PNH achieved transfusion independence during complement inhibition, compared to 6 out of 8 (75%) of patients with BMD-PNH on complement inhibition. One patient developed Neisserial gonococcal

sepsis, but no meningococcal infections nor deaths due to complement inhibition were noted. Notably, extravascular hemolysis (EVH) with positive direct antiglobulin test was noted in 42% of all patients being treated with terminal complement inhibition.

Conclusion: In the largest single-center pediatric cohort of patients with PNH to date, time from symptom onset to diagnosis remains a challenge, likely due to non-specific presenting symptoms. Complement inhibition used in 72% of our patients was a safe and effective strategy at mitigating IVH and avoiding thrombosis. However, it is important to note that C5 inhibition can result in EVH. Additionally, our data support the use of complement inhibition to reduce transfusion need in patients with BMD-PNH and IVH.

POSTER # 321 | NEUROCOGNITIVE OUTCOMES IN PATIENTS WITH SHWACHMAN-DIAMOND SYNDROME: RESULTS FROM A FOLLOW-UP SURVEY

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Background: Shwachman-Diamond Syndrome (SDS) is a rare inherited bone marrow faillure syndrome with known concerns with neurocognitive developmental issues.

Objectives: To understand the current spectrum of cognitive, behavioral and neurocognitive functioning and issues of patients with genetically confirmed SDS.

Design/Method: A follow-up REDCap survey was distributed to all patients enrolled on the Shwachman Diamond Registry. To evaluate the current spectrum of neurocognitive outcomes we analyzed the referral process for neuropsychological evaluation, findings and management strategy recommendations provided to patients from these neuropsychological evaluations, and any barriers to obtaining neuropsychological evaluation.

Results: Forty-four patients and/or families completed the follow-up survey. Genetic confirmation of diagnosis was available for 31 patients (70%). The majority (n = 25, 81%) of these patients had biallelic mutations in the *SBDS* gene. The median age of this cohort was 11.5 years (range 1-39 years) old. The majority of the patients did not report any current or previous diagnosis of mood disorders (n = 22, 58%). For patients who reported any mood disorders, anxiety was the most common (n = 9, 24%), followed by major depressive disorder (n = 6, 16%). Additionally, 50% (n = 16) reported no current or previous diagnosis of behavioral disorders. The most common behavioral disorder reported by survey respondants was attention-deficit hyperactivity disorder (ADHD) (n = 7, 22%). The vast majority of patients with referrals for neuropsychological evaluation (n = 19, 61.2%) successfully completed initial evaluation (n = 18, 94.7%). Of these patients, 68.2% (n = 13) had folllow-up neuropsychological evaluations. Reported neuropsychological findings were variable from these evalluations including but not limited to pertinent findings in areas of developmental delay (n = 11, 14%), cognition/learning disabililty (n = 11, 14%), and overall functioning (n = 5, 7%). Fourteen patients (77.8%) who completed neurocognitive evaluation reported findings from in at least two different areas. Recommendations on management strategies from these evaluations included use of ancillary therapy services (n = 14, 33%), school services (n = 10, 23%), behavioral management strategies (n = 6, 14%), medication for mood and behavioral disorders (n = 4, 9%) and psychotherapies (n = 5, 12%). The majority of patients (77.8%) reported neuropsychological evaluation occurred in a timely manner. Financial (32.3%) and medical insurance (29%) issues were not reported to major barriers to compelting neuropsychological evaluation.

Conclusion: Early identification of concerns and implementation of evidence-based interventions for these concerns is crucial in promoting optimal development. Neurocognitive concerns seen in patients with SDS are not unique to children with SDS. Evidence-based interventions developed for other populations with similar symptoms are likely to be effective for children with SDS who display these symptoms.

POSTER # 322 | TREATMENT RELATED PATIENT REPORTED OUTCOMES IN PEDIATRIC SEVERE APLASTIC ANEMIA

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Background: Additional study of the quality of life (QOL) and patient reported outcomes (PROs) of pediatric patients with severe aplastic anemia (SAA) is greatly needed to optimize care of such patients. Prior QOL studies in SAA patients focused on adult bone marrow transplantation (BMT) patients, were deficient in proxy/caregiver analysis of patient QOL, were retrospective in-nature and lacked extensive validated PRO assessments.

Objectives: Quantitatively analyze QOL, self-image and PROs of pediatric patients treated for SAA with immunosuppressive therapy (IST) or BMT. Assess the feasibility of a multi-institutional web-based assessment of QOL and PROs for pediatric patients with SAA via direct patient evaluations and caregiver/proxy assessments.

Design/Method: Pediatric SAA patients (age 5-17.9 years) or their primary caregiver completed both demographic and health history information as well as QOL and PRO measures via a secure online platform at initial diagnosis and every 3 months following treatment with BMT or IST. Survey tools included PedsQL, PedsQL Self-Image and patient-reported outcomes measurement information system (PROMIS®) short forms, with the following PROs assessed: anger, anxiety, depression, fatigue, mobility, pain, cognitive function, and peer relationships. Surveys were scored according to their respective scoring manuals.

Results: Nineteen institutions participated from 2019-2022. Twenty-five total unique survey evaluations were completed by 8 separate patients (7 males and 1 female; age 5 – 12 years at initial survey).

Evaluations were completed by both patients and caregivers. All patients underwent BMT including two patients who received IST followed by BMT. Sixty-three percent of patients completed>1 survey with data collected up to two years post-treatment initiation.

Prior to treatment initiation patients had low QOL and self-image scores with mental health, physical well-being, and peer relationships reduced compared to relevant healthy reference populations. There was improved QOL, physical well-being and psychosocial health following treatment with improvements more substantial as a patient progressed further from treatment. Anger, cognitive function, peer relationships and mobility were least impacted by treatment. Both patients and caregivers noted an improvement in PROs and QOL following treatment. Differences in proxy and patient results were noted but small sample size limited the evaluation of such results, including assessment of the comparative impact of BMT versus IST treatment modalities. Strong associations between numerous mental and physical health PROs were noted.

Conclusion: A diagnosis of SAA and subsequent treatments substantially impacts the QOL and PROs of pediatric patients. Completion of a multi-institutional longitudinal prospective web-based survey investigation directed at PROs and QOL in patients with SAA is feasible.

POSTER # 323 | IMMUNOLOGICAL FUNCTION IN CHILDREN WITH SHWACHMAN-DIAMOND SYNDROME

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Background: Shwachman Diamond Syndrome (SDS) is an inherited bone marrow failure syndrome characterized by neutropenia and pancreatic insufficiency. The current understanding of immune function in SDS is limited. Abnormalities in innate and adaptive immunity have been reported in a small subset of SDS patients.

Objectives: This is a retrospective study to characterize immunologic function in patients with SDS.

Design/Method: Data were obtained from chart review of 223 patients with biallelic mutations in *SBDS* enrolled on the SDS registry or followed clinically at participating institutions with IRB approval (n = 5).

Results: Immunologic data were available from 373 time points on 111 well patients including lymphocyte subsets, immunoglobulin subsets, and antigen/mitogen stimulation. Assessment of quantitative abnormalities demonstrates at least one low absolute lymphocyte count (ALC) in 27% of subjects (n = 19/70; median of all values [median-ALL] = 2500; median of low values [median-LOW] = 1435). In 55 patients with lymphocyte subpopulations, 18% had at least one low CD3 value (n = 10/55; median-ALL = 2151; median-LOW = 773); 16% had at least one low CD4 value (n = 9/55; median-ALL = 1221; median-LOW = 490); 15% had at least one low CD8 value (n = 8/55; median-ALL of 778; median-LOW = 238); 42% had at least one low CD19 value (n = 23/55; median-ALL = 305; median-LOW = 84); and 27% had at least one low CD16/56 value (n = 14/52; median-ALL = 182; median-LOW = 69). Of the patients with low CD19 counts, 4 patients had low IgG levels (n = 4/20; 20%) and 16 had normal IgG levels (n = 16/20; 80%).

Qualitative assessment of the B cell compartment based on immunoglobulin levels showed 17% of patients with a least one low IgG level (n = 13/77; median-ALL = 865; median-LOW = 512); 18% with at least one low IgA level (n = 14/79; median-ALL = 83; median-LOW = 33); 52% with at least one low IgM level (n = 38/73; median-ALL = 42; median-LOW = 28); and 14% of patients with high IgE levels (n = 4/28) with a median of 13.

Of the 17 patients with antigen/mitogen stimulation testing, 14 (82%) had normal responses to tetanus, PHA, and/or Candida; 2 (12%) had one abnormal response to tetanus, PHA, or Candida; and one patient (6%) had an abnormal response to all three on multiple occasions.

Conclusion: Overall, these results indicate limited immune deficits, largely quantitative and qualitative changes in the B cell compartment, in a small subset of patients with SDS. Initial immunological evaluation including a complete blood count and lymphocyte subpopulations may be of benefit. However, it is reasonable to reserve more detailed assessment for patients with recurrent or serious infections.

POSTER # 324 | LENTIVIRAL-MEDIATED GENE THERAPY FOR FANCONI ANEMIA [GROUP A]: RESULTS FROM RP-L102 CLINICAL TRIALS

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Background: Fanconi anemia (FA) is an inherited deoxyribonucleic acid (DNA) repair disorder that results in progressive bone marrow failure (BMF) in 80% of patients within the first decade of life. Allogeneic hematopoietic stem cell transplant (alloHSCT) is potentially curative for FA-related BMF. Although survival exceeds 80% in experienced transplant centers, adverse effects including 100-day mortality and increased cancer risk limit success. The current studies utilize autologous FA-A CD34+ enriched hematopoietic stem and progenitor cells (HSPCs) and rely upon the proliferative advantage of gene-corrected FA HSPCs, enabling engraftment without conditioning. We report results from global RP-L102 studies.

Objectives: To assess efficacy of RP-L102 to treat FA-A related BMF.

Design/Method: Patients with FANCA mutations, age ≥1 year with no HLA-matched sibling donor and ≥30 CD34+ cells/μL in bone marrow (BM) are eligible. Peripheral blood (PB) cells are collected via leukapheresis. Following CD34+ enrichment, HSPCs are subsequently transduced with a lentiviral vector carrying the FANCA gene, and infused without cryopreservation or conditioning. Patients are followed for 3 years for safety assessments (including insertion site analysis [ISA]) and evidence of efficacy (increasing vector copy number [VCN], mitomycin-C [MMC] resistance in BM colony forming cells [CFCs]), and stabilization/correction of cytopenias).

Results: As of October 2022, 12 patients age 2 to 6 years have received RP-L102. Sustained engraftment has been demonstrated in 7 of 10 evaluable patients with ≥12 months of follow up as indicated by peripheral blood mononuclear cell (PBMC) VCN. Six of these 7 patients have increasing BM CFC MMC resistance with concurrent hematologic stabilization. One patient with increasing PBMC and BM VCN has had recent development of BM CFC MMC resistance and relative hematologic stability. One patient without genetic correction had progressive BMF and underwent successful alloHSCT. A transient serious Grade 2 RP-L102 infusion-related reaction was observed in one patient and resolved without sequelae. No patients have developed RCL. One patient developed T cell lymphoblastic lymphoma determined to be unrelated to gene therapy. There has been no evidence of RP-L102 related bone marrow dysplasia, clonal dominance or insertional mutagenesis.

Conclusion: RP-L102 conferred phenotypic correction as demonstrated by sustained increase in BM CFC MMC resistance, genetic correction and hematologic stabilization in at least 6 patients with ≥1 year of follow up. Sustained engraftment, phenotypic correction, and hematologic stability was achieved in the absence of conditioning. RP-L102 represents a potentially curative therapy for FA-related BMF, which can be administered without transplant-conditioning related toxicities.

Supported by Rocket Pharmaceuticals, Inc.

POSTER # 325 | MODELING REMISSION IN A MURINE RPL5 MODEL OF DIAMOND BLACKFAN ANEMIA

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Background: Diamond Blackfan Anemia (DBA) is a rare inherited bone marrow failure syndrome that manifests as a variably penetrant macrocytic anemia, which can spontaneously enter remission for unclear reasons. *RPL5* is one of the commonly mutated genes in DBA and is associated with a severe phenotype including morphological defects and reduced likelihood of spontaneous remission. We previously characterized a murine genetic model of *Rpl5* haploinsufficiency ($Rpl5^{Skax23\text{-}Jus/1/+}$) with a CFU-E/proerythroblast differentiation block at E12.5 that begins to resolve by E14.5.

Objectives: Our objective is to perform unbiased studies to determine dysregulated pathways that contribute to variable anemia penetrance and remission in DBA utilizing our *Rpl5* haploinsufficient model.

Design/Method: We generated E12.5 embryos from timed matings with wild type (WT) females x $Rpl5^{Skax23\text{-}Jus/1/+}$ males and isolated fetal liver (FL) cells. Fetal liver cells were stained with Ter119 and CD71 antibodies and the CFU-E/proerythroblast (CD71+/Ter119-) population was sorted and RNA-seq performed.

Results: We first used the DESeq2 to perform differential expression analysis on the gene counts from 9 FL samples (3 WT, 6 mutants). We applied log2-scaled fold-change (LFC) filtering, abs (LFC) ≥ 0.99 and set the significance level with adjusted p-value ≤0.005 and found 329 up-regulated genes and 79 down-regulated genes. We then used clusterProfiler to perform the gene ontology (GO) enrichment analysis on the up- and down-regulated genes from the mutant-WT comparison. We queried the mouse gene annotation database in Bioconductor using the gene names. The significance levels were set as p-value ≤ 0.001 and q-value ≤ 0.005. When combining the significant genes together, they were enriched in 90 terms. Down-regulated genes in this GO analysis were in the erythrocyte differentiation, development and homeostasis groups consistent with the erythroid differentiation block observed in $Rpl5^{Skax23\text{-}Jus/1/+}$ E12.5 FL. G2/M transition genes were also significantly differentially expressed in GO analysis while p53 pathway genes were overall not different in our WT-mutant comparison.

Conclusion: Our preliminary data indicates that the erythroid differentiation block in E12.5 FL from $Rpl5^{Skax23\text{-}Jus/1/+}$ mutant animals may be mediated by cell cycle dysregulation and will be investigated further in our future studies. We are also involved in validating novel genes and pathways that may be involved in the erythroid failure in our model.

POSTER # 326 | PEDIATRIC EVANS SYNDROME DUE TO CTLA-4 INSUFFICIENCY: A NOVEL MUTATION AND RESPONSE TO ABATACEPT

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Background: Pediatric Evans syndrome is an autoimmune disorder diagnosed by the presence of two or more immune mediated cytopenias. Recent literature suggests that pediatric Evans syndrome may be a manifestation of an underlying, primary immunodeficiency (PID). Heterozygous loss of cytotoxic T lymphocyte antigen-4 (CTLA4), a key gene regulating T-cell proliferation, leads to a phenotype of systemic autoimmunity known as "CTLA4 haploinsufficiency with autoimmune infiltration" (CHAI). Identification of this mutation allows for the opportunity to treat refractory disease with abatacept, a CTLA4 analog; however, there is limited data on the use of abatacept for CTLA4 haploinsufficiency in children.

Objectives: To describe a case of refractory pediatric Evans syndrome secondary to CHAI caused by a novel mutation in the CTLA4 gene, and

to describe the clinical response of various autoimmune manifestations to abatacept.

Design/Method: Case report

Results: A 16-year-old female was initially referred to hematology for leukopenia (WBC 1.9 k/mm^3) and thrombocytopenia (3 k/mm^3) discovered after several months of easy bruising and heavy menstrual bleeding. She was found to have severe neutropenia (ANC 200 cells/mm^3) and splenomegaly. After an unnrevealing bone marrow aspirate and biopsy, she was diagnosed with Evan's syndrome based on the presence of neutrophil and platelet auto-antibodies. She was trialed on Cellcept followed by IVIg with limited response. Due to refractory disease and family history of autoimmunity/deficiency +/- lymphoma, a PID panel was obtained which revealed a heterozygous, germline mutation in the CTLA4 gene (deletions of exons 2-4), confirming the diagnosis of CTLA4 haploinsufficiency. Upon further probing, she disclosed experiencing months of hematochezia. A thrombopoietin receptor agonist (TPO-RA) was started with limited response, so she was rechallenged with IVIg and a platelet transfusion prior to a endoscopy. Biopies revealed lymphocytic colitis consistent with CTLA4 enteropathy. Due to multi-organ autoimmune involvement, IV abatacept infusions were initiated at 2-week intervals. After just two doses, her colitis and cytopenias improved (ANC 1,970 cells/mm^3 and platelets 77 k/mm^3). After her first 3 induction doses, an attempt to space infusions to four weeks resulted in recurrence of cytopenias. Upon resuming treatments every two weeks, she has had a sustained response (ANC>500 k/mm^3 and platelets>150 k/mm^3) and currently is undergoing wean of her TPO-RA.

Conclusion: PID should be suspected in Pediatric Evans syndrome in patients with refractory disease, multiorgan autoimmunity, and/or positive family history for autoimmunity. Furthermore, the diagnosis of CTLA4 haploinsufficiency allows for targeted therapy with abatacept which may have beneficial effects on autoimmune cytopenias and enteropathy.

POSTER # 327 | OUTCOMES OF COLLABORATION BETWEEN CLINICIAN AND GENETIC COUNSELOR IN GENETIC EVALUATION OF PEDIATRIC PATIENTS WITH CHRONIC NEUTROPENIA

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Background: Genetic testing for inherited forms of neutropenia may involve focused testing for familial variants, selection of gene(s) based on phenotype, or broad genetic testing via large gene panels or whole-exome sequencing. Broad genetic testing in a pediatric population poses unique challenges, including increased risk for variants lacking sufficient evidence to influence medical management and incidental findings with medical repercussions in adulthood. Collaboration between physicians and genetic counselors when offering broad genetic testing allows both the family and medical team to weigh perceived risks versus benefits of testing and prepare for potential outcomes of testing.

Objectives: Here we report the implementation and outcomes of broad genetic testing in pediatric patients with suspicion of inherited neutropenia, with attention to variants of uncertain significance and incidental findings defined as variants in genes associated with conditions that do not include chronic pediatric-onset neutropenia as a feature.

Design/Method: A 19-month-old (patient A), a 3-year-old (patient B), and a 6-year-old (patient C) were referred to our outpatient clinic for chronic neutropenia. Patient A was offered a 429 gene panel for primary immunodeficiencies. Patients B and C were offered a 574 gene panel for inherited causes of immunodeficiency or cytopenia.

Results: Testing in patient A yielded 6 reported variants: 6 (100%) were classified as "of uncertain significance"; a causative variant was not identified on testing. Patient B was offered genetic counseling prior to testing for consideration of possible incidental findings and discussion of existing genetic discrimination protections. The family decided to decline testing due to panel inclusion of 22 (~38%) genes associated with adult-onset cancer predisposition. Testing in patient C yielded 2 reported variants: one variant (50%) was a *CXCR4* variant pathogenic for WHIM syndrome, and one variant (50%) was an incidental finding in *RNASEH2B*.

Conclusion: Genetic counselor review of variants identified occurred in all three cases. Post-test counseling for patients A and C addressed parental confusion around medical significance of non-diagnostic results (88% of reported variants), counseling focused on variant classification criteria, reportable variants versus medically actionable variants, and newly identified reproductive risks associated with autosomal recessive conditions. Pre-test counseling provided to Patient B allowed for consideration of potential unexpected findings, possible implications to unprotected insurance policies, and discussion of alternate testing options with reduced risk for incidental findings. Involvement of genetic counselors in test selection and consenting promotes shared decision-making and impacts the course of care and provides support and education to families and clinical providers faced with non-diagnostic results.

POSTER # 328 | A PRESENTATION OF PEDIATRIC EVANS SYNDROME SECONDARY TO CTLA-4 INSUFFICIENCY

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Background: Evans syndrome is the presence of both immune thrombocytopenic purpura (ITP) and autoimmune hemolytic anemia (AIHA). Most children with Evans syndrome also have an underlying autoimmune deficiency, most commonly ALPS. Less commonly, 6% of patients with Evans syndrome have an underlying CTLA-4 insufficiency, an

immune dysregulation syndrome caused by a heterozygous mutation of a key protein (CTLA-4) in immune suppression. Patients with this gene mutation can present with manifestations of hypogammaglobulinemia including recurrent respiratory infections, autoimmune conditions, and lymphoid malignancies.

Objectives: To describe an atypical ITP presentation and highlight Evans syndrome as an important differential diagnosis in pediatric patients presenting with thrombocytopenia.

Design/Method: Case report and PubMed review of literature. Data was collected using retrospective chart review of hospital records.

Results: An 8-year-old female presented to the hospital with a 1-week history of petechiae and ecchymosis on her legs that progressed to the upper extremities over a few days. There was a preceding viral upper respiratory tract infection 3 weeks prior to presentation. Laboratory studies showed remarkably low platelet counts (1 x 10^3/mcL), with normal Hb (14.3 g/dL) and WBC counts (6.4 x 10^9L). She was treated with IVIG but relapsed 6 days later with a platelet count of 4 x 10^3/mcL, Hb of 9.7 g/dL and a Coombs positive hemolytic anemia. Subsequent bone marrow biopsy was normal with no signs of myelodysplasia or leukemia. The patient was diagnosed with Evans syndrome. Given family history of CTLA-4 insufficiency, genetic testing was done, which revealed CTLA4 insufficiency in the patient. She was treated with oral prednisolone and sirolimus. Initial immunoglobulins and comprehensive antinuclear antibody panel were normal. However, subsequent visits found dropping IgG and the patient was started on Hizentra infusions. She was weaned off prednisolone after 7 months and is currently stable on sirolimus with normal Hb and platelet counts.

Conclusion: ITP can sometimes present atypically, such as in Evans syndrome. Development of ITP and AIHA most commonly occurs sequentially, rather than simultaneously, making Evans syndrome a challenging condition to diagnose. Although a rare condition, it is important to recognize in order to manage life-threatening relapses. Evans syndrome in a pediatric patient warrants further immunological evaluation, as genetic and immunologic factors substantially increase the risk of mortality.

POSTER # 329 | USE OF CAPLACIZUMAB IN PEDIATRIC THROMBOTIC THROMBOCYTOPENIC PURPURA PATIENTS

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Background: Thrombotic Thrombocytopenic Purpura (TTP) is a rare disorder characterized by microangiopathic hemolytic anemia, thrombocytopenia, and severely reduced or absent von Willebrand factor (VWF)-cleaving protease, ADAMTS13. In immune-mediated TTP (iTTP), autoantibodies against ADAMTS13 result in accumulation of high molecular weight VWF multimers, platelet-rich microthrombi, and red blood cell fragmentation. While traditional TTP treatment involves therapeutic plasma exchange (TPE) and immunosuppression, a new anti–VWF nanobody, caplacizumab, has the potential to further transform management. Caplacizumab blocks the A1 domain, preventing platelet-VWF interaction and microthrombi formation. Limited data exists regarding use of caplacizumab in pediatric iTTP patients as it only became FDA approved for adults in 2019.

Objectives: To describe clinical features, treatments, and outcomes in three pediatric iTTP patients treated with caplacizumab.

Design/Method: Chart review and laboratory analysis.

Results: Though each patient presented with varying symptoms, all demonstrated direct antiglobulin negative microangiopathic hemolytic anemia and thrombocytopenia. ADAMTS13 activity levels ranged from <3-20% with positive anti-ADAMTS13 inhibitors. All were treated with TPE, steroids, and rituximab. In 2 of 3 cases, caplacizumab was added with prompt normalization of platelet count. Case 1: A previously healthy 11 year old black male presented with headache, fatigue, emesis, and diarrhea. Though initially refractory to treatment, requiring 19 total TPE sessions, he achieved clinical response 4 days after starting caplacizumab. He remains in remission with no further exacerbations or clinical relapses. Case 2: 17 year-old black male with complex medical history presented with septic shock & acute respiratory failure in setting of a bowel perforation. Caplacizumab was added, but he ultimately died from complications of septic shock. Case 3: 11 year old Caucasian female presented to outside hospital with headache, unilateral weakness, and confusion. She started caplacizumab after transfer and platelet count normalized within 2 days. She had no bleeding complications and remains in remission.

Conclusion: Caplacizumab appears to be well-tolerated with the potential to impact prognosis in children. TTP can be life threatening and some children are refractory to standard treatment of TPE and immunosuppression. As evident by our institutional experience, caplacizumab can safely hasten clinical response, thereby reducing risk of ischemic injury and its long-term complications. Prospective clinic trials utilizing caplacizumab in pediatric patients could help to standardize treatment and better understand optimal usage of this potentially life-saving drug.

POSTER # 330 | THE EXPANDING ROLE OF ELTROMBOPAG IN CHRONIC IMMUNE THROMBOCYTOPENIC PURPURA POST-SPLENECTOMY

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Background: Immune Thrombocytopenic Purpura (ITP) is the acquired, immune-mediated destruction of platelets. Although mostly self-limiting, approximately 20% of patients progress to achieve chronic status. Medical management for ITP includes corticosteroids and immunoglobulin therapy with varying levels of efficacy. A small subset of patients ultimately undergo splenectomy for resistant disease. Eltrombopag is a non-competitive thrombopoietin receptor agonist that is increasingly being used in the management of patients with

chronic primary ITP. Its efficacy has been established in refractory ITP by increasing platelet count and decreasing bleeding risk.

Objectives: Early evidence supports eltrombopag use in the management of ITP. There is limited data defining its role in the post-splenectomy patient. This case report describes the successful use of eltrombopag in a patient with persistent chronic ITP post splenectomy.

Design/Method: Case report with literature review.

Results: A 3-year-old male presented with one week of bruising to the limbs. Laboratory investigations revealed a platelet count of 21,000/uL. Being otherwise well with no evidence of ongoing bleeding, he was diagnosed with ITP. His thrombocytopenia persisted with platelet counts remaining below 20,000/uL. When platelet counts dropped to less than 5000/uL corticosteroid therapy was initiated. A short-lived response was seen with counts increasing to 198,000/uL however this quickly reverted to pre-medication levels. A similar response occurred with use of intravenous immunoglobin.

Eltrombopag was commenced with no significant platelet response. Vincristine, rombiplostim, 6MP, rituximab, mycophenolate, dapsone and sirolimus were similarly unsuccessful. Laparoscopic splenectomy was therefore performed. Post-operative thrombocytosis occurred however thrombocytopenia recurred within two months. Eltrombopag was restarted at 50 mg per day and platelets trended up to 400,000/uL. At this point eltrombopag was held but had to be restarted within 10 days because of a steady decline in platelets once more. Ultimately, alternate day dosing of 25 mg then 50 mg was administered with maintenance of platelets above 200,000/uL.

Conclusion: Indications for eltrombopag use in patients with chronic ITP began with its role in pre-splenectomy patients to avoid the morbidity associated with asplenia. Newer evidence, as seen in this patient, suggests it may play a role in post-splenectomy patients with relapsing disease. Previous failure in the pre-splenectomy phase of management does not preclude its use in the post-splenectomy patient. The dosing regimen may be commenced at the recommended dose and titrated to effect. Its long-term efficacy and toxicity are to be determined, but thus far results are promising, despite lack of pre-splenectomy efficacy.

POSTER # 331 | CAPLACIZUMAB IN PEDIATRIC ACQUIRED THROMBOTIC THROMBOCYTOPENIC PURPURA

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Background: Thrombotic thrombocytopenic purpura (TTP) is a thrombotic microangiopathy (TMA), characterized by thrombocytopenia, microangiopathic hemolytic anemia (MAHA) and ADAMTS13 deficiency. Since acquired TTP is rare in children no standard treatment guidelines are available. Caplacizumab is a humanized, bivalent variable-domain-only immunoglobulin fragment, that inhibits the interaction between von Willebrand factor multimers and platelets, approved for the treatment of acquired TTP in adults. There is limited data on the use of Caplacizumab in pediatric acquired TTP.

Objectives: We report a case of refractory acquired TTP in a pediatric patient treated with Caplacizumab.

Design/Method: Case report

Results: A 13-year-old girl presented with intermittent left-sided paresthesia, facial numbness and headaches. Past medical history was notable for asthma. Family history was unremarkable. On admission, examination was remarkable for petechiae. Laboratory data showed mild renal impairment (serum creatinine 0.94 mg/dl), hemolytic anemia (lactate dehydrogenase 1,070 U/L, hemoglobin 5.6 g/dl, indirect bilirubin 2.43 mg/dl, reticulocyte count 40.4 $\times$ 104/μl, and negative Coombs test), low platelet count (10 $\times$ 103/mm3), and schistocytes (3+) in the peripheral blood smear. C3 complement fraction was low (67 mg/dL). Head imaging was negative for intracranial abnormality. Clinical and laboratory data suggested the diagnosis of TTP, supported by a PLASMIC score of 6 (high risk) and confirmed by the ADAMTS13 activity (<1%) and presence of high titer anti-ADAMTS13 antibodies. Plasmapheresis (PLEX) was immediately initiated and continued until the platelet count increased above 150 for two consecutive days. She also received steroids and Rituximab. Two days after stopping PLEX, thrombocytopenia recurred so plasmapheresis was restarted, though it was stopped following a transfusion reaction and caplacizumab was added to her treatment regimen. Three days later, the platelet counts normalized. She was discharged home on oral steroid taper and Caplacizumab. Anti-ADAMTS13 antibodies remained high, and ADAMTS13 activity was low at the time of discharge. Four weeks after starting Caplacizumab, ADAMTS13 activity increased to 75% and ADAMTS13 inhibitor was undetectable. ADAMTS13 activity levels were followed until 8 weeks after withdrawal of therapy and levels continued to be normal.

Conclusion: The 2020 International Society on Thrombosis and Hemostasis Guideline makes a conditional recommendation in favor of using caplacizumab for adult patients with acquired TTP having severe features, though it has not been approved for children in the US. We present a case of successful off-label treatment of refractory acquired TTP with caplacizumab, which was well tolerated. Caplacizumab may be considered for therapy in children and adolescents with acquired TTP.

POSTER # 332 | THROMBOCYTOPENIA IN SIBLINGS WITH MERCURY POISONING

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Background: Mercury poisoning is rare, and diagnosis is often delayed because it may present with over 250 symptoms including central nervous system (CNS), gastrointestinal, cardiovascular, and/or hematologic abnormalities. We present two siblings who simultaneously developed symptomatic, severe thrombocytopenia due to acute mercury poisoning.

Objectives: Review the presentation of mercury poisoning as a rare etiology of severe thrombocytopenia.

Design/Method: Case report obtained by comprehensive chart review.
Results: **Patient 1**, a five-year old female, and her 15-year-old maternal half-brother, **Patient 2**, presented to Connecticut Children's with three days of petechial rash, epistaxis, oral ulcers, malaise and fever. Physical exams for both siblings were significant for diffuse petechial rash of trunk and extremities, wet purpura, and diffuse abdominal tenderness with splenomegaly. Abnormal laboratory findings of both patients included severe thrombocytopenia (<2K/μL), elevated inflammatory markers, and elevated LDH. Patient 1 had anemia (hemoglobin 9.9 g/dL). Patient 2 had hypoalbuminemia, elevated transaminases, hematuria and proteinuria. Their thrombocytopenia was unresponsive to platelet transfusions and IVIG. Patient 1′s bone marrow demonstrated trilinear hematopoiesis, megakaryocytic hyperplasia and 80% cellularity. Infectious evaluations were negative. Both siblings had elevated serum Mercury levels of 315, 518 and urine mercury levels of 409,>1000, respectively. Patient 1 revealed that she discovered and spilled a jar of mercury in her bedroom two weeks earlier when the family moved into a 1940s home. Patient 2 cleaned the mercury spill. Dimercaptosuccinic acid (DMSA) treatment was initiated, and Patient 2 responded well and was discharged on Hospital Day 15 with platelet count of 47K/μL. Despite extended chelation with DMSA, Patient 1 had persistent refractory thrombocytopenia. With weekly romiplostim injections, her platelets increased to 250K/μL within one month.
Conclusion: The simultaneous presentations of severe thrombocytopenia in these siblings were likely due to high blood mercury levels. When multiple household members present with similar symptoms, environmental exposures need to be considered. Mercury poisoning, although rare, must remain on the differential for severe refractory thrombocytopenia.

POSTER # 333 | CEREBRAL ARTERIOPATHY IN A CASE OF SHIGA TOXIN-PRODUCING ESCHERICHIA COLI HEMOLYTIC UREMIC SYNDROME

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Background: Hemolytic-uremic syndrome (HUS) is an acute thrombotic microangiopathy typically caused by Shiga toxin. Microangiopathic hemolysis, thrombocytopenia, and end organ damage are the most common clinical manifestations, but neurologic complications have been reported in 10.4% to 33% of cases. Children with HUS and cerebral involvement have an increased risk of mortality with the most common types of neurologic complications being encephalopathy, hemorrhage, infarction, anoxic brain injury, and edema. We report the first known case of HUS presenting as transient ischemic attack (TIA) with radiological evidence of cerebral vasculitis.
Objectives: To describe an unusual case of cerebral vasculitis in a patient with Shiga toxin-producing *Escherichia coli*-HUS (STEC-HUS).
Design/Method: A single subject case report.
Results: A 13-year-old male with a history of autism, migraines, and a chromosomal disorder presented to an outside hospital with an 8 day history of diarrhea, vomiting, jaundice, and an acute neurologic event involving altered mental status, aphasia, and left arm weakness. Head computed tomography was normal and the event resolved within 4 hours of onset, consistent with a TIA. He was transferred to our hospital with severe thrombocytopenia and renal failure. A positive Shiga-toxin assay, stool culture positive for E. coli O157, and normal ADAMTS13 levels confirmed STEC-HUS. Due to multiorgan dysfunction, atypical HUS genetic studies were sent which revealed a variant of unknown significance on the CFHR5 gene: p.Ser128Ser. A brain magnetic resonance imaging/magnetic resonance angiography (MRI/MRA) showed no evidence of cerebral infarction, but severe narrowing was noted in the left internal carotid artery (ICA). Prophylactic heparin was initiated. On day 3 of admission, despite plasmapheresis, follow up brain MRI/MRA showed progression with bilateral ICA involvement and increased narrowing of the left ICA; additionally, there was clinical deterioration. Eculizumab was then started. At the time of his second eculizumab dose (7 days later), his platelets and hemoglobin had stabilized and a brain MRI/MRA showed significant improvement of his arteriopathy.
Conclusion: HUS is a life-threatening condition that can cause renal injury and serious neurologic complications. Although not previously mentioned as a neurologic complication of HUS, progressive cerebral arteriopathy was noted in our patient. Early intervention with eculizumab seemed to reverse the progression of neurovascular disease, suggesting complement deposition is possibly the mechanism behind cerebral arterial narrowing noted on brain MRA. Children presenting with neurologic manifestations of HUS should have brain MRA in addition to MRI. Continued research on the use of eculizumab for the treatment of HUS-associated neurologic complications is needed.

POSTER # 335 | IRON DEFICIENCY ANEMIA AND STROKE IN CHILDREN: CASE REPORT AND LITERATURE REVIEW

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Background: Iron deficiency is a major cause of childhood anemia and is associated with poor neurodevelopmental outcomes. Although the association of iron deficiency anemia (IDA) and thrombosis in children is well-recognized, descriptions of IDA-associated stroke are limited to case series and case control studies.
Objectives: Discuss a pediatric case of IDA-associated cerebral sinus venous thrombosis (CSVT) with hemorrhagic stroke and summarize published pediatric cases of IDA-associated stroke.
Design/Method: Case Report and Literature Review.
Results: A 22-month-old female presented to the ED via ambulance from home with acute seizure. Initial hemoglobin was 3.8 g/dL, mean corpuscular volume (MCV) 40fl and platelets 319,000. CT showed transverse sinus venous thrombosis with significant associated

hemorrhagic infarction, resulting in profound neurologic deficits. Parents describe a healthy toddler with gastrointestinal illness two days prior and a long history of excessive cow's milk intake. Review of published literature for cases of IDA-associated stroke identified 16 papers (37 unique patients). There were 18 cases (47.4%) of arterial ischemic stroke (AIS), 19 cases of CSVT (50.0%) and 1 case of both CSVT and AIS (2.6%). Ages ranged from 6 months to 15 years (average: 42.6 months). The average hemoglobin level was 5.9 g/dL (n = 32), platelets 573K (n = 32), ferritin 8.6 ng/mL (n = 17) and MCV 54.9fL (n = 28). Nutritional deficiency was the most reported cause of IDA. Additional thrombotic risk factors were identified in 72% of cases, with recent illness/infection in 51%. Mann-Whitney U tests and independent samples t-tests comparing cases with and without additional thrombosis risk factors showed no statistically significant difference in laboratory values. Comparing stroke type, independent samples t-test revealed higher platelet levels in CSVT group (716K) versus AIS group (443K) (p = .033), without significant differences in hemoglobin or ferritin.

Conclusion: While IDA-associated stroke is rare in the pediatric population, our analysis indicates that it is more frequently observed in patients with concurrent illness or other risk factors, yet occurs in 28% of cases without additional trigger. Multiple hypotheses regarding the pathophysiology of IDA-associated stroke have been proposed, including the role of thrombocytosis. In our analysis, platelet counts were significantly higher with CSVT compared to AIS, however cases with normal platelet levels are also reported underscoring the complex pathophysiology. This review highlights the importance of iron deficiency anemia in promoting childhood stroke.

POSTER # 336 | A CASE OF HEMOLYTIC DISEASE OF THE NEWBORN TREATED WITHOUT BLOOD PRODUCTS

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Background: Hemolytic disease of the newborn (HDN) affects 3/100,000 – 80/100,000 patients yearly. The three phases of HDN include fetal anemia, acute anemia, and late anemia. Fetal anemia can lead to hydrops fetalis and death and is treated with intrauterine blood transfusions. Acute anemia is treated with exchange transfusion and hyperbilirubinemia is treated with phototherapy. Late anemia occurs 2-4 weeks after birth and is likely a production issue due to marrow suppression from intrauterine transfusion therapy. Late anemia is treated with recurrent blood transfusions until there is evidence of marrow recovery. There have been a handful of case reports of using recombinant human erythropoietin (RHuEPO) to minimize/prevent late anemia.

Objectives: This case report describes a patient with HDN and severe, symptomatic acute anemia requiring NICU admission. The family were Jehovah's Witnesses and refused blood transfusions. The patient was successfully treated with RHuEPO, folic acid, and ferrous sulfate and did not require blood products.

Design/Method: The patient was born full term, weight was appropriate for gestational age, and APGARS were 8 and 9. Maternal blood type was O+/antibody negative, and the patient's blood type was B+/Coombs positive. The patient had hyperbilirubinemia and was started on phototherapy at 2 hours of life. Hematocrit at birth was 28.5% and symptoms of anemia included temperature instability, oxygen desaturations, and poor feeding. Although blood transfusion was recommended in this case, RHuEPO (200 units/kg), folic acid, and ferrous sulfate were used. The lowest hematocrit was 18.6% on day of life 8 and lowest hemoglobin was 7.7 g/dL on day of life 15. The patient was discharged home on day of life 16 and RHuEPO, folic acid, and ferrous sulfate were continued until 6 weeks of age at which time hemoglobin had improved to 10.4 g/dL. The patient was meeting developmental milestones, gaining weight appropriately, and had no difficulty with feeding.

Results: This is a unique case in which a patient with HDN with profound symptomatic anemia and hyperbilirubinemia was successfully treated without the use of blood products. The use of RHuEPO to treat HDN without the use of blood products has been reported in one other case report. However, the patient had seemingly no symptoms of anemia and hemoglobin nadir was 8.7 g/dL, which is strikingly higher than our patient.

Conclusion: Although blood transfusion and phototherapy are the standards of care, this case supports that RHuEPO may be considered as an alternative if the family does not consent to blood transfusions.

POSTER # 337 | HEMOLYTIC ANEMIA & APLASTIC CRISIS WITH COVID INFECTION IN THE SETTING OF HEREDITARY STOMATOCYTOSIS

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Background: Hereditary stomatocytosis (HSt) is a rare genetic disorder that presents with various degrees of hemolytic anemia and abnormal red blood cell morphologies characterized by alterations in RBC hydration and cell membrane, resulting in increased permeability to cations and inappropriate shrinkage or swelling of erythrocytes. Most patients with non-syndromic forms of HSt show mild anemia, which typically requires folic acid or vitamin B12 supplementation. Occasionally, transfusions are needed for either intermittent hemolysis or transient aplastic crisis, often caused by active viral infections, as seen in our patient.

Objectives: To describe the case of an infant with severe hemolytic anemia and aplastic crisis, found to have underlying hereditary stomatocytosis, triggered in the setting of active COVID and Rhinovirus infection.

Design/Method: A 2-month-old female, born at 37 weeks gestation via C-section with no complications, presented with jaundice, bilious emesis, dark stools, and lethargy, associated with upper respiratory illness for 2 days. She was otherwise healthy with unremarkable medical and

family history. At birth, patient was A (+) and direct antibody testing (DAT) negative; mother is O (-). No history of hyperbilirubinemia or blood transfusion during newborn period.

Results: Patient was found to be positive for COVID-19 and Rhinovirus on admission. Labs were significant for severe anemia (Hgb 2.0 g/dl, Hct 3.3%) with hyperbilirubinemia, elevated lactate dehydrogenase, decreased haptoglobin, and DAT positive with multiple warm and cold autoantibodies, consistent with severe intravascular and extravascular hemolysis. Single-cell lineage suppression was noted (reticulocyte count 2.4%), consistent with aplastic crisis secondary to active viral infection. A comprehensive hereditary hemolytic anemia genetic panel revealed variations in PIEZO1 gene, which is one of the major genes responsible for hereditary stomatocytosis. Treatment included supportive care with pRBC transfusions, intravenous immunoglobulin (IVIG), and high-dose steroids with resolution of anemia.

Conclusion: Literature review revealed several unusual findings of autoimmune hemolytic anemia in adults associated with COVID infection. This case report demonstrates a unique pediatric patient with new-onset severe hemolysis in the setting of active COVID infection and associated hereditary stomatocytosis. Unprovoked hemolytic anemia in infancy hence requires thorough diagnostic evaluation for appropriate therapeutic intervention.

POSTER # 338 | THE G.O.A.T. DIAGNOSIS—A RARE AND UNCOMMON DIAGNOSIS OF MACROCYTIC ANEMIA

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Background: The differential diagnosis of macrocytic anemia is broad and includes many etiologies but can also be suggestive of rarer, yet serious underlying diseases. The most important initial step in diagnosing the etiology of macrocytic anemia is obtaining a peripheral smear to evaluate for hypersegmented neutrophils. Megaloblastic anemias are most commonly caused by folate or B12 deficiency. Non-megaloblastic anemias can be indicative of various etiologies including; hemolysis, acute blood loss, liver disease, myelodysplastic disorders and hypothyroidism.

Objectives: Describe a rare cause of macrocytic anemia in a child with bicytopenia and a constellation of other symptoms, leading to the diagnosis and discuss the red herring which nearly led to a misdiagnosis.

Design/Method: Single subject case report.

Results: A 3 month-old Caucasian male was transferred for chronic bicytopenia. This was first noted at 2 months of age, and he was evaluated for failure to thrive, developmental delay, noisy breathing, GERD and was recently diagnosed with cow's milk-protein allergy. After attempting different formulas, he was switched to a goat's milk formula 1 month prior to presentation. Physical exam revealed a well appearing infant with slightly abnormal facies, generalized pallor, right sided strabismus, stridor at rest, hepatomegaly, and mildly decreased tone. Lab work revealed: hemoglobin 6.5gm/dL, MCV 95.7FL, reticulocyte 5.6%, platelets 90k, and a normal white count. Based on the history of goat's milk and macrocytic anemia, a diagnosis of folate deficiency was suggested. However, the constellation of additional symptoms warranted a further work-up. Both LDH and red blood cell folate were found to be elevated. Peripheral blood smear demonstrated dysplastic and enucleated RBCs, decreased number of platelets, many vacuolated neutrophils with myeloid precursors and activated lymphocytes, and no hypersegmented neutrophils. A skeletal survey revealed diffusely increased bone mineral density throughout vertebral bodies and long bones. Genetic testing confirmed the diagnosis of infantile malignant osteopetrosis [double heterozygous TCIRG1 exon 12 mutations]. He underwent a matched unrelated donor bone marrow transplant 3 months after diagnosis and continues to be doing well>14 months post-transplant with normal CBC parameters and improvements in growth and developmental delay.

Conclusion: While there are many etiologies of macrocytic anemia, some are more common than others, it is imperative to obtain a detailed history and work up including a peripheral smear to support your diagnosis. The history of goats milk use in the setting of a macrocytic anemia could have delayed the diagnosis of osteopetrosis leading to irreversible damage if early intervention was not made.

POSTER # 339 | AN UNUSUAL CASE OF ABO HEMOLYTIC DISEASE INVOLVING MATERNAL BLOOD TYPE A AND NEONATAL BLOOD TYPE AB

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Background: ABO hemolytic disease is a common cause of hemolytic disease in the newborn, which almost exclusively occurs in babies with type A or type B blood group born to mothers with type O blood group. Anti A, B antibody which is an IgG antibody present in mother with type O blood group is considered culpable for this. However, hemolytic disease in newborn due to ABO incompatibility, with maternal blood A or B has not been reported. Here, we report a case of neonatal hemolytic disease occurring in a baby with type AB blood group born to a mother with type A blood group.

Objectives: To review clinical presentation of an unusual case of ABO hemolytic disease secondary to incompatibility between maternal A and AB blood group in the newborn.

Design/Method: Case Report

Results: A male baby was born from a second pregnancy at 36 weeks 4 days via spontaneous vaginal delivery with a birth weight of 3,100 gm. The baby developed hyperbilirubinemia

(Total bilirubin level of 9.18 mg/dl and direct bilirubin of 0.59 mg/dl at 15 hours of life) along with hemoglobin level of 16.1 g/dl, hematocrit 45 % and 6.6 % reticulocytes. The peripheral blood smear showed occasional spherocytes and was otherwise unremarkable. Cord blood Direct Antiglobulin Test (DAT) was positive and Anti-B antibodies were detected in the cord blood.

Maternal blood group was A positive and the infant's blood group was AB positive. Maternal indirect antibody test was negative. The patient received phototherapy for 28 hours until the serum total bilirubin level dropped down to 10 gm/dl. The baby was thereafter stable and maintained normal bilirubin and blood counts without evidence of hemolysis at 4 weeks of age.

Conclusion: Hemolytic disease in newborn due to ABO incompatibility in mothers with blood group O occurs due to the presence of anti- A, B antibody which is an IgG type of antibody and can easily cross the placenta. In type A blood group, the serum contains anti B antibody which is IgM type of antibody and cannot cross the placenta. Our case is an exeption as maternal anti B antibody crossed the placental barrier and caused significant hemolysis in the newborn requiring treatment.

In our literature search, till date there has not been any case reported with such unusual ABO hemolytic disease secondary to incompatibility between maternal A and AB blood group in the newborn.

POSTER # 340 | SITOSTEROLEMIA PRESENTING AS HEMOLYTIC ANEMIA IN PEDIATRIC PATIENTS

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Background: Sitosterolemia is a condition in which lipids from plant sterols in dietary sources accumulate in blood and tissues. While atherosclerosis and cutaneous, tendinous or muscular xanthomas are most traditionally associated symptoms. Hemolysis can be a rare, or in some occasions, only presenting symptom of the disease. Serology can be significant for abnormally shaped red blood cells(RBC), known as stomatocytes, or macrothrombocytopenia. Sitosterolemia is caused by mutations in two adjacent adenosine triphosphate-binding cassette (ABC) subfamily G members 5 and 8 (ABCG5 and ABCG8) encoding sterolin-1 and sterolin-2 and is inherited in an autosomal recessive pattern. The resultant defective sterolin transporters, impair elimination of plant sterol. The excess plasma sterols can change the lipid composition of the RBC, making the membrane stiff, misstructured and prone to rupture, leading to hemolytic anemia.

Objectives: To describe hemolytic anemia as presenting symptom of sitosterolemia.

Design/Method: Case series

Results: Case one- A term male infant born without complication, with a history of significant hyperbilirubinemia requiring phototherapy. He was noted to have symptomatic hemolytic anemia with Hemoglobin of 6.1 g/dl, reticulocyte count 11.7% with associated pallor and jaundice at 1 month of life, required pRBC transfusion x2. Peripheral smear revealed microcytic, hypochromic RBC with polychromasia, poikilocytosis, target cells, elliptocytes, spherocytes and tear drop cells. Genetic panel for hemolytic anemia revealed a c.55G>C mutation in ABCG8. Patient maintained on folic acid with stable hemoglobin values of>9 g/dl without the requirement of any additional transfusions.

Case two—A female infant with family history of hereditary spherocytosis and hyperbilirubinemia requiring phototherapy. Presenting Hemoglobin was 11.0 g/dl with reticulocyte count of 1.7%. Peripheral smear significant for normocytic normochromic RBC with polychromasia and few spherical cells. Patient with pallor, but otherwise asymptomatic, growing and developing appropriately. Osmotic fragility testing showed slightly increased osmotic fragility and rare spherocytes. Genetic panel for hemolytic anemia revealed c.55G>C mutation in ABCG8, as well as mutations in NT5C3A and SEC23B, which are of uncertain significance. Patient maintained on folic acid with stable hemoglobin values of>11 g/dl without any transfusions.

Conclusion: These cases present an example of hematologic manifestations in infants as the only presenting symptoms of sitosterolemia with confirmatory c.55G>C mutation in ABCG8. Moreover, these cases emphasize the importance of the consideration of sitosterolemia in the diagnosis of hemolytic anemia and the necessity of genetic testing in unprovoked hemolysis. A definitive early diagnosis of sitosterolemia may significantly impact medical management and will help tailor therapies to secure optimum clinical benefit.

POSTER # 341 | SPLENIC LACERATION IN A PATIENT WITH BETA THALASSEMIA TRAIT: EVALUATION FOR ALPHA TRIPLICATION

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Background: Beta thalassemia intermedia is a diagnosis with very diverse clinical findings thought to be attributable to the disorder's significant genetic heterogeneity. While these patients do not require chronic transfusions as in seen with beta thalassemia major, intermittent transfusions may be required. Anemia and iron overload are common, due to extramedullary erythropoiesis with splenomegaly.

Objectives: We describe a case of a previously undiagnosed 16-year-old patient with beta thalassemia intermedia, who presented to the trauma service with a splenic laceration.

Design/Method: Case Report.

Results: A 16-year-old male of Indonesian and Taiwanese descent with a history of beta thalassemia trait presented after a bicycle related traumatic fall. Computed tomography revealed a grade IV splenic laceration with marked splenomegaly. Initial workup revealed a hemoglobin of 7.9 g/dL, mean corpuscular volume 72, red cell distribution width 22, plasma free hemoglobin 80, lactate dehydrogenase 1440 followed by subsequent hemoglobin drop to 6.6. He was managed non-operatively and received one blood transfusion. On review of his previous records, his hemoglobin range was chronically in the 7 - 9 range. Beta globin gene DNA analysis done in our hemoglobinopathy laboratory revealed a beta 0 mutation, with heterozygosity on codon 41/42 (-TTCT). After conventional reverse dot blot hybridization testing for an alpha triplication was inconclusive we performed an alpha multiplex ligation dependent probe amplification assay revealing an anti-4.2 alpha-globin

gene triplication. With co-inheritance of a beta 0 mutation and an alpha triplication in setting of moderate anemia and splenomegaly the patient was diagnosed with beta thalassemia intermedia also known as non-transfusion-dependent thalassemia.

Family history was significant for a sister with beta thalassemia major requiring bone marrow transplant. His father and paternal grandfather were diagnosed with beta thalassemia trait and also exhibited splenomegaly. Additional testing for both parents was pursued. His mother was found to have beta thalassemia trait and his father had our patient's same genotype. He and his father are now followed closely in our thalassemia clinic.

Conclusion: This provides further evidence that co-inheritance of an anti 4.2 alpha-globin triplication with beta thalassemia heterozygotes increases chain imbalance, converting a typically asymptomatic carrier state to that of a beta thalassemia intermedia.

POSTER # 342 | COPPER DEFICIENCY: AN OFTEN FORGOTTEN CAUSE OF MACROCYTOSIS

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Background: Common causes of macrocytic anemias include folate deficiency, vitamin B12 deficiency, secondary to drugs, hemolysis or bleeding, liver diseases, hypothyroidism, and myelodysplasia. Micronutrient deficiencies like copper can also cause macrocytosis and macrocytic anemias as it is an essential cofactor for various enzymatic reactions and hematologic, skeletal, neurologic, and vascular functions; the daily requirement being 15 mg/day

We describe the case of a 9-year-old female with a complex medical history who presented with macrocytic anemia that improved with copper replacement.

Objectives: To highlight the importance of evaluating for trace element deficiencies in patients with macrocytosis of unclear etiology.

Design/Method: Case report

Results: A 9 year old female with severe cerebral palsy, autonomic dysfunction, and chronic lung disease was admitted to the pediatric ICU for urosepsis and was noted to have a macrocytic anemia. She had a history of recurrent urinary tract infections (UTI), and was on nitrofurantoin for UTI prophylaxis. She is G-J tube dependent. She was febrile, tachycardic and tachypneic on admission. CBC showed a Hb of 6.6 g/dl with MCV 111 Fl (78-91). She had elevated inflammatory markers with mild transaminitis. Her MCV had been steadily increasing over the past 2 years.

We transfused her with packed red blood cells and initiated a workup for macrocytosis, which showed normal Vitamin B12, Folate, and methylmalonic acid levels. A hemolytic disease panel, haptoglobins, reticulocyte count, D dimer, and thyroid function tests were also normal.

On further workup, she had extremely low copper and ceruloplasmin levels and slightly low zinc levels. We started her on copper and zinc supplementation, which she received for eight months. We discontinued them following the normalization of Hb and MCV. Interestingly, her copper and ceruloplasmin levels began down-trending with increasing macrocytosis off the supplementation. Her zinc levels remained stable. The patient had to be restarted on copper supplementation. GI consult and work up did not reveal any disorders of copper metabolism/ other causes of copper deficiency.

Conclusion: Our patient's macrocytosis was most likely due to copper deficiency due to correction with copper supplementation and a linear correlation between the increasing macrocytosis and dropping copper and ceruloplasmin levels. This report is to emphasize the importance of evaluating for micronutrient deficiencies in patients with macrocytosis/ macrocytic anemias if all other work up is negative. The cause of her copper deficiency remains unclear though her GJ feeds could be contributory as copper is predominantly absorbed in the stomach and proximal duodenum.

POSTER # 343 | CONGENITAL TRANSFUSION DEPENDENT ANEMIA: A NOVEL PRESENTATION OF GFI1B D262N MUTATION

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Background: Growth factor-independent 1B (GFI1B) is a transcription factor essential for the development and differentiation of erythroid and megakaryocytic lineages. GFI1B aberrations have been implemented in patients with erythroleukemia, acute myeloid leukemia (AML), and megakaryocytic leukemia. Mice deficient for GFI1B failed to produce mature erythrocytes and showed a fetal liver containing arrested development of erythroid and megakaryocytic precursors however, this phenotype has not been described in clinical literature. D262N mutation of the GFI1B has been associated with an autosomal dominant platelet-type bleeding disorder which can be described as a gray platelet syndrome by light microscopy.

Objectives: Describe novel presentation of GFI1B D262N mutation

Design/Method: Case Report

Results: A fetus was found to have hydrops fetalis on prenatal ultrasound, requiring four intrauterine transfusions of packed red blood cells (pRBC). He was delivered at 32 weeks and found to have hypospadias, ASD/VSD, hypoglycemia, respiratory failure, thrombocytopenia, and anemia. The patient was admitted to the neonatal intensive care unit for 5 weeks, requiring 4 pRBC and 6 platelet transfusions. Work-up for anemia and thrombocytopenia including TORCH infections, was found to be negative aside from positive parvovirus IgG with negative maternal parvovirus IgM and negative parvovirus PCR. Coombs testing was negative and peripheral smear showed microcytic anemia with thrombocytopenia. Platelets appeared to be adequately granulated, normal in size and color on peripheral smear [AM1] .

Upon discharge, anemia with hemoglobin ranging from 6.5-9.0 g/dL and thrombocytopenia with platelet counts 22,000-67,000 continued. At two months of age, bone marrow aspiration and biopsy were obtained.

Bone marrow biopsy was notable for dyserythropoiesis with bilobed erythroid precursors and nuclear karyorrhexis involving at least 20% of erythroid precursors and noted reticulum fiber deposition with clustered megakaryocytes. The specimen was notable for iron deposition. Myelodysplastic syndrome (MDS) panel via FISH was negative and flow cytometry was normal. Next-generation sequencing was negative for common causes of congenital dyserythropoietic anemia and 116 causes of bone marrow failure. Whole exome sequencing revealed D262N mutation of GFI1B.

At 5 months of age, the patient continues to have transfusion dependent anemia and significant thrombocytopenia. He has an elevated ferritin of 643 and will undergo iron overload evaluation with T2* MRI and discuss the utility of hematopoietic stem cell transplant.

[AM1]Has he had light microscopy?

Conclusion: D262N mutation of GFI1B is previously described with platelet-related bleeding disorder, AML and MDS however can present with hydrops fetalis and transfusion-dependent anemia with dyserythropoesis.

POSTER # 344 | EPSILON-GAMMA THALASSEMIA TRAIT: A HETEROZYGOUS DELETIONAL MUTATION

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Background: Epsilon-, and gamma- globin gene mutations have been associated with beta- and delta- globin gene mutations resulting in rare thalassemias ranging from asymptomatic to severe hemolytic anemia.

Objectives: We report a heterozygous large deletional mutation in the epsilon-, gamma(G)-gamma(A) genes in the absence of mutations in beta- and delta- gene mutations.

Design/Method: A 2-month-old healthy female was referred for abnormal newborn hemoglobin (HGB) screen with AF pattern. There was no intrauterine or neonatal blood transfusions, or family history of anemia. Her sclerae were anicteric. She had no hepatosplenomegaly. At 2.5 months, HGB electrophoresis showed HGB A 90.5%, A2 4.1%, F 5.4% compared to 11 months, HGB A 95.2%, A2 4.8%, and F 0%. Complete blood cell counts remained normal. Beta globin gene nucleotide sequence analysis was normal. Multiplex polymerase chain reaction (PCR) amplification assay for epsilon-, gamma(G)-, gamma(A)-, delta-, and beta- globin genes, and the locus control region (LCR) was performed, designed to detect deletions and / or duplications.

Results: Results showed one copy of a deletion involving the epsilon-globin gene, gamma (G)-globin gene, and gamma(A)-globin gene. This deletion included the Beta-Globin pseudogene but not the LCR or the delta and beta-globin genes.

This child with unique heterozygous large deletion mutation in the epsilon-, gamma(G)-, gamma(A)- globin genes in the presence of normal beta- and delta- globin genes with insignificant deletion in the beta-globin pseudogene.

Since hemoglobin F consists of 2 alpha globin and 2 gamma globin chains, this mutation caused an abnormally low HGB F at 2 months and abnormal newborn screen AF rather FA pattern.

This mutation deletion did not cause microcytic anemia, hypochromasia or hemolysis.

Genetic counselling is recommended for this patient to address patient's future children's possibility of mutation inheritance and to know he status of hemoglobin genes of her future male partner.

Conclusion: This child with epsilon-, gamma-, thalassemia trait, manifests with abnormal newborn screen, elevated HGB A2 and no clinical symptoms.

POSTER # 345 | BONE MARROW FAILURE SECONDARY TO MECOM MUTATION: CASE REPORT

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Background: Inherited Bone Marrow Failure Syndromes (IBMFS) are a group of blood disorders that typically present with cytopenias and possibly pancytopenia, which are associated with genetic mutations. Some commonly known IBMFS are Fanconi anemia, dyskeratosis congenita, Diamond Blackfan anemia, and Shwachman Diamond syndrome. Molecular testing methods, including whole exome sequencing (WES) and next generation sequencing (NGS) of large panels of genes have become standard tools in the diagnosis and understanding of the underlying biology of complex disorders, including the IBMFS. One of the new genomic discoveries is the MECOM gene mutation, which was first identified in 2015. MECOM-associated syndrome is known to cause a congenital amegakaryocytic thrombocytopenia and radioulnar synostosis, however, further case reports have shared variable expression of symptoms in patients with the MECOM mutation.

Objectives: This case seeks to demonstrate diagnostic and clinical management of bone marrow failure in a 2-month-old female with MECOM mutation.

Design/Method: We present a case report of a 2-month-old female that initially presented with severe pancytopenia and subarachnoid hemorrhage.

Results: The patient had a bone marrow biopsy with hypocellular marrow with 30% cellularity. Her initial work up was unremarkable for an etiology. She had negative infection test for EBV, CMV, HHV6, parvo-virus B19, Hepatitis A, B, C, HIV, and varicella. Metabolic evaluation with normal TSH, free T4, iron panel, B12, RBC folate, zinc, and copper. Negative non-accidental trauma lab and imaging. From a hematologic/oncologic work up her marrow had normal karyotype, no malignancy or fibrosis, negative myelodysplastic syndrome panel and she had normal PNH in erythrocytes and leukocytes. As for classic IBMF testing she had negative chromosomal breakage studies, telomere length, bone marrow failure panel that included 60 genes. The patient subsequently had

multiple hospitalizations following the initial admission for complications from the pancytopenia. A whole exome sequencing was sent, which identified a heterozygous, de novo, variant of uncertain significance in the MECOM gene (c. 1763G>A, protein change p.Ser588Asn). The patient was then referred for allogeneic bone marrow transplant, with successful engraftment and resolution of pancytopenia.

Conclusion: MECOM is a relatively new identified gene mutation that causes bone marrow failure. Upon literature review, this patient's specific gene mutation of MECOM is the first reported. This case also emphasizes the need for early whole exome sequencing in patients with a negative infectious, metabolic, oncological, and standard of care bone marrow failure panels.

POSTER # 346 | UNUSUAL PRESENTATION OF DIAMOND-BLACKFAN ANEMIA WITH NORMAL BONE MARROW FINDINGS

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Background: Diamond-Blackfan anemia (DBA) is a rare congenital form of erythroid aplasia, characterized by onset in infancy, macrocytic anemia, reticulocytopenia, and presence of congenital anomalies in 50% of patients. A diagnostic feature of DBA is a bone marrow biopsy that shows normal cellularity with erythroid aplasia.

Objectives: We describe an unusual presentation of DBA in a patient who did not exhibit the typical bone marrow findings associated with this condition.

Design/Method: This is a case report.

Results: A full-term female patient with congenital hypothyroidism, congenital hip dislocation, vesicoureteral reflux, and autoimmune enteropathy, presented at 2 months of age, with severe anemia, hemoglobin 5.3 g/dL, reticulocyte count 5%, and normal other cell lines. Bone marrow aspiration and biopsy were performed on three separate occasions during the first 14 months of life, and each time they revealed a normocellular marrow with a predominance and left shift of the erythroid series. The patient had required red blood cell transfusions every 4 to 5 weeks for the first year of life. Subsequently, the patient's anemia resolved, and she became transfusion independent. However, the patient continued to have persistent macrocytosis and reticulocyte count ranging between 1.2 to 2.4%. The patient represented at age of 14 years with shortness of breath with exertion and was found to have recurrence of anemia with a hemoglobin level of 6.2 g/dL, mean corpuscular volume 108.8 fL, and inadequately low reticulocyte count of 0.8% with absolute reticulocyte count 17,000 per microliter. Bone marrow biopsy showed a mildly hypocellular marrow for age (75% cellular) with normal erythroid maturation. Genetic testing was performed and returned positive for an RPS19 mutation, which is consistent with DBA. The patient was started on steroid treatment.

Conclusion: This case report challenges the established paradigm that DBA always presents with erythroid aplasia in the bone marrow. It also provides an example of an atypical DBA presentation that involves a long period of transfusion independence followed by a sudden recurrence of anemia. This case report emphasizes the significance of considering DBA as a potential diagnosis when encountering a patient with a characteristic clinical presentation, even in the absence of typical bone marrow findings. It also highlights the need for a broad differential diagnosis and the utility of genetic testing in cases where DBA is suspected.

POSTER # 347 | GRANULOCYTE TRANSFUSION: BRIDGE TO STEM CELL TRANSPLANT IN APLASTIC ANEMIA WITH REFRACTORY PROCTITIS

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Background: Idiopathic aplastic anemia (IAA) is a rare form of bone marrow failure characterized by multilineage cytopenias and hypocellular bone marrow. Profound neutropenia associated with very severe aplastic anemia (vsAA) is a significant risk factor for development of life-threatening fungal and bacterial infections. Perirectal cellulitis and perianal abscess are associated with high morbidity rates. Absence of neutrophil recovery limits the eradication of such infections prior to treatment with immune suppressive therapy (IST) or hematopoietic stem cell transplant (HSCT).

Objectives: Describe the use of adjuvant granulocyte transfusion to treat antibiotic-refractory proctitis/perianal abscess in a profoundly neutropenic child with vsAA.

Design/Method: Case report

Results: 7-year-old female presented with febrile pancytopenia in the setting of Human Metapneumovirus and Parainfluenza. Bone marrow biopsy showed hypocellularity (60-70%) with granulocytic and megakaryocytic hypoplasia, favoring viral suppression. She progressed to transfusion dependence. Repeat bone marrow aspirate/biopsy revealed marrow aplasia. DEB chromosomes, telomere lengths, and PNH clones were negative, confirming vsAA. She was admitted for febrile neutropenia (F&N) and found to have COVID-19 with rectal pain, attributed to constipation. After defervescing on IV antibiotics (negative cultures), she was discharged. Within a week, she re-presented with hematochezia and F&N. MRI confirmed proctitis with perianal fistula; GI PCR panel was +Enteroaggregative E. coli. Despite clinical improvement and 2 weeks of IV antibiotics, she re-developed fever; imaging showed persistent proctitis with peri-rectal abscess. Due to limited antibiotic response alone, we trialed a course of granulocytes with improvement in anorectal inflammation by CT. She was discharged with a plan to continue IV piperacillin-tazobactam until achieving radiographic cure. Imaging after another 2 weeks of antibiotics showed evolving proctitis. She was re-admitted with F&N

and rising inflammatory markers. Failure to eradicate her peri-rectal infection despite>1-month of antibiotics, along with her previous response to the course of granulocytes, prompted us to prescribe a prolonged 10-day course of granulocytes with continued antibiotics. Post-granulocyte CT revealed resolution of perirectal abscess and proctitis. She subsequently underwent HSCT without recurrence of her infection.

Conclusion: Conventional granulocyte transfusions are considered in patients with severe neutropenia, bacterial or fungal infection refractory to antibiotics, and reasonable expectation of neutrophil recovery. Evidence for efficacy is limited. In our patient without expectation of bone marrow recovery, infection persisted despite prolonged antibiotics with resolution only after we re-attempted an extended course of granulocytes, allowing our patient to proceed with HSCT. We suggest an expanded application for granulocyte use in profoundly neutropenic patients without anticipated recovery for severe, antimicrobial-refractory infection.

POSTER # 348 | A UNIQUE CASE OF PAROXYSMAL NOCTURNAL HEMOGLOBINURIA IN AN ADOLESCENT MALE

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Background: Paroxysmal nocturnal hemoglobinuria (PNH) is an uncommon disorder in pediatrics. The primary risks of morbidity and mortality relate to symptoms of hemolytic anemia, a concomitant bone marrow failure (BMF), or myelodysplastic syndrome, and an elevated risk of thrombosis. Nonspecific symptomatology and variations in clinical presentations may lead to a delayed diagnosis. Incidence of PNH is 1-10 people per 1 million people in the general population with the average age of onset in the fourth decade of life. Diagnosis includes flow cytometry repeated at least twice at independent time intervals, which recognizes the PNH population of blood cells. Treatment is guided by one's PNH subtype and can include clinical monitoring, C5 complement inhibitors, and/or hematopoietic cell transplant.

Objectives: We report the case of a fourteen-year-old male with a history of chronic thrombocytopenia and macrocytosis, subsequently diagnosed with PNH.

Design/Method: Case report. An literature review was performed to review PNH pathophysiology, diagnostic measures, and treatment modalities.

Results: Our patient is a fourteen-year-old male with history of ITP in infancy, who re-presented at age eleven with a new petechial rash and increased bruising. Platelet count was 54.000 with a concurrent subtle yet progressive macrocytic anemia (maximum MCV of 105 fL and minimum hemoglobin of 10.4 g/dL). Work-up displayed no evidence of autoimmune lymphoproliferation syndrome, malignancy, or immunodeficiency. Bone marrow analysis revealed a mildly hypocellular marrow without evidence of malignancy, myelodysplasia, or severe aplasia. Insurance denied genetic testing for inherited BMF and cancer predisposition syndromes.

Two years later, he experienced two episodes of hematuria during first morning voids associated with abdominal pain and nausea. Three independent flow cytometry results revealed blood cells with a PNH-type phenotype (78.98%, 81.79%, and 84.08% of neutrophils and 56.62%, 59.48%, and 63.51% of red blood cells respectively). Repeat bone marrow analysis showed a normocellular marrow without abnormalities. Insurance again denied genetic testing. A sponsored genetic testing program found the patient was a carrier for Fanconi anemia with presence of heterozygous FANCE gene. Chromosomal breakage testing with diepoxybutane was negative.

Conclusion: PNH requires a comprehensive diagnostic approach, with its wide variety of clinical manifestations. This case highlights that the clinical presentation of pediatric PNH may be wider than what is considered common. A standardized and tiered approach to complex cytopenias would be advantageous in the care of these pediatric patients. Additionally, increased payor support for genetic testing is an important policy issue to help guide treatment decisions in rare pediatric conditions.

POSTER # 349 | A NOVEL DE NOVO FRAMESHIFT PATHOGENIC VARIANT UNDERLYING SAMD9L-ASSOCIATED AUTOINFLAMMATORY DISEASE

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Background: *SAMD9* and *SAMD9L* proteins promote degradation of cytokine receptors through endosomal trafficking. Germline heterozygous missense pathogenic variants in *SAMD9/SAMD9L* are associated with various disorders including MIRAGE, ataxia pancytopenia, and monosomy 7 with myelodysplasia and leukemia syndromes. These missense variants lead to gain-of-function that suppress cell growth. Development of myeloid malignancy can occur with loss of the mutated gene through revertant mosaicism. Recently, a distinct inflammatory disorder known as *SAMD9L*-associated autoinflammatory disease (SAMD9L-SAAD) has been described. SAMD9L-SAAD is caused by frameshift *SAMD9L* variants leading to a truncated protein with gain-of-function activity that appears to be interferon-driven. Clinical manifestations include neutrophilic skin infiltration, interstitial lung disease, cerebral calcifications, cytopenias, and decreased B and NK cells.

Objectives: To describe a patient with a novel heterozygous *SAMD9L* truncating variant leading to SAMD9L-SAAD.

Design/Method: Case report.

Results: An 8-week-old male infant was born at 32 weeks gestation with hydrops fetalis, respiratory failure, and poor cardiac function. He developed ventriculomegaly, anemia and thrombocytopenia, hepatosplenomegaly, poor growth, neutrophilic

dermatosis on biopsy of diffuse rash, *Enterobacter* urinary tract infection, and disseminated fungal disease. He was transferred to our institution for evaluation of suspected immunodeficiency. His course was complicated by retinal detachment, failed extubation attempts, multiple infections including *Enterococcus* bacteremia, severe B-cell deficiency, and brain imaging showing white matter volume loss with possible left parietal calcification. Whole exome sequencing identified a novel *de novo* frameshift *SAMD9L* truncating variant c.2804_2805delCT (p.Ser935Tyrfs*8). While this variant has not been previously reported, his phenotype was consistent with SAMD9L-SAAD. Cytogenetics revealed a normal male karyotype, and chromosomal microarray showed a 15q11.2 deletion. Peripheral flow cytometry demonstrated mild immunophenotypic abnormalities of the circulating CD34+ stem cell populations. He was treated with prolonged corticosteroids and immune globulin therapy. Given his comorbidities, he was not deemed a candidate for interleukin or Janus kinase inhibitors or hematopoietic cell transplantation. Although B cells were undetectable at 2 months of age, repeat flow cytometry at 4 months demonstrated a small population of B cells at 1.2%. The patient unfortunately succumbed to his disease at the age of 5 months after compassionate extubation.

Conclusion: *SAMD9/SAMD9L* syndromes can exhibit diverse manifestations and outcomes. This is the first known report of a patient with SAMD9L-SAAD due to this novel truncating variant. Truncating variants downstream of this variant have been described in individuals with SAMD9L-SAAD, with reported improvement of cytopenias and immunodeficiency after 1 year of age. Further research is warranted to illuminate the pathogenesis of *SAMD9/SAMD9L* variants.

POSTER # 350 | AUTOIMMUNE LYMPHOPROLIFERATIVE SYNDROME: A UNIQUE PRESENTATION

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Background: Autoimmune lymphoproliferative syndrome (ALPS) is an immune regulatory disorder. ALPS is classically due to mutations in the FAS gene and clinical presentation includes systemic lymphoproliferation, characterized by chronic lymphadenopathy, organomegaly, and multilineage cytopenia(s). Making the diagnosis of ALPS includes the above required criteria with the addition of various accessory findings including elevated biomarkers (sFASL, vitamin B12, IL-10, IL-18) and/or abnormal T cell subsets with double negative T cells (CD3+TCR$\alpha\beta$+CD4−CD8− DNTs).

Objectives: To review a case of an infant who presented with a chief complaint of fever and emesis, who was diagnosed with ALPS.

Design/Method: Case Report

Results: A 1 month old ex-40 week female infant (born from consanguineous parents), meeting all prior growth parameters and developmental milestones presented with fever, decreased oral intake, and emesis. She was initially found to be positive for rhino-enterovirus but due to abdominal distension on physical exam, imaging was done which showed hepatosplenomegaly and profound axillary and abdominopelvic lymphadenopathy concerning for a lymphoproliferative process. Initial labs showed a white blood cell count of 30,400/uL, hemoglobin of 5.7 gm/dL and platelets of 132,000/uL, with peripheral flow cytometry showing an absolute lymphocytosis, but without any malignant blast population. An extensive infectious work-up was performed which was non-revealing. With an initial concern for primary HLH or an underlying malignant oncologic process, a bone marrow and lymph node biopsy were performed. The lymph node biopsy revealed a double negative (CD4-/CD8-) T cell population and accessory blood work showed elevated levels of sIL2-R, IL18, vitamin B12, and ferritin. Soluble FAS ligand was markedly elevated at 117,391 (normal: 69-493) and a fas-mediated apoptotic assay was 1% (normal:>56%) all suggesting a diagnosis of ALPS. Genetic testing later confirmed the clinical diagnosis with the presence of a homozygous pathogenic truncating variant in the FAS gene.

Conclusion: ALPS is a rare pediatric immune regulatory disorder, and this case illustrates a unique presentation of an early-onset neonatal diagnosis. Given the clinical findings observed in ALPS are heterogeneous, differential diagnoses remain broad including infectious, oncologic, and/or related to a primary immunodeficiency all of which were evaluated and excluded in this patient. ALPS requires certain clinical and diagnostic criteria, which was ultimately fulfilled, and treatment was initiated with a steroid-sparing immunosuppressive therapeutic agent which has thus far shown to provide a sustained clinical response.

POSTER # 351 | IMMUNE CTYOPENIAS IN 22Q11.2 DELETION SYNDROME

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Background: 22q11.2 deletion syndrome is a rare genetic disorder that could present with immunodeficiency and immune dysregulation. It predisposes to secondary immune cytopenia that tend to be recurrent and difficult to manage. Here we present 2 cases of Evan syndrome in a background of 22q11.2 deletion syndrome with an absence of typical phenotypic features.

Objectives: To discuss treatment modalities of immune cytopenias in patients diagnosed with 22q11.2 deletion syndrome.

Design/Method: Case report and literature review.

Results: Patient A, an eighteen-year-old male who was previously healthy presented at age sixteen with mucocutaneous bleeding and thrombocytopenia with a positive Coombs test but no evidence of active hemolysis. He was clinically diagnosed with ITP but did not respond to IVIG and his response to steroid was suboptimal. Subsequently, he was initiated on thrombopoietin receptor agonist (TPO-RA), romiplostin, with improvement in his platelet counts. One year later, he presented with warm autoimmune hemolytic anemia (AIHA)

and had good response with steroid. Due to persistent lymphopenia and evolving hypogammaglobinemia, genetic panel for immunodeficiency was initiated and revealed a gross deletion in *TBX1*. Further SNP microarray confirmed 22q11.2 deletion syndrome.

Patient B, an eight-year-old male with history of partial cleft palate was initially diagnosed with Evan syndrome when he was one year old. He subsequently had two additional episodes of warm AIHA treated with steroids and rituximab. Due to persistent cytopenia, he underwent bone marrow evaluation and SNP microarray identified 22q11.2 deletion. He had recurrent episodes of immune cytopenia triggered by infections, for which, he was started on a romiplostin that could improve his platelet counts.

In depth immunophenotyping on both patients revealed mild hypogammaglobulinemia, moderate T cell lymphopenia, significantly reduced CD4+ naïve T cells, and decreased class switched memory B cells.

A literature review was performed and identified 14 cases of immune cytopenias secondary to 22q11.2 deletion syndrome. Five of them had ITP, 3 had Evan syndrome, 4 with pancytopenia, and 2 had ITP and neutropenia. Among those, different therapies were used including IVIG, steroids, rituximab, sirolimus, mycophenolate, and TPO-RA with variable responses. New treatment modalities such as bortezomib were highlighted.

Conclusion: Managing Evan syndrome in a background of 22q11.2 deletion syndrome remains controversial and there is no standard approach. We suggest those patients to be treated differently as their disease course is much more complicated. Our two patients responded well to the TPO-RA after trying multiple regimens.

POSTER # 352 | PEDIATRIC CASE WITH SHORT TELOMERE SYNDROME AND HLH COMPLICATED BY IMMUNE DYSREGULATION OF THE GUT

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Background: Short Telomere Syndromes (STS) are caused by mutations that interfere with telomere maintenance, resulting in an accelerated telomere shortening. These conditions are characterized by a predisposition to immunodeficiency, bone marrow failure and a wide spectrum of disease involving the immunologic, pulmonary, and gastrointestinal (GI) systems. One rare finding in STS is immune dysregulation of the gut, with colitis presenting as very early onset Inflammatory Bowel Disease (VEO-IBD). There is no current standard of care for immune dysregulation of the gut in patients with STS, and this complication leads to increased morbidity and mortality.

Objectives: To present a pediatric patient with failure to thrive (FTT), immunodeficiency, bone marrow failure and STS complicated by immune dysregulation of the gut and Hemophagocytic Lymphohistiocytosis (HLH).

Design/Method: This is a case report highlighting unique complications in a pediatric patient with STS.

Results: We present a 17-month-old female with history of prematurity presenting with fever, FTT and persistent diarrhea. Initial evaluation revealed rotavirus and norovirus infection. Her hospital course was complicated by respiratory failure secondary to Pneumocystis jiroveci pneumonia (PJP). She developed pancytopenia with hypogammaglobulinemia warranting further workup. Bone marrow biopsy revealed hemophagocytosis leading to diagnosis of HLH and subsequent treatment with decadron and Emapalumab. Whole Exome Sequencing revealed a heterozygous mutation in the RTEL1 gene, with Telomere Length Analysis supportive of STS. Diarrhea persisted, prompting further investigation. CT demonstrated left sided colitis. Flexible sigmoidoscopy grossly revealed diffuse moderate inflammation characterized by altered vascularity, congestion, erythema, and friability from the rectum to descending colon. Pathology was consistent with severely active colitis with ulceration, architectural distortion, and absent plasma cells with a broad differential. Viral staining was negative. Her colitis was refractory to Budesonide, Mesalamine, and Infliximab. Unfortunately, an inflammatory colonic stricture with obstruction developed, requiring ileostomy. She passed away secondary to recurrent bacteremia, intestinal failure, and respiratory failure.

Conclusion: While a wide array of GI symptoms can develop in STS, immune dysregulation of the gut presenting as VEO-IBD remains a unique manifestation. This colitis was refractory to multiple medical treatments, including biologics and diversion of the fecal stream. Upon review of the literature, one documented case reflects a patient with a homozygous RTEL1 mutation and STS diagnosed with VEO-IBD (Ziv et al, J Clin Immunol, 2020). Our case report supports the need to investigate patients with STS and FTT for immune dysregulation of the gut and early onset colitis. This case report highlights the need for further investigation into future novel treatments.

POSTER # 353 | ACUTE KIDNEY INJURY IN SICKLE CELL DISEASE HOSPITALIZATION

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Background: Pediatric patients with sickle cell disease (SCD) are at increased risk of development of chronic kidney disease (CKD)[1]. Acute kidney injury (AKI) events increase the long-term risk for CKD[1]. Non-steroidal anti-inflammatory drugs (NSAIDs) may contribute to AKI events, however, are often used as treatment for SCD-related pain.

Objectives: To determine the incidence and prevalence of AKI complicating hospitalizations in a longitudinal cohort with SCD and to characterize the relation to NSAID use during hospitalization.

Design/Method: The Sickle Cell Clinical Research and Intervention Program (SCCRIP) is a SCD lifespan cohort study. SCRIPP was used

to perform a retrospective chart review of all SCD-related hospitalizations. Pediatric and young adult participants with a history of AKI at presentation or developed during hospitalization were identified. AKI was defined as a 1.5 times or a ≥ 0.3 mg/dL increase in serum creatinine (SCr) from baseline. Baseline creatinine was defined as the SCr level obtained during the most recent routine clinic visit. Participant demographics, SCD-modifying therapies, NSAID use during hospitalization, and hematological parameters were studied in relation to AKI development using generalized linear mixed effect model, adjusting for age at admission. Data was analyzed using SAS 9.4, $p < 0.05$ was considered significant.

Results: Of the 328 participants with at least one hospitalization and available SCr measurements, 22% (72/328) had a hospital-associated AKI. There was no difference in sex and genotype among participants who experienced AKI and those who did not. In most participants (58/72, 80.6%), AKI was identified on presentation. Participants prescribed hydroxyurea (73.6% vs 58.2%, $p = 0.02$), on chronic transfusions (CTX) (45.8% vs 25.8%, $p = 0.001$), and had increased hospitalizations (16.6 vs 9.4, $p = <0.001$) experienced higher rates of AKI. From the 328 participants, 2,284 hospitalizations were identified. AKI events occurred in 6% ($n = 142$) of hospitalizations. AKI was associated with higher admission total bilirubin (3.88 mg/dL vs 2.96 mg/dL, $p = 0.01$) and white blood cell (WBC) counts (19.66 $x10^3$/uL vs 15.40 $x10^3$/uL, $p < 0.0001$). There was no difference in fetal hemoglobin, disease-modifying therapy exposure (hydroxyurea or CTX), or in-hospital NSAID use between participants with hospitalizations complicated by AKI compared to those who did not.

Conclusion: We identified a prevalence of AKI in 6% of hospitalizations that was associated with markers of hemolysis and inflammation. NSAID exposure during hospitalization was not associated with AKI; however, AKI was frequently noted on admission. Longitudinal studies are needed to determine additional risk factors for AKI development at presentation or during hospitalization.

1Ataga, Nature Reviews Nephrology, 2022

POSTER # 354 | A HEALTH EQUITY ECHO FOR PROVIDERS OF INDIVIDUALS WITH SICKLE CELL DISEASE

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Background: Studies have shown individuals with sickle cell disease (SCD) are often stigmatized and racialized due to implicit bias by healthcare providers during interactions. Biases can result in inequities in healthcare delivery, affecting health related quality of life and clinical outcomes.

Objectives: The Sickle Treatment and Outcomes Research in the Midwest (STORM) network developed a health equity training curriculum for a continuing education course using the Project ECHO ® virtual telementoring framework. A pilot Health Equity ECHO was held March—September 2022 to asses feasibility, acceptability and potential impact on provider bias. The curriculum addressed foundations of racial justice, race, racism, whiteness, along with applications and implementation strategies for institutional change.

Design/Method: Using the Project ECHO © framework, the Health Equity ECHO consisted of hour-long monthly sessions, with didactic presentations and interactive discussion typically including a case presentation, via Zoom. Canvas Learning Management System was used for supplemental materials and discussion post prompts for participant self-reflection. Optional post session "debrief" sessions were held for deeper reflective dialogue. A six question pre and post survey tool assessed awareness and impact of racism and participant's self-efficacy using a five point Likert scale.

Results: Thirty-two participants from 9 states participated in at least one session. Nearly half of participants reported their racial identity as white, with 30% African-American; 5% Asian; 5% multi-racial and the remaining preferring not to answer (11%). Roles of participants included physicians, nurse practitioner, registered nurses, pharmacists, psychologists, newborn screening coordinators, and patient advocates. Collectively, participants provide care to over 1,000 pediatric patients with SCD. At pre-registration, 25% of participants felt the impact of racism on their ability to deliver quality care was high or very-high; 64% of participants reported feeling as effective at caring for white patients as they are at caring for patients of color; and 62% of participants felt well-equipped to care for patients of color. Participants showed high awareness of racism which was associated with low impact of racism affecting participants' ability to deliver care ($p < 0.0001$). Over 25 MOC Part 2 credits, over 15 CME credits, and 10 nursing continuing education credits were awarded to participants for joining live sessions.

Conclusion: Feasibility and acceptability data, including qualitative data, from the Health Equity ECHO pilot cohort show this to be a promising training platform for healthcare providers to raise self-awareness about implicit bias and racism, build a safe community of practice, and leverage tools to address health inequities within healthcare settings.

POSTER # 355 | SICKLE CELL DISEASE TRANSITION CLINIC 2007 - 2022 : CELEBRATING 15 YEARS OF SUCCESS IN CONNECTICUT

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Background: Young adults with sickle cell disease (SCD) who do not successfully transition to an adult provider are at higher risk of mortality. We developed a combined pediatric/adult transition program between Connecticut Children's Medical Center (CCMC) and UCONN in 2007. Our published outcomes on the first five years of this transition program demonstrated a 68% transition success rate. Risk factors associated with unsuccessful transition included clinical markers of milder disease severity (SC and SB+ genotypes and no chronic

transfusion therapy [CTT]). This discrepancy was noted to be due to more effort involved on the part of providers to ensure transitioning patients who are on CTT and who have more severe genotypes (SS/SB0) get to their first transition visit.

Objectives: Improve transition success rate to 100% through enhanced tracking and reengagement of all patients transitioning to the adult SCD program regardless of genotype or CTT status

Design/Method: A quality improvement process was undertaken in 2012 to enhance transition outcomes. A shared Excel spread sheet was created to track patients. The CCMC nurse and the UCONN social worker (SW) reviewed all transitioned patients monthly. Patients who had not kept their appointment to be seen at the UCONN adult SCD center were contacted by CCMC staff to ascertain if they had been connected to another hematologist or if they still needed an adult hematology provider. The importance of transitioning was reiterated. If a provider was needed, an appointment was rescheduled at UCONN. UCONN SW staff apprised CCMC of patient attendance, no-shows, or cancellations for initial appointments. The process continued until the patient made their first visit to UCONN.

Results: 58 of 59 patients transitioned successfully from 2012-2022.

Conclusion: Goals of "readiness" for transition are often abstract, difficult to define and vague. There are also limits to achieving such readiness in a defined time. Changes on the part of the providers are in many ways easier to implement and can improve communication, provide consistent messages to patients and lead to a smoother transition process. Having quality improvement programming as part of the transition process by both the pediatric and adult SCD providers, and holding all accountable, can dramatically improve transition outcomes. Our use of a close tracking system and improved communication between the two institutions led to a 98.3% transition success rate. Further research will identify if our enhanced transition success is associated with improved health outcomes.

Andemariam et al 2014). Identification of risk factors.. Pediatric Blood & Cancer, 61(4)

POSTER # 356 | THE RELATIONSHIP BETWEEN MEDICATION ADHERENCE, BARRIERS, AND QUALITY OF LIFE IN SICKLE CELL DISEASE

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Background: Sickle cell disease (SCD) requires lifelong treatment and management. While hydroxyurea, voxelotor and/or crizanlizumab reduce complications and improve health related quality of life (HRQOL), adherence remains suboptimal, especially among adolescents and young adults (AYA). Further, patient barriers to adherence are poorly understood.

Objectives: Assess the relationship of patient medication adherence to barriers and HRQOL domain scores and understand factors contributing to variation in medication adherence among AYA with SCD.

Design/Method: Sixty-one patients (10-25 years old) with SCD (all genotypes), receiving hydroxyurea, voxelotor and/or crizanlizumab participated in this single-institution longitudinal study over 12-months. Participants completed the Adherence to Refills and Medications Scale 7 (ARMS-7), Brief Medication Questionnaire (BMQ), and Patient Reported Outcomes Measurement Information System (PROMIS) HRQOL measures every 3-4 months. Patient characteristics were analyzed using descriptive statistics, and Wilcoxon rank-sum test, Kruskal-Wallis test, chi-square, and spearman tests to assess the relationships.

Results: Participants (52% Female; 93% Black; median age of 14 years [IQR 12-18], at enrollment, had a median (IQR) fetal hemoglobin (HbF) of 12.1% (7.9-24.9) and mean corpuscular volume (MCV) of 93.5 fL (80- 104.2). Self-report adherence rates (median 12 [IQR 10-14]) were correlated with HbF ($r = -0.44$, $P < 0.001$) and MCV ($r = -0.27$, $P = 0.03$). Participants reported medication recall barriers or forgetfulness (41%), negative beliefs about medication (23%), and difficulty with access to medications, such as paying for refills (32%). Most patients endorsed ≥1 barrier domain (n = 40, 66%).

Patients with lower medication adherence were significantly more likely to report forgetfulness ($P < 0.01$), access barriers ($P < 0.01$) and negative beliefs ($P = 0.04$), compared to patients with higher adherence. Patients with lower adherence reported worse physical stress ($P = 0.01$), psychological stress ($P < 0.01$), anxiety ($P < 0.01$), depression ($P < 0.01$) and self-efficacy managing symptoms ($P = 0.02$). Furthermore, participants with negative beliefs reported significantly worse anxiety ($P = .03$) and depression ($P < 0.01$) a trend toward significantly more fatigue ($P = 0.06$) and social isolation ($P = 0.08$) than those without negative beliefs. Participants with reported medication access barriers trended toward significantly worse physical stress ($P = 0.06$), anxiety ($P = 0.08$) and pain ($P = 0.08$), compared to those without access barriers.

Conclusion: A significant number of AYA with SCD have at least one medication adherence barrier related to access, forgetfulness, or negative beliefs. Lower medication adherence and negative beliefs were significantly associated with impaired HRQOL. These findings suggest that mitigating barriers to medication access, helping to reduce forgetfulness, and overcoming negative beliefs could contribute to improved HRQOL.

POSTER # 357 | ASSESSING PSYCHOSOCIAL RISK FACTORS FOR FAMILIES OF CHILDREN WITH SICKLE CELL DISEASE

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Background: Most individuals with sickle cell disease (SCD) in the U.S. identify as Black or African American, a minoritzed population who experiences disparities in healthcare access and treatment. For

individuals managing a chronic health condition like SCD, psychosocial stressors resulting from and impacted by systemic racism can lead to worse health outcomes.

Objectives: The purpose of this study was to assess the utility of the Psychosocial Assessment Tool (PAT), a validated caregiver-report screener, in identifying psychosocial risk factors for families caring for children with SCD at a comprehensive pediatric sickle cell center.

Design/Method: The PAT is administered annually as part of the clinical visit and scored by the SCD Social Worker to provide tailored resources to families. Scores are stratified into 3 categories indicating level of psychosocial need/concerns—Universal, Targeted, or Clinical (least to most). PATs administered between July 2021-December 2022 were analyzed, with descriptive statistics performed to determine demographics, experiences, beliefs, and overall risk categorization, as well as regression analyses to compare PAT category to individual variables.

Results: Two hundred fifty-one PATs were distributed to 236 caregivers over this timeframe with 236 completed for analysis. Four families refused to complete the PAT; the remaining were incomplete. Most caregivers identified as Black, single women over 21 years of age with at least a high school degree. The average patient age was 8.19 years (range 0-22 years). Sixty-six percent of PATs fell into the Universal range, 28% in the Targeted range, and 5% in the Clinical range. Caregivers/patients that scored in the Targeted or Clinical category were more likely than those in the Universal category to report financial hardship, caregiver mental health concerns, family stressors, developmental concerns with a sibling, and fewer people who support patient/family ($p < 0.05$). Forty-eight percent of families reported some form of financial difficulty, including 39% of all families in the Universal category. Nine families had more than one screen during this timeframe, 2 of whom moved categories due to increased risk, mostly related to change in caregiver support or stressors.

Conclusion: Implementation of a psychosocial risk screener in the SCD clinic helped identify financial challenges for many families, as well as caregiver burden and mental health concerns, allowing for timely resource support. Many of these families, however, were categorized as Universal, indicating that distribution of resources and support for families of patients with SCD must not be based on total PAT score/category alone.

POSTER # 358 | OUTPATIENT PAIN MANAGEMENT PLANS FOR PEDIATRIC PATIENTS WITH SICKLE CELL DISEASE

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Background: Patients with sickle cell disease (SCD) experience recurrent vaso-occlusive crises (VOC) as a primary manifestation of their illness. Pain may be present as acute, chronic or acute-on-chronic. These crises often require emergency room visits and hospital admissions to appropriately manage pain. The American Society of Hematology (ASH) guidelines recommend that individuals with SCD have individualized outpatient pain plans to effectively begin pain management at home prior to presenting to the emergency room (1). Rady Children's Hospital-San Diego(RCHSD) serves over 100 patients with SCD, however there was no standardized approach for the provision of outpatient pain plans (OPP).

Objectives: By applying quality improvement (QI) methodology, our interprofessional team aimed to improve outpatient pain management and quality of life for patients with SCD.

Our Smart Aim was: Between November 2021- May 2022, 50% of patients with SCD, seen at the RCHSD Comprehensive Sickle Cell Clinic, will have an OPP provided.

Design/Method: Qualitative interviews with families, hematology providers and staff informed QI tools (process mapping, key driver and Ishikawa diagrams) to identify barriers and facilitators to implementation. Interventions were evaluated using PDSA cycles with each monthly comprehensive clinic (CC).

OPPs were modeled after an existing asthma action plan, with green, yellow and red zones to indicate different levels of pain management. Pain medication dosages and supportive care measures for each zone were discussed at CC and families were given printed color copies prior to their visit completion. Families were contacted by phone within 1 week of the CC to review and confirm OPP receipt.

Results: Eighty-four percent (16/19) of patients seen in CC between November 2021 and May 2022 received an OPP. Three patients did not receive an OPP due to issues with the electronic medical record.

Feedback from follow-up calls with parents/patients revealed appreciation for having the OPP with up-to-date medication dosages to reference during a VOC. Adolescents expressed interest in learning more about supportive care measures. Provider feedback highlighted the benefits of a new streamlined workflow.

Conclusion: Our interprofessional QI team surpassed our SMART aim of implementing the OPP for our patients with SCD. Next steps include formal evaluation of the clinical impact of the OPP.

1. Brandow et al.; "American Society of Hematology 2020 guidelines for sickle cell disease: management of acute and chronic pain." Blood Adv 2020; 4 (12)

POSTER # 359 | THROMBOPROPHYLAXIS IN SICKLE CELL PATIENTS HOSPITALIZED FOR COVID-19, A QUALITY IMPROVEMENT STUDY

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Background: The inflammatory response to COVID-19 infection leads to a procoagulant state and coagulopathy and has been associated with an increased risk of thromboembolic event. Several studies

demonstrated improved outcome using anticoagulation in adult populations hospitalised for Sars-Cov2 infection. The rate of thromboembolic events also seems to be increased in the pediatric population, but data are scarce and conflicting. Following those observations, recommendations for anticoagulant thromboprophylaxis in children hospitalized for COVID-19 infection were emitted early in the pandemic, including for children with sickle cell disease (SCD) a condition also known for higher risk of thrombotic complications.

Objectives: Since March 2020, our institutional guidelines recommended anticoagulation at a prophylactic dose in every SCD patient older than 6 months of age hospitalized in the context of a Sars-Cov2 infection, for the duration of the hospital stay or a maximum of 14 days (whichever came first). Our goal was to evaluate the application, the efficacity and the safety of thromboprophylaxis in those patients.

Design/Method: As part of a quality improvement review, charts of every SCD patients aged 6 months or older hospitalized at our institution (Montreal, Canada) in the context of a Sars-Cov2 infection between April 2020 and February 2022 were revised.

Results: Twenty-three SCD patients were hospitalized during the study period in a context of Sars-Cov2 infection. Institutional recommendations were followed for 18 (78.3%) patients. Two patients didn't receive prophylactic anticoagulation due to mild thrombocytopenia at admission. All others received prophylactic anticoagulation until their discharge, with mean hospital stay of 3 days.

Non-conformities were observed in 5 patients (21.7%): anticoagulation not prescribed within 24 hours of admission (2), or not prescribed as deemed non necessary per the treating physician (2), or unexplained (1).

Mild bleeding was observed in one patient on thromboprophylaxis, who experienced an epistaxis that stopped after the application of a topic antifibrinolytic agent. One patient developed thrombocytopenia after the introduction of anticoagulation. No thromboembolic event was observed.

Conclusion: Although the dose and duration of anticoagulation in children remains uncertain, we will continue to reinforce the use of thromboprophylaxis for SCD patients aged 6 months to 18 years hospitalized in the context of COVID-19 infection. The retrospective nature of this study and the limited number of patients prevent us to make further recommendations notably on the dose of the anticoagulant. We will continue to monitor the application and safety of our recommendation as COVID-19 pandemic evolves.

POSTER # 360 | IMPROVING EFFICIENCY OF VASO-OCCLUSIVE CRISIS CARE IN AN INFUSION CENTER THROUGH STANDARDIZATION

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Background: Sickle cell vaso-occlusive crises (VOC) occur unpredictably, leading to same-day add on visits in our infusion center staffed by a provider of the day. A retrospective data review of infusion appointments identified inconsistent pain management across different encounters in the same patients. Research supports the effectiveness of individual pain plans (IPP) in the inpatient and emergency room settings however, the impact has not been well described in the ambulatory infusion center.

Objectives: The objective of this quality improvement initiative was to increase the consistency of effective pain management in the ambulatory infusion center through development of easily accessible IPPs in the electronic health record (EHR) coupled with a plan of care huddle with the provider, nurse, and patient regarding their treatment plan at that visit.

Design/Method: A multidisciplinary quality improvement team engaged with key stakeholders to gain support for this initiative. Initial surveys were completed by infusion nurses and physician providers. This data informed a root cause analysis that guided the intervention, specifically: 1) standard formatting of the IPP, 2) Standard location in the EMR of the IPP, and 3) a patient-focused huddle at every encounter with the bedside nurse, provider, and patient. A prospective data collection tool was developed and utilized by the nurses to track quantitative data to measure the frequency and effectiveness of implementing IPPs, with a goal frequency set at 70%.

Results: Results were collected from 141 appointments over a six-month period. Pain medication administered within the first hour increased from 72% to 79%. Dose consistency across episodes increased from 54% to 71%. Pre-intervention, 52% of analgesic orders were placed as one-time orders, while 41% were every hour PRN for up to three doses. Post-intervention data revealed a 28% reduction in one-time orders and a 34% increase in PRN doses leading to an average additional 700 minutes saved over 6 months (one order takes an estimated 10 minutes from placement to verification). Only 6 encounters resulted in hospital admissions or transfer to the emergency department for continuation of care.

Conclusion: Implementation of an IPP in the ambulatory setting that is easily accessible in the patient's electronic health record, coupled with a plan of care huddle can expedite consistent, effective pain management and decrease hospital admissions and emergency room visits for VOC.

POSTER # 361 | IMPACT OF PSYCHOSOCIAL STRESSORS ON MENTAL HEALTH AND QUALITY OF LIFE IN SICKLE CELL DISEASE

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Background: Individuals with sickle cell disease (SCD) suffer from a myriad of complications, including severe pain and stroke. Higher rates of depression and anxiety than the general population are also characteristic of the population. Yet, access to screening and follow-up services are limited, and structural inequities in education and

healthcare contribute to the significant healthcare disparities experienced by this neglected population.

Objectives: The purpose of our study is to evaluate the potential association of psychosocial family stressors and child mental health and quality of life through relevant screens in a comprehensive SCD clinic.

Design/Method: The PAT is a validated caregiver-reported questionnaire administered annually as part of the clinical visit. Scores are stratified into 3 risk tiers indicating level of psychosocial intervention necessary—Universal, Targeted, or Clinical (least to most). The PedsQL is distributed annually to patients 2 years and older and caregivers, and the PHQ9 is a validated screen for depression distributed annually to patients ages 12 and up during routine clinical visits. All screens are reviewed by the SCD Social Worker and/or Psychologist. Univariate and multivariate analyses were performed as relevant.

Results: There were 236 completed PATs for analysis. Sixty-six percent of patients fell into the Universal range, 28% in the Targeted range, and 5% in the Clinical range. Forty-eight percent of families reported some form of financial difficulty, with housing, utility bills, and car costs as the most common.

Sixty-nine unique patients had also completed a PHQ9. Median PHQ9 scores based on PAT category were significantly higher for those in the Clinical category than the Universal ($p < 0.05$).

Forty-six patients/caregivers had completed the Child/Caregiver PedsQL and the PAT. Total Child and Caregiver PedsQL Scores in the Targeted and Clinical Categories were lower than the Universal Category ($p < 0.05$). Caregiver subscale scores were also lower, with significant associations with the Hurt, Impact, and Worry total scores ($p < 0.05$). Child subscale scores were also lower in Targeted and Clinical Categories compared to Universal, all of which showed similar statistically significant associations as Caregiver subscale total scores.

Twenty patients and 15 caregivers had completed all 3 screens at the time of this analysis, but multivariate analysis did not demonstrate a statistically significant association of screening results and PAT categories.

Conclusion: Our study demonstrated an association between caregiver-reported psychosocial risk factors, quality of life, and depression screening, highlighting the importance of mental health and psychosocial screening for families of children with SCD as part of routine care.

POSTER # 362 | CLINICAL FACTORS AFFECTING 6-MINUTE WALK TEST PERFORMANCE IN CHILDREN WITH SICKLE CELL DISEASE

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Background: In sickle cell disease (SCD), hemoglobin polymerizes in the deoxygenated state resulting in vaso-occlusion, tissue hypoxia, acute chest syndrome, and stroke. Cardiopulmonary complications of SCD are associated with higher morbidity and mortality in adults but are poorly understood in children. The 6 minute-walk test (6MWT) is a validated submaximal exercise test used to measure cardiopulmonary functional capacity. Previous studies suggest children with SCD have abnormal 6MWT results; however, the results of these studies are equivocal and risk factors for abnormal 6MWT parameters are unclear.

Objectives: We aimed to describe 6MWT results in children with SCD and the clinical factors associated with a reduced walk distance and the presence of desaturations during the 6MWT.

Design/Method: We performed a retrospective chart review of children with SCD followed at Children's Medical Center in Dallas, TX who had a 6MWT between 2013-2020. Patient demographics and clinical data were manually abstracted, including baseline hemoglobin level, use of hydroxyurea, frequency of hospitalizations in the previous 3 years, tricuspid regurgitant jet velocity on echocardiogram, pulmonary function tests, diagnosis of asthma, nighttime hypoxemia, and home oxygen requirement. Descriptive statistics were calculated for all study variables using the statistical software SAS. An abnormal walk distance was defined as less than 80% of predicted based on published models by Geiger et al. Desaturations during the 6MWT was defined as a 3% decrease in oxygen saturation from baseline. In comparing clinical variables to 6MWT outcomes, t-test was utilized for quantitative variables and Chi-square or Fisher's exact test for categorical variables. Linear and logistical regression were performed to predict walk distance and odds of desaturation during the 6MWT, respectively.

Results: There were 43 patients included in the study (median age 11 years, 72% female). Walk distance was reduced in 72% of patients. Male gender and the number of hospital admissions were associated with a reduced walk distance (p-value 0.019 and 0.013, respectively). A history of home oxygen use was associated with 6MWT desaturations (p-value 0.012). Univariate linear regression showed prescribed home oxygen and the number of admissions were predictive of walk distance (p-value 0.005 and 0.030, respectively). Univariate logistic regression revealed the odds of desaturation was greater for patients with home oxygen (OR 5.9, p-value 0.028).

Conclusion: Gender, frequency of hospital admission, and the requirement of home oxygen all may contribute to poorer cardiopulmonary performance in children with SCD as assessed by the 6MWT.

POSTER # 363 | EVALUATION OF THE ROLE OF C-REACTIVE PROTEIN IN FEBRILE CHILDREN WITH SICKLE CELL DISEASE

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Background: Pediatric patients with sickle cell disease (SCD) suffer from multi-systemic complications. Repeated sickling of red blood cells within the splenic tissue compromises function, precipitating tissue ischemia and auto-infarction. This increases the susceptibility to infection by encapsulated bacteria. Hydroxyurea (HU), by inducing fetal hemoglobin production, may serve to decrease hemolysis and inflammation. C-reactive protein (CRP) is a cytokine responsible for activating the classical complement system by acting as an opsonin.

CRP levels are used as an indicator of inflammation and are included in the evaluation of these patients.

Objectives: 1. Assess the association between HU use and CRP levels. 2. Assess the correlation between CRP levels and bacteremia or hospital admission in patients with febrile SCD.

Design/Method: A retrospective study was conducted at the Acute Care Clinic (ACC) at St. Jude Children's Research Hospital evaluating all febrile SCD encounters at the ACC from January 2020 through December 2021. Electronic medical records were accessed to gather medication use, acute diagnosis, CRP levels, blood culture results, and disposition status. Normal to minor elevations in CRP were defined as values from 0.0 through ≤ 1.0 mg/dL while moderate to marked elevation included values from 1.1 through ≤ 10.0 mg/dL. Data analysis included descriptive data in percentages. A Chi-square test of independence or Fishers-exact test was conducted for further indagating on variable relationships.

Results: Ninety-four children with SCD had 115 clinical encounters for fever at the ACC during the study period with 107 having CRP levels for the encounter. The median age was 4.3 years (range 0.2-18.9 years) and 50.5% were male. Patients on HU had a normal to mildly elevated CRP 46.8% of the time and moderate to marked elevation 53.2% of the time (p = 0.83). Bacteremia occurred in 2 patients (1.74%) with *Staphylococcus epidermididis* and coagulase-negative *Staphylococcus*, but both cases were associated with normal CRP levels. For patients admitted to the hospital, 68.2% had a moderate to marked elevated CRP compared to 31.8% which had a normal to mildly elevated CRP (p = 0.15).

Conclusion: HU did not appear to impact CRP levels. Bacteremia was rare with no cases of *Streptococcus pneumoniae* isolated, and both cases were associated with a normal CRP. While patients admitted to the hospital had a higher prevalence of marked CRP elevation, this was not statistically significant in this cohort. Further studies are necessary to evaluate the value of CRP levels in the setting of a fever in patients with SCD to aid clinicians in decision-making.

POSTER # 364 | THE IMPACT OF ILLNESS PERCEPTION AND STIGMA ON PATIENT-REPORTED OUTCOMES IN SICKLE CELL DISEASE

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Background: Stigma and illness perceptions of adolescents and young adults (AYA) with sickle cell disease (SCD) are not well-studied. These socio-emotional factors may have implications on patient-reported outcomes, including health-related quality of life (HRQOL) and medication adherence.

Objectives: Describe illness perception and stigma among AYA with SCD and examine the relationship between illness perceptions and stigma of AYA with SCD and HRQOL and medication adherence

Design/Method: Patients, 10 to 25 years old, English-speaking, and taking hydroxyurea, voxelotor and/or crizanlizumab for SCD treatment were recruited and enrolled from outpatient hematology clinics at a single academic institution. Participants completed the Brief-Illness Perception Questionnaire (B-IPQ), Measure of Sickle Cell Stigma Questionnaire (MoSCS), Patient Reported Outcomes Measurement Information System (PROMIS) HRQOL Domains, and Adherence to Refills and Medications Scale 7 (ARMS-7) every 3 months over a 1-year period. Patient characteristics were analyzed using descriptive statistics, and Wilcoxon rank-sum, Kruskal Wallis and spearman's correlations to assess the relationships.

Results: Sixty-one participants completed all assessments (93% Black; 52% Female; median age 14 years [IQR 12-18]). Older participants (18+ years) reported a better understanding of SCD (10 vs 8, $p = 0.02$) but worse emotional response to SCD (6 vs 3, $p = 0.03$) compared to younger participants (10-17 years). Patients with higher self-reported medication adherence reported less perceived SCD-related consequences (4 vs 0, $p = 0.03$) and symptoms (4 vs 2, $p = 0.01$) and had better treatment control (10 vs 8, $p = 0.03$). Patients with less perceived personal control of SCD and more emotional response to SCD had worse social isolation ($r_s = -0.29$, p = 0.03; $r_s = 0.33$, p <0.01), mobility ($r_{s=}0.34$, p <0.01; $r_s = -0.26$, p = 0.04), anxiety ($r_s = -0.26$, p = 0.04; $r_s = 0.41$, p <0.01), depression ($r_s = -0.27$, p = 0.03l; $r_s = 0.48$, p <0.001), and fatigue ($r_s = -0.39$, p <0.01; $r_s = 0.32$, p = 0.01), respectively. Further, patients with more perceived personal control had with less physical stress ($r_s = -0.50$, p <0.001), pain ($r_s = -0.30$, p = 0.02), and greater mobility ($r_s = 0.34$, p <0.01). Participants with higher negative perceptions of SCD-consequences and concerns reported more physical stress ($r_s = 0.30$, p = 0.02; $r_s = 0.26$, p = 0.04), depression ($r_s = 0.40$, p <0.01; $r_s = 0.52$, p <0.001), and fatigue ($r_s = 0.32$, p = 0.01; $r_s = 0.41$, p <0.01). Most patients (80%) endorsed ≥1 statement related to stigma and those who reported greater stigma had more perceived SCD-related consequences (p = 0.03), concerns (p = 0.02) and emotional response (p = 0.04).

Conclusion: Patients with more perceived stigma, as well as negative perceptions of SCD and related medications reported lower medication adherence and worse HRQOL. These multifaceted and dynamic relationships potentially offer new targets to improve HRQOL and medication adherence in AYA with SCD.

POSTER # 365 | RELATIVE RETICULOCYTOPENIA, ERYTHROPOIETIN, AND KIDNEY FUNCTION IN PATIENTS WITH SICKLE CELL DISEASE

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Background: The two key features of SCD are chronic hemolytic anemia and vaso-occlusion. Elevated reticulocyte counts are necessary to maintain stable hemoglobin levels. Inappropriately low reticulocyte levels could result from the decreased capacity of the bone marrow

vs. decreased stimulation by erythropoietin. Relative reticulocytopenia (RR) has been defined by the Multi-Center Study of Hydroxyurea Follow-Up Study (MSH-FU) as reticulocytes <250×109/L despite hemoglobin <9 g/dl. As previously reported in patients with SCD erythropoietin levels are elevated, but they are lower than expected for a healthy patient with chronic anemia.

Objectives: Investigate relationship between markers of kidney function, erythropoietin levels, and RR in patients with SCD. We hypothesize that patients with measured kidney damage will have RR due to decrease in erythropoietin levels and patients on disease modifying therapy (hydroxyurea) will have better reticulocyte responses.

Design/Method: Data collected through retrospective chart review of patients with SCD disease followed at St. Christopher's Hospital, Philadelphia. Using EMR, we selected 100 patients who met inclusion criteria. Patients in the study had the diagnosis of Hb SS and S beta0. They had available laboratory parameters including CBC, reticulocyte count, kidney function and erythropoietin levels. To evaluate kidney function we used creatinine, cystatin C, GFR calculated based on cystatin C, urine microalbumin/creatinine ratio, and proteinuria. Patients were excluded if they were on chronic PRBC transfusion, had underlying kidney disease, or if labs were obtained during a disease exacerbation. A series of contingency tables with Spearman correlation and ANOVA tests were used to analyze the data.

Results: One hundred patients were included in the study, with ages ranging from 1-28 years, mean age of 11.8 years, 47 females, and 53 males. Ninety-one patients had Hb SS disease and 9 Hb S beta0 thalassemia. Twenty-eight patients had RR. Using nonparametric correlations in patients with RR, erythropoietin levels were significantly negatively correlated with urine creatinine ($r = -0.621$, $p = 0.003$) and significantly positively correlated with GFR ($r = 0.420$, $p = 0.037$), although showed no significant correlations with cystatin C. A significant negative correlation was seen between erythropoietin and hemoglobin as well as between erythropoietin and age in both the RR and no RR groups (not seen with platelet $p = 0.065$ in no RR group). Patients on hydroxyurea had higher erythropoietin levels.

Conclusion: In patients with SCD who have RR, erythropoietin levels inversely correlate with markers of kidney damage and directly correlate with GFR. Erythropoietin levels were inversely correlated with Hgb in both the RR and no RR groups.

POSTER # 366 | TRAINING MEDICAL STUDENTS AS PATIENT NAVIGATORS FOR A SICKLE CELL DISEASE TRANSITION CLINIC

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Background: Transitioning from pediatric to adult care is a challenging process for adolescents and young adults (AYAs) with sickle cell disease (SCD). AYAs with SCD are at an increased risk of death soon after they are discharged from pediatric practices and have a mortality rate that quadruples when compared to younger children and older adults.[1] This population often has no formal transition planning prior to transfer to adult care, leading to patients that feel unready to be transitioned and an increased dependence on emergency departments for medical care during this period.[2,3] Sickle Cell Superheroes is a service-learning program that trains medical students to become patient navigators for AYAs with SCD who are transitioning to adult medicine. Using a 3-year, transition focused curriculum, medical students work one-on-one with AYAs and their families across several sessions to help bridge this gap in care through counseling and advocating efforts.

Objectives: To convene a multidisciplinary team to help AYAs with SCD develop the skills necessary for a successful transition to adult medicine.

Design/Method: Medical students applied to Sickle Cell Superheroes and were selected by student leaders. New participants completed a 1-hour workshop to understand their role as patient navigators. Each semester, participants worked with their patients for at least 3 hours and attended 1 group reflection session with an attending physician. Volunteers evaluated the patient navigator workshop using pre- and post-participation surveys. The curriculum was modeled after St. Jude's SCD transition course, supplemented with resources from Got Transition, and evaluated by patients using pre-, during-, and post-transition surveys.[4] Each year, patients will complete a transition readiness questionnaire adapted from materials published by the American Society of Hematology and an SCD quiz.

Results: As of December 2022, 14 medical students and 13 patients have participated in the Sickle Cell Superheroes service-learning program. Assessments completed by the patients so far have found working with patient navigators helpful and the sessions useful for improving transition readiness.

Conclusion: Preliminary data from this service-learning curriculum suggests students and patients are satisfied with the program and advocacy skills they develop through their participation. We plan to continue recruiting participants, integrate transition clinic progress into electronic medical records, and involve patient navigators in verifying a patient's successful transfer of care.

References:

1. Shankar et al., American Journal of Hematology, 2005
2. Brousseau et al., *JAMA*, 2010
3. Hemker et al., *American Journal of Hematology*, 2011
4. Sulsberry et al., *Hematology Am Soc Hematol Educ Program*, 2019

POSTER # 367 | A CLINICAL REGISTRY TO IMPROVE CARE DELIVERY TO PEDIATRIC PATIENTS WITH SICKLE CELL ANEMIA

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Background: The United States Military Health System (MHS) cares for 9.6 million beneficiaries, including children and teens with sickle cell anemia (SCA), HgbSS and HgbS-beta-thalassemia-zero. These patients

receive open-access no-cost or low-cost care in either military or civilian facilities.

The National Heart Lung and Blood Institute (NHLBI) published guidelines of preventive care for SCA include: prescribing and managing hydroxyurea; antimicrobial prophylaxis; asplenia vaccinations; proteinuria screening; retinopathy screening; and neuroimaging. Reported rates of good adherence to hydroxyurea based on pill counts or refill data, apart from clinical trial data, is 30-61%. Barriers to hydroxyurea adherence include frequent lab checks for monitoring which are complicated by physical distance and traffic to the tertiary pediatric hematology centers.

Objectives: Our objective is to identify the pediatric patients with SCA within the MHS and maximize their delivery of NHBLI recommended preventative care, first targeting hydroxyurea adherence.

Design/Method: A clinical registry for MHS pediatric patients with SCA was developed. Patients were identified by algorithm based on diagnosis codes: two encounters with SCA specific International Classification of Disease (ICD) codes with further restriction that theses codes where input by a pediatric or adult hematologist. The registry was audited through iterative chart reviews to increase the sensitivity and specificity of patient identification. NBHLI preventive care guidelines were matched to perspective codes in Current Procedural Terminology or Healthcare Common Procedure Coding Systems. The registry used logic based on patients' age and timing of care to determine adherence with NHLBI clinical guidelines.

Overdue hydroxyurea prescriptions were defined as more 90 days since last medication fill, these patients were identified through the registry. Process mapping was used to develop a standardized efficient workflow: identification by registry; notification; lab order; more convenient lab draw locations, and the option of a virtual or face-to-face encounter.

Results: The registry identified 300 patients with sickle cell anemia total in the MHS. In the pilot region 24 patients were identified for the quality improvement project. Prior to the first Plan-Do-Study-Act (PDSA) cycle 43% of patients with SCA were dispensed hydroxyurea within the last 90 days at the pilot institution. After one PDSA cycle of implementation this rate improved to 82%.

Conclusion: Our SCA clinical registry proved to be a valuable tool to effect improvement in the delivery of hydroxyurea to patients with SCA at a pilot care center. The next goals include sustainment of hydroxyurea adherence and expanding to the approximately 300 pediatric patients with SCA in the MHS.

POSTER # 368 | PREVALENCE OF ADVERSE CHILDHOOD EXPERIENCES IN A SAMPLE OF CHILDREN WITH SICKLE CELL DISEASE

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Background: Adverse childhood experiences (ACEs) negatively impact the trajectory of a child's life. Traditional ACEs (tACEs) include abuse, neglect, and household challenges. Over half of adults report having experienced at least one ACE in their lifetime. Studies have suggested a relationship between autonomic stress reactivity and vaso-occlusive events (VOEs) in children with sickle cell disease (SCD). There is limited research describing the prevalence of tACEs and additional adversities in children with SCD.

Objectives: (1) To describe the prevalence of tACEs and additional adversities in children with SCD as reported by family caregivers and (2) compare our findings with a reference sample.

Design/Method: Caregivers of children with SCD (n = 42) completed the Pediatric Screen for ACEs and Related Life Events (PEARLS) during a clinic visit at a Sickle Cell Comprehensive Center in Oakland from 2019 to 2021. PEARLS is a rigorously designed and validated 17-item standardized screen for tACEs and additional adversities, including discrimination, food insecurity, community violence, housing instability, and caregiver absence. Clinical and demographic information was collected by chart review. Descriptive statistics and two-sample proportion and t-tests were conducted.

Results: In this sample of children with SCD, mean age was 7.66 ± 5.05; 45% female; 57% HbSS; 81% non-Hispanic Black; and 79% publicly insured. Caregivers reported cumulative tACEs as follows: 59.5% none, 35.7% 1-3, and 4.8% ≥ 4 (median 0; IQR 0-1). The most frequently reported tACE was changes in caregiver relationship status (53% of those reporting ≥ 1 ACE). Caregivers reported additional adversities: 67% none, 26% 1-2, and 7% ≥ 3. Housing instability occurred most frequently (43% of those reporting ≥ 1 additional adversity). Children in this sample were older than those in a reference sample receiving primary care in the same geographic region (mean age 5.91 ± 3.57, $p < 0.01$). The proportion of children with SCD without tACEs was lower than the reference sample ($p = 0.04$, 95% CI: 0.02, 0.47); likewise, the proportion with at least 1 tACE was also lower than the reference sample, approaching statistical significance ($p = 0.05$, 95% CI: −0.49, 0).

Conclusion: The lower prevalence of ACEs in this sample of children with SCD, compared with the reference sample, may reflect a protective effect of multimodal care in a comprehensive center. Future research with larger sample sizes will determine relationships between ACEs, VOEs, other complications, and healthcare utilization. Early screening for ACEs and additional adversities can guide interventions and trauma-informed care for children with SCD.

POSTER # 369 | CYP2D6 ALLELE AND PHENOTYPE FREQUENCIES IN CHILDREN WITH SICKLE CELL DISEASE TAKING HYDROCODONE

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Background: The *CYP2D6* gene encodes for the CYP2D6 drug-metabolizing enzyme, which is responsible for the metabolism of

hydrocodone to hydromorphone. Hydrocodone is often used in children with sickle cell disease (SCD) to manage pain related to vaso-occlusive episodes (VOE). Based on the allelic variants of *CYP2D6*, individuals may have a phenotype of poor, intermediate, normal, or ultra-rapid metabolizer corresponding to no, decreased, normal, or increased *CYP2D6* enzyme activity, respectively. Due to mixed and limited studies, certain guideline recommendations from the Clinical Pharmacogenetics Implementation Consortium (CPIC) for *CYP2D6*-hydrocodone are weakly rated. The literature on clinical response of hydrocodone in children with sickle cell disease based on *CYP2D6* is even more limited and warrants investigation.

Objectives: To determine the frequency of *CYP2D6* alleles and phenotypes in patients with sickle cell disease prescribed hydrocodone for VOE.

Design/Method: We performed a chart review to identify patients with sickle cell disease who were prescribed hydrocodone. Demographic data was collected and *CYP2D6* genotype was determined as part of a 10-gene pharmacogenetic panel utilizing ThermoFisher TaqMan Assays performed on the QuantStudio 12K FLEX platform. *CYP2D6* copy number was determined by a tier 2 TaqMan copy number assay. Phenotypes were assigned from diplotype activity score based on the following CPIC definitions: poor metabolizer (0), intermediate (0.1-1.24), normal (1.25-2.25), and ultrarapid (> 2.25). Duplicated alleles were reported as a range of phenotypes due to testing limitations in determining which allele is duplicated. Categorical variables are reported as frequency (percentage).

Results: We enrolled 44 subjects for study participation. We detected the following *CYP2D6* alleles and their frequencies: **1* (35.2%), **2* (21.6%) **17* (15.9%), **5* (8%), **29* (6.8%), **10* (4.5%), **4* (3.4%), **41* (2.3%), **9* (1.1%), and **36* (1.1%). There were 11 (27.5%) intermediate metabolizers, 3 (6.8% intermediate to normal, 28 (70%) normal, 1 (2.5%) normal to ultra-rapid, and 1 (2.5%) ultra-rapid metabolizers. Seventy-five percent (75%) of participants carried at least 1 decreased function allele of *CYP2D6*.

Conclusion: This study describes the frequency of *CYP2D6* alleles and phenotypes in children with sickle cell disease prescribed hydrocodone. In this cohort, nearly 28% of subjects are predicted to have reduced CYP2D6 enzyme activity. Further studies are needed to investigate the clinical impact of these phenotypes on hydrocodone efficacy. Understanding these mechanisms may promote personalized care for these children with sickle cell disease to better manage their pain and improve quality of life.

POSTER # 370 | IMPROVING TREATMENT OF SICKLE CELL DISEASE-RELATED ACUTE PAIN IN PEDIATRIC EMERGENCY DEPARTMENTS

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Background: Annually, sickle cell disease (SCD) results in>200,000 emergency department (ED) visits, most commonly for pain[1]. According to American Society of Hematology (ASH) guidelines, children with SCD-related pain should receive analgesia within one hour of arrival to the ED with frequent reassessment thereafter.[2] Despite these recommendations, treatment of SCD-related pain in pediatric EDs is inconsistent. Historical data shows just 37.5% of pediatric patients at "KiDS ED" at NYU Langone and Bellevue's Pediatric Emergency Service (PES) receive their first opioid within this timeframe.

Objectives: Improve rate of 'first opioid in <60 minutes' from 37.5% of pediatric ED encounters for SCD-related pain to 50% within 18 months

Design/Method: We conducted a quality improvement project to study the treatment of SCD-related pain in the KiDS ED and PES. Included patients were $\leq$21 years who follow at Hassenfeld Center for Cancer and Blood Disorders for SCD care. Patient charts were reviewed for SCD-related pain from January 2019 - December 2020; time to first opioid administration and admission rates were collected. Personalized pain plans ("intervention") specifying medication dosing were created for 76 patients. The intervention was entered as a 'Treatment Note' in each patient's chart in January 2021, and all pediatric ED staff (primary drivers) were educated about the rollout. Post-intervention data was collected for pain-related ED visits from January 2021 - April 2022. Statistical analysis included Mann-Whitney U tests (with Z score approximation) comparing pre- vs. post-intervention data for the domains of time to first opioid and hospital admission rate.

Results: Seventy-six patients had 72 ED encounters for SCD-related pain, and 57 required opioid administration (32 pre-intervention, 25 post-intervention). The average time to first opioid was 120.0 minutes pre-intervention (SE = 20.7) and 100.9 minutes post-intervention (SE = 16.8) ($p = 0.395$), with 48% of post-intervention encounters having time to first opioid within goal of 60 minutes as per ASH guidelines, approximating our SMART aim. Admission rates for pain management were 72.1% pre-intervention and 58.6% post-intervention ($p = 0.335$), with an absolute risk reduction of 13.5% and a relative risk reduction of 18.7%.

Conclusion: It is feasible to create and utilize personalized pain plans for pediatric patients presenting to the ED with SCD-related pain. We report a small improvement in time to first opioid and small decrease in admission rate which were not statistically significant but may be clinically significant. The next PDSA cycle will focus on making the personalized pain plans more easily accessible within the medical record to further improve SCD-related pain treatment.

POSTER # 371 | REAL-WORLD EFFECTIVENESS OF VOXELOTOR IN CHILDREN WITH SICKLE CELL DISEASE AGED 4 TO <18 YEARS

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Background: Sickle cell disease (SCD) requires comprehensive, lifelong management, often entailing blood transfusions and frequent hospitalizations due to vaso-occlusive crises (VOCs). Voxelotor, a sickle hemoglobin polymerization inhibitor, is approved in the US for patients with SCD aged ≥4 years.

Objectives: To examine real-world impacts of voxelotor on transfusions, VOCs, and hospitalizations in pediatric patients with SCD.

Design/Method: Healthcare claims data for patients aged ≥4 years who started voxelotor between November 2019 and June 2022 were obtained from the Symphony Health claims database. Patients with ≥1 year of data before the index date (date of first voxelotor claim) were included. Annualized study outcomes per patient-year pre- and post-index were calculated for patients with ≥1 occurrence of the corresponding event in the 3-month pre-index period; 95% CIs and *P* values for outcome changes were based on bootstrapping. Outcomes from a 90-day lookback are reported.

Results: As of June 2022, 4521 patients were included. Of these, 830 were aged 4 to <18 years (mean: 13.2 years; 52.3% female; median follow-up [Q1, Q3]: 82 [45, 159] days). In pediatric patients, lower annualized rates of transfusions, VOCs, and hospitalizations, and lower annualized mean number of inpatient days were observed over the 3-month post-index period compared with the 3-month pre-index period. Annualized event rates (95% CI) declined by 77.1% (−108, −44.9) for transfusions (n = 23), 38.9% (−49.8, −26.6) for VOCs (n = 203), 54.4% (−68.6, −39.7) for VOC-related hospitalizations (n = 103), and 50.7% (−62.6, −36.9) for all-cause hospitalizations (n = 139). The annualized mean number of inpatient days declined by 50.3% (−73.1, −28.0) for VOC-related hospitalizations (n = 103) and by 43.2% (−63.8, −18.8) for all-cause hospitalizations (n = 139). Similar trends were observed in the overall population; however, reductions were numerically greater for pediatric patients.

Conclusion: These results suggest that voxelotor may provide additional clinical benefits beyond Hb improvement by reducing the frequencies of transfusions, VOCs, and hospitalizations and decreasing inpatient days. Reductions were numerically greater in pediatric patients than in the total population; potential explanations for this difference include the smaller pediatric sample size and pediatric patients having historically greater treatment compliance and fewer SCD-related complications, enabling a greater clinical response. Limitations include the nonrandomized design, reliance on claims data, and possible changes in healthcare use due to COVID-19. Overall, this real-world evidence supports the use of voxelotor to treat SCD and potentially mitigate associated complications in pediatric patients.

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POSTER # 372 | ACCESS AND UTILIZATION OF TELEMEDICINE BY PEDIATRIC PATIENTS WITH SICKLE CELL DISEASE

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Background: Pediatric patients with sickle cell disease (SCD) require routine specialty care at academic medical centers but encounter logistical challenges accessing care. Telemedicine is a strategy for improving access.

Objectives: We sought to characterize and describe utilization of telemedicine by SCD patients during the COVID pandemic.

Design/Method: At Mayo Clinic, 201 patients with SCD aged 25 or younger were identified, along with demographics, healthcare utilization, and medical history, between March 2020 and December 2021. Telemedicine visits were identified between March 2020 and March 2022 using CPT4 procedure codes and modifiers. Area Deprivation Index (ADI) scores were calculated at the census block level. Kruskal-Wallis and Fisher exact t-tests were used to compare patient characteristics and outcomes according to telemedicine use.

Results: Of 201 patients, 40 (20%) had a telehealth visit. Telemedicine users were more likely to be older (average age of 14.3 years vs. 8.8 years; p = 0.0016), female (72.5% vs. 51.6%, p = 0.0206), from the primary site in Rochester (52.5% vs. 37.9%, p = 0.0040), and have an activated online portal to access a telemedicine (85% vs. 65.2%, p = 0.0207). Patients with a history of chronic pain, stroke, avascular necrosis, or opioid prescription were more likely to utilize telemedicine (32.5% vs. 4.3%, p <0.001; 10.0% vs. 1.2%, p = 0.0151; 10.0% vs. 0.6%, p = 0.0059; 40.0% vs. 13.7%, p = 0.0005). There was no difference in average number of hospitalizations or ER visits. ADI scores did not differ with telemedicine use.

Conclusion: Following the emergence of telemedicine during the COVID pandemic, 20% of SCD patients utilized telemedicine. Incongruent online patient portal access between groups may indicate barriers such as lack of smart phones and/or the internet. Community wide broadband internet may increase accessibility. Telemedicine users were more likely to be older, female and seen at the main clinic in Rochester, indicating that even local patients use telemedicine. Mean ADI scores did not differ between groups and reflect general ADI scores in patients with SCD, indicating that the socioeconomic status of our SCD population is comparable to the national average of SCD population. Patients with a history of chronic pain, stroke, avascular necrosis, and opioid prescription were more likely to utilize telemedicine, suggesting that patients with severe disease require greater access to their providers. These findings indicate that telemedicine is not solely

a benefit for patients who live far from an academic medical center. Towards a post-COVID model of health care delivery, maintaining patient access to telemedicine is crucial in providing comprehensive care for SCD patients.

POSTER # 373 | IMPACT OF SOCIAL DETERMINANTS OF HEALTH ON CLINICAL OUTCOMES IN CHILDREN WITH SICKLE CELL DISEASE

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Background: Social Determinants of Health (SDOH) are socioeconomic factors that influence health and well-being and are largely responsible for health disparities. SDOH include economic, housing, food and medical needs and have been associated with worse health outcomes for people with chronic illness. Individuals with Sickle Cell Disease (SCD) are at increased risk of mortality, disability, and healthcare utilization in addition to being disproportionately burdened by poverty and systemic racism. Prior studies show that children with SCD from lower income families have higher healthcare utilization rates. However, there is limited data linking specific social needs with disease outcomes in this population.

Objectives: Identify unmet social needs of children in our Sickle Cell clinic and their impact on self-reported healthcare utilization and disease complications.

Design/Method: Patients ages 1-18 years and their guardians were approached during routine appointments at our Sickle Cell clinic. Children in acute crisis were excluded. Consented guardians (n = 114) completed the "WECARE" SDOH screening questionnaire developed by Boston Medical Center along with information regarding their child's disease. We defined an unmet social need as any positive answer to the "WECARE" survey and disease outcome variables were Emergency Department (ED) visits and hospitalizations in the previous six months, missed school/activities related to pain and acute SCD events in the past year. Percentages and exact tests were used to examine the relationship between unmet needs and disease outcomes variables.

Results: 52% of subjects reported an unmet need in at least one of the categories of the WECARE survey with food insecurity (36%), trouble paying utility bills (28%), and unemployment (16%) being the most prevalent needs out of the total study sample. Subjects with at least one unmet social need were significantly more likely to report one or more hospitalizations in the previous six months than those without an unmet need (31% vs 14%) and miss school/activities due to pain in the month prior (63% vs 31%) (p <0.05). Subjects with an unmet need also reported higher ED visits and acute SCD complications than those without, but these were not statistically significant.

Conclusion: Over half of our study sample reported at least one unmet social need; the most common being reliable access to food which is an important area for intervention. Furthermore, specific social needs have an association with healthcare utilization and SCD-related complications. By identifying which needs exist in our population, we can provide more equitable care and improve the lives of children with SCD.

POSTER # 374 | PATIENT AND CLINICIAN BELIEFS ABOUT NEUROPATHIC PAIN IN CHILDREN WITH SICKLE CELL DISEASE

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Background: Pain is the hallmark symptom causing morbidity for people with sickle cell disease (SCD) and may present as nociceptive, neuropathic, or mixed type pain. Risk factors for neuropathic pain (NP) in SCD patients include older age, female sex, hydroxyurea therapy, and increased acute care visits for pain (Brandow, 2014; Cregan, 2022). NP is underrecognized and undertreated in SCD patients and is associated with decreased patient-reported quality of life (Román, 2020). There are likely patient- and clinician-related barriers to effective management of SCD-related NP.

Objectives: We sought to understand patient and clinician attitudes about NP and explore potential barriers to management of SCD-related NP.

Design/Method: Survey metrics were developed to assess clinician and patient attitudes and beliefs about SCD-related NP and potential interventions to manage NP. Surveys were sent electronically to clinicians caring for pediatric SCD patients in the outpatient setting. SCD patients (ages 14-18) at increased risk of NP completed a patient-facing survey at a scheduled clinic visit.

Results: The clinician completion rate was 35% (n = 17). 94% of respondents agreed that NP contributes significantly to pain symptoms in some SCD patients. Providers believed that NP medications are effective for reducing chronic pain (63%) and decreasing opiate need (44%), but less likely to prevent acute pain events (18%). Clinician-identified barriers to prescribing NP medications included concerns about medication adherence (84%), lack of formal guidelines for NP medications in children (71%), and perceived patient concern about side effects (69%). More than 1/3 (35%) of clinicians reported that they were not comfortable managing NP medications. Clinician-identified barriers to referral to a pain management specialist included scheduling concerns (88%) and perceived patient/family lack of interest (76%). Most clinicians (76%) believed that nonpharmacologic interventions for chronic pain are effective in some patients. Of 70 patient responses, most indicated that they would be willing to take a medication for NP (73%), see a pain management specialist (82%), or learn more about nonpharmacologic interventions (71%) if recommended. Most patients (59%) reported some concerns about taking a medication for NP, citing insufficient knowledge (34%) and concern about side effects (26%). A minority of respondents (17%) reported concern about seeing a pain management specialist. The most common concern was that others might not believe their pain is real (11%).

Conclusion: Clinician and patient perspectives provide insights that may guide targeted education efforts or other interventions to improve treatment of SCD-related NP. More research is needed to establish NP guidelines for patients with SCD.

POSTER # 375 | ASSOCIATION OF PROMIS PARENT PROXY PROFILE WITH CLINICAL OUTCOMES IN PEDIATRIC SICKLE CELL PATIENTS

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Background: Patient reported outcomes (PRO) allow clinicians to understand patients' perspectives on their quality of life and functioning while fostering shared decision-making and individualized care. Patients with sickle cell disease (SCD) often experience a high symptom burden and understanding how their quality of life and functioning is affected is vital. Since children may be too young for self-assessment, parent proxy reports can provide important insight to providers. There is little published data linking parent proxy reports of their children's quality-of-life with health outcomes in this population.

Objectives: To examine the relationship between six domains of the parent proxy version of the Patient Reported Outcome Measurement System (PROMIS) to healthcare utilization and functional limitations in children with SCD.

Design/Method: Patients (ages 5-18) and their guardians were approached while attending outpatient appointments; children who were ill or in pain during the visit were excluded. Consented parents ($n = 87$) completed questions on recent healthcare utilization and the PROMIS Parent Proxy Pediatric Profile assessing the five domains of depression and sadness, pain interference, fatigue, anxiety and fear, mobility, and peer relations during the prior seven days. Outcome variables included emergency department (ED) utilization; hospitalizations in the previous six months; acute SCD medical events in the prior year and missed school days/planned activities due to SCD in the past months. T-tests were used to examine the relationship between domains of the PROMIS and outcome variables of interest.

Results: 39% of parents reported an ED visit and 26% reported a hospitalization in the previous six months; 30% reported an acute event SCD medical event in the previous year and 53% reported missed activities due to SCD. Healthcare utilization (ED visits and hospitalizations), acute medical events and missed days were all significantly associated with higher levels of pain interference ($p < 0.001$), fatigue ($p < 0.05$), and anxiety/fear ($p < 0.05$); having an ED visit, acute medical events, and missed activities were associated with decreased mobility ($p < 0.05$). None of the outcomes were associated with depression and sadness or peer relationships.

Conclusion: Our data demonstrates that deficits in multiple quality-of-life domains as reported via parent proxy were associated with healthcare utilization in the prior six months, acute medical events in the past year and missed school days in the past month. The association of these PROs with clinical outcomes suggests that the PROMIS parent proxy reports may be used to help identify and prevent further disease-related impairment and healthcare use for children with SCD.

POSTER # 376 | COUNSELING TO INFANTS WITH SICKLE CELL TRAIT: INITIAL REPORT OF A QUALITY IMPROVEMENT PROJECT

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Background: Newborn screening (NBS) for sickle cell trait (SCT) was adapted by New York state in 1975 and all the US by 2006. According to CDC, carriers are up to 1 in 13 Black or African American newborn babies. New York Department of health (NYDH) recommends counseling by primary care physician (PCP) or genetic specialist once the NBS is abnormal. Counseling patients and caregivers about possible complications is substantial.

Objectives: Assess the rate of counseling of newly diagnosed patients with Sickle cell trait

Assess the quality of the counseling

Design/Method: We conducted a retrospective chart review of patients with positive NBS for Hemoglobin AS, collected at Metropolitan Hospital Center between September 2019 and December 2022. NYDH provided patients list. Primary outcome was the rate of counseling, defined as any evidence of results discussion. Variables included counseling by PCP or Genetics, education points as family planning (FP), sport and renal complications, parental status. Data was analyzed using R4.2.2. Chi-square and Fisher exact tests were used when appropriate with alpha-risk of 5%.

Results: We included 107 patients. Forty-seven percent were males. Mothers had Sickle cell variants and unknown status in 52% and 4% respectively. Fathers had unknown status and Sickle cell variants in 14% and in respectively. Only 67% of patients had documented counseling. PCP counseled 34% of patients. Fifty-three percent were referred to genetics and of those 71% of were seen. One patient was referred to Hematology but did not show up. During PCP counseling, FP for the patient, FP for patient's parents, renal complication and family testing were discussed for 39%, 8%, 3% and 6% of patients respectively. Sports precautions were not discussed. During Genetics counseling, FP for the patient, FP for patient's parent, renal complication, sports, parent's referral for testing and family testing were discussed for 56%, 39%, 2%, 2%, 30% and 7% respectively. No statistically significant difference was noted in overall counseling and Genetic referral between genders. Only 8% of Male were counseled by PCP versus 25% of female. No statistically significant difference was noted on counseling depending on maternal status.

Conclusion: Counseling about Sickle cell trait is a critical part of preventive medicine. As of now, our hospital lacks consistency in approaching this matter. We identified the lack of documentation and

insufficient quality of counseling. Intervention must be done to standardize and improve counseling. Next step is adapting a systematic approach and educate physicians about pertinent counseling points.

POSTER # 377 | AN OVERLOOKED FACTOR THAT IMPACTS CHRONIC PAIN IN CHILDREN WITH SICKLE CELL DISEASE

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Background: Psychological stress has been identified as a trigger for acute pain crises and acute exacerbation of chronic pain in sickle cell disease (SCD). This leads to frequent emergency room visits and hospitalizations. These complications put children with SCD at profound risk for low school performance, persistent absences, and cognitive impairment. Furthermore, the resulting anxiety and depression of these academic and medical challenges require a multifaceted treatment approach. At one pediatric SCD center with ~ 200 patients, aggressive use of SCD-related therapies has resulted in effective disease management with a remarkedly low rate of patients with chronic pain. Despite the application of all-embracing therapies such as exchange transfusions, gabapentin, cognitive behavioral therapy, anti-depressants, opioids as needed, and an academic 504 plan, some patients still experience breakthrough pain episodes. Many non-pharmacological treatment modalities are utilized to treat chronic pain, yet there are limited reports regarding the impact of homebound school programs on acute care utilization in pediatric patients with chronic pain in sickle cell disease.

Objectives: This project aimed to assess the acute care utilization of pediatric sickle cell patients with chronic pain receiving maximum biopsychosocial therapies, before and after the implementation of a home-bound school program.

Design/Method: Patients were selected based on provider experience. Charts were reviewed via the electronic health record system, and raw counts of healthcare utilization instances were documented for set time periods before and after the start of the home hospital intervention. Utilization was then broken down by type (inpatient admissions; emergency department visits without admission; infusion center appointments; and outpatient visits including those hematology/oncology providers, pediatric providers, and urgent care centers).

Results: After gathering basic utilization data, the portion constituting acute care utilization (defined as encounters involving inpatient admission and emergency department visits without inpatient admission) was compared to the overall amount of utilization for each patient. Only two of ~ 200 pediatric patients qualified as having chronic pain. For the first patient, there was a 36% decrease in acute care utilization as a portion of all SCD-related care, and a 12% decrease for the second. De-escalation and subsequent discontinuation of opioids occurred in both patients

Conclusion: Students with SCD and chronic pain receive insufficient support to address their academic and social-emotional needs and have high rates of school absenteeism. While children with SCD are encouraged to maintain participation in normal routines, educational services such as homebound programs ought to be utilized to impact chronic pain in SCD.

POSTER # 378 | INTERIM SAFETY AND EFFICACY OF VOXELOTOR IN CHILDREN AGED 2 to <4 YEARS WITH SICKLE CELL DISEASE

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Background: Sickle cell disease (SCD) is driven by polymerization of deoxygenated sickle hemoglobin (HbS), resulting in chronic hemolytic anemia and vaso-occlusive crises. Ischemic injury and inflammation that begins early in children with SCD are associated with progressive end-organ damage, substantial morbidity, and early mortality. Voxelotor, a HbS polymerization inhibitor, is approved in the US for patients aged ≥4 years.

Objectives: To assess the safety and efficacy of voxelotor in children with SCD aged 2 to <4 years.

Design/Method: Patients with baseline hemoglobin (Hb) ≤10.5 g/dL received once-daily voxelotor 1500 mg weight-based–equivalent dosing for up to 48 weeks (HOPE-KIDS Part D; NCT02850406). Concomitant hydroxyurea was allowed if stable for ≥1 month at enrollment. Efficacy outcomes included change from baseline to week 24 in Hb and markers of hemolysis. Safety was assessed by treatment-emergent adverse events (TEAEs).

Results: As of July 29, 2022, 23 patients aged 2 to <4 years (median [range] age, 2.0 [2-3] years; median [range] weight, 14.6 [10-19] kg; 60.9% male) were enrolled; 82.6% were HbSS and 17.4% were HbSβ^0 in genotype; 69.6% were receiving hydroxyurea. At baseline, mean (SD) Hb was 8.4 (1.0) g/dL. Efficacy evaluation was performed in 20 patients with hematology measurements who completed the week 24 assessment. At week 24, the mean (SD) increase in Hb from baseline was 0.6 (1.0) g/dL, with 45% (95% CI: 23.1-68.5) of patients achieving a Hb response>1 g/dL. Seventy-five percent of patients achieved a Hb response>1 g/dL at some time point during the study. Reductions in hemolysis markers—indirect bilirubin (mean change from baseline: −24.5%; n = 18) and reticulocytes (mean change from baseline: −3.65%; n = 19)—were observed. At least 1 non–SCD-related TEAE occurred in 91.3% of patients (21/23). The majority of TEAEs were grade 1 or 2. Three patients had ≥1 TEAE considered related to study drug (nausea, abdominal pain, diarrhea). No patients permanently discontinued treatment due to TEAEs.

Conclusion: Voxelotor increased Hb and decreased markers of hemolysis in children with SCD aged 2 to <4 years. Voxelotor was well tolerated, and no new safety signals were detected. These results,

which are consistent with those in children aged 4 to <12 years (HOPE-KIDS Part C) and adolescents and adults aged ≥12 years (HOPE trial), support the use of voxelotor as a potential strategy for early mitigation of hemolysis and anemia associated with SCD in children aged ≥2 years.

Global Blood Therapeutics, Inc., a wholly owned subsidiary of Pfizer Inc.

POSTER # 379 | APPLYING THE YOUTH ACUTE PAIN FUNCTIONAL ABILITY QUESTIONNAIRE IN PATIENTS WITH SICKLE CELL DISEASE

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Background: Pain assessment in sickle cell disease (SCD) is traditionally performed through unidimensional measures such as the numeric pain scale. Inter-patient variability in interpretation of numeric scores and difficulty of differentiating between acute and chronic pain limit the use of pain scores in assessing improvement or return of function. The Youth Acute Pain Functional Ability Questionnaire (YAPFAQ) was validated by Zempsky et al. in 2013 for pediatric patients with vaso-occlusive pain episodes due to SCD.

Objectives: By applying quality improvement (QI) methodology, our interprofessional team aimed to implement YAPFAQ administration in adolescents with SCD at Rady Children's Hospital San Diego. Our SMART Aim was to increase the proportion of patients with SCD ≥ 12 years admitted to the inpatient pediatric hematology unit who had YAPFAQ scoring performed and documented in the electronic medical record (EMR) at least once during their hospitalization from 0% to 50% from February through September 2022.

Design/Method: QI tools included process mapping, key driver, and Ishikawa diagrams to identify barriers and facilitators to implementation. Interventions were evaluated using Plan-Do-Study-Act cycles. We designed interventions to increase implementation uptake, including posting the newly-developed YAPFAQ administration workflow in the provider work area and sending targeted reminders to on-service attending physicians and fellows. All inpatients ≥ 12 years with SCD received a copy of the YAPFAQ to complete every morning. The medical team obtained completed YAPFAQs from patients, reviewed results, and entered responses into the EMR. Daily responses and score trends over time were included in daily progress notes and available for clinical decision-making.

Results: Prior to YAPFAQ implementation, 60% of providers (n = 15) were unfamiliar with the YAPFAQ, with 87% stating they had never used it, and 67% expressing dissatisfaction with current methods of pain assessment for SCD vaso-occlusive episodes. From February-September 2022, 12 of 18 eligible admissions (67%) had completed and documented YAPFAQs. Of the 12 patients who completed the YAPFAQ, 100% had at least one result documented in the EMR. After YAPFAQ implementation, all hematology physicians had administered the questionnaire and stated that it provided useful information not captured by pain scores.

Conclusion: Our interprofessional QI team surpassed our SMART aim of implementing the YAPFAQ in>50% patients admitted with SCD. We obtained buy-in from providers, and patients shared that YAPFAQ completion allowed them to describe the impact of their pain more accurately and receive targeted interventions. Future QI initiatives include YAPFAQ use in clinical decision-making.

POSTER # 380 | AWARENESS OF SICKLE CELL DISEASE AMONG ADOLESCENTS AND YOUNG ADULTS

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Background: Sickle hemoglobinopathy occurs in 1:2,647 births and is identified through the state mandated newborn screening program.Sickle cell disease is associated with enormous health burden. Because sickle cell trait is a benign condition, its knowledge for an individual may be lacking even though it's identified at birth. Awareness of sickle hemoglobinopathy status for each parent is not highly emphasized in the US for prenatal genetic screening. Assessing awareness of this condition is important among adolescents given high rates of teenage pregnancy.

Objectives: We set out to assess awareness of sickle cell disease among adolescents and young adults.

Design/Method: We performed a cross sectional study of 180 adolescents who sought care at one of the outpatient clinics at Children's Hospital of New Jersey in Newark, NJ by administering an anonymous questionnaire to volunteers 12-21 years of age from January 2020-June 2022. The study was approved by our local IRB and an informed consent and/or assent was obtained from each enrolled subject. Demographics and questions to assess knowledge about sickle cell disease were asked. Incomplete questionnaires were not included in analysis.

Results: Of the 180 adolescents, 72% were of age 14-18 years, 59% were females and 92% were African Americans or Hispanic. More than 30% of subjects' parents were high school graduates and 25% were college graduates. Seventy-six percent had heard of sickle cell disease and 44% reported that they knew about sickle cell disease. Only 12% were able to identify that it is a genetic disease that may cause complications. One hundred and eighteen patients (66%) were unaware of their sickle cell status. Of those with sexual partners, 53% did not think that knowing their partner's sickle cell status would influence their choice; however, 59% wouldn't consider having a child with someone who has sickle cell disease. Only 5 individuals (2.8%) were able to correctly identify the inheritance pattern of sickle cell disease. Only 1 out of 4 individuals with children reported that they were aware of their child's sickle cell status. Majority (92%) were interested in learning more and identified their doctor, internet and school as primary forms of obtaining health information.

Conclusion: Sickle cell disease is associated with significant health burden. While we cannot prevent sickle cell disease, as health care

providers, we should make every effort to educate youth about this condition by reviewing newborn screening hemoglobinopathy status during adolescent well visits, especially for those with sickle cell trait.

POSTER # 381 | INITIATION OF SICKLE CELL EDUCATION IN PEDIATRIC HEMATOLOGY ANNUAL VISITS

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Background: Sickle cell disease (SCD) is an autosomal recessive blood disorder affecting approximately 100,000 Americans, making it the most common inherited blood disorder in the United States. In 2010, it was estimated to be responsible for 113,000 hospitalizations and $488 million dollars in hospitalization costs annually. Given that SCD is mostly diagnosed by routine neonatal screenings it requires a lifelong commitment by patients and their families to manage their healthcare. Therefore, effective education is necessary for maintaining the health of patients and reducing hospitalizations and their associated costs.

Objectives: The purpose of this research was to assess the efficacy of a patient education curriculum by physicians, child-life specialists, and nurse practitioners in the Division of Pediatric Hematology/Oncology at the University of Maryland Medical Center. The curriculum includes an annual education visit with age-appropriate information packets and activities for teaching patients and their families about SCD. Topics covered include general understanding of the disease, the importance of the patient's medications, and when to seek medical care.

Design/Method: A total of 14 patients between the ages of 0-22 years of age with a diagnosis of SCD, including variations, were identified. Prior to the annual teaching session, patients able to give assent or consent and all guardians of underaged patients were given brief surveys where they rated their knowledge in different areas related to their disease on a scale of 1 to 5. A post-education survey with the same questions was then administered via phone one week and at least one month after the visit. Differences in overall knowledge as well as knowledge in individual areas of understanding (e.g. medications, triggers) were assessed.

Results: Of the 12 guardians and 2 patients surveyed, 7 showed an increase in their overall knowledge of their disease and 6 maintained the same level of knowledge. On average, the total knowledge score increased by 4.06 points at 1-week post-education and 1.09 at 1-month.

Conclusion: Based on the survey results, the education provided has demonstrated efficacy in increasing knowledge of disease in patients and their guardians. The goal is to implement the education curriculum for 100% of the sickle cell patients at this institution to benefit their knowledge as they transition to adult care.

POSTER # 382 | ARE CHILDREN WITH SICKLE CELL DISEASE AT INCREASED RISK OF HARMS FROM AIR POLLUTION?

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Background: Key pathophysiologic pathways of both sickle cell disease (SCD) and air pollution exposure include increased inflammation, oxidative stress, and endothelial damage. It is therefore plausible that children with SCD are especially prone to harms from air pollution.

Objectives: We aimed to determine if increases in city-wide, daily ambient (outdoor) pollutant levels were associated with more emergency department (ED) visits among a large cohort of children with SCD and a comparison group of children without SCD. We hypothesized that children with SCD would be more affected by increases in city-wide air pollution as compared to children without SCD.

Design/Method: Patient data were retrospectively collected from a single pediatric hospital system in Atlanta, GA, forming an urban/peri-urban cohort of children with confirmed SCD and a comparison group of children without SCD, ages 1-17. Daily ambient concentrations of fine particulate matter ($PM_{2.5}$) were collected via NASA satellite-derived remote-sensing products, and carbon monoxide (CO), nitrogen dioxide (NO_2), and ozone were collected from local monitoring stations. We used multivariable negative binomial regression to quantify associations of pollutant levels (main exposure variable) with daily counts of ED visits (main outcome variable), accounting for weather and time trends.

Results: From 2010-2018, there were 17,731 ED visits by 1740 children with SCD (64.8% HbSS/HbSβ0). Vaso-occlusive events (57.8%), respiratory illness (17.1%), and fever (16.1%) were most common cause of visits. Three-day (lags 0-2) rolling mean $PM_{2.5}$ and CO levels were associated with daily ED visits among those with SCD ($PM_{2.5}$ incident rate ratio (IRR) 1.051 (95% CI 1.010-1.094) per 9.4 $\mu g/m^3$ increase; CO 1.088 (1.045-1.132) per 0.5 ppm). NO_2 showed positive associations in secondary analyses; ozone levels were not associated with ED visits. When we stratified the cohort by severe SCD (i.e. HbSS, HbSβ_0) vs. all other genotypes, IRR were higher for the severe group, though confidence intervals overlapped and no conclusions could be drawn. However, the comparison (non-SCD) group demonstrated lower IRR for all four pollutants. Our models were robust to various distributional assumptions, different time and time-trend lags, and 1- and 2- day lead analyses.

Conclusion: Our results suggest that increases in short-term ambient air pollution levels may be potential triggers for SCD events and that children with SCD may be more vulnerable to harms from air pollution than those without SCD. Targeted pollution-avoidance strategies could have significant clinical benefits in this population.

POSTER # 383 | BILATERAL CALCANEA CLOSTRIDIOIDES DIFFICILE OSTEOMYELITIS IN A PATIENT WITH SICKLE CELL DISEASE

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Background: Osteomyelitis is a well-known and described complication seen in patients with sickle cell disease (SCD) as a result of functional asplenia that places patients at increased risk for infection and sepsis. The most common organism causing osteomyelitis in SCD is *Staphylococcus aureus*. Very few cases have reported osteomyelitis caused by *Clostridioides difficile*, but reports indicate it is characterized by a prolonged and difficult course. We present a case of a patient with SCD and osteomyelitis due to *C. difficile* and outline the ongoing management plan and course.

Objectives: This case report demonstrates a patient with SCD with bilateral calcanea osteomyelitis due to *C. difficile*.

Design/Method: Single subject case report.

Results: A 14-year-old male with SCD presented for three days of bilateral heel pain that differed from his typical vaso-occlusive episodes. He was febrile during admission, which led to a sepsis workup being initiated. He was started on intravenous (IV) clindamycin and x-ray was obtained and negative. Due to persistent pain and fevers, magnetic resonance imaging of bilateral calcanea were obtained and showed multifocal areas of signal abnormality involving the calcaneus on the left and extensive abnormal signal and lack of enhancement throughout the calcaneus on the right, consistent with bilateral calcanea osteomyelitis. Blood cultures subsequently grew *C. difficile*. The patient underwent irrigation and debridement (I&D) and intraoperative wound cultures grew *C. difficile*. The patient had placement of vancomycin coated beads, yet had continued wound drainage with several subsequent I&Ds. Wound cultures again grew *C. difficile*. Over six months, patient had a waxing and waning course due to severe antibiotic side effects and per Infectious Disease, antibiotic management was transitioned from IV vancomycin + metronidazole, to oral metronidazole, back to IV metronidazole, to oral linezolid, and back to oral metronidazole. He underwent forty days of hyperbaric oxygen therapy due to its role enhancing wound healing and was started on monthly exchange transfusions to improve tissue oxygenation. Despite this, he had persistent abscess formation in the calcanea with another bilateral calcanea I&D planned.

Conclusion: This case highlights the difficulty in treating osteomyelitis caused by an uncommon organism, *C. difficile*, in patients with SCD. Limited data is available on the treatment of *C. difficile* osteomyelitis in patients with SCD. Therefore, with a multidisciplinary approach, our team treated this patient with therapies including metronidazole, vancomycin, and linezolid, multiple I&Ds, hyperbaric oxygen therapy, and regular exchange transfusions. The patient continues to undergo active treatment for recurrent intraosseous abscess formation.

POSTER # 384 | MOYA-MOYA SYNDROME IN AN INFANT WITH SICKLE CELL DISEASE: A CASE REPORT

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Background: Moyamoya is a disorder that affects blood vessels in the brain and is characterized by narrowing (stenosis) of the distal internal carotid arteries or branches with the development of compensatory collateral vessels. Patients can present with stroke, transient ischemic attacks, or bleeding in the brain; and can also lead to cognitive and developmental delays. Moya-moya is associated with a variety of disorders including sickle cell disease. The presence of moyamoya in patients with SCD is an important finding that has been found to be a predictor of recurrent stroke and it can affect the management as well as the prognosis.

Objectives: This case highlights the importance of recognizing symptoms of stroke and or transient ischemic attacks in infants and children, especially in those with sickle cell disease.

Design/Method: A retrospective chart review of the patient was conducted to investigate the patient's initial presentation, imaging and treatment.

Results: We report a case of an 8-month-old male infant with sickle cell disease who presented to our institution with left sided weakness and a convulsive episode. CT angiogram of the brain showed bilateral focal narrowing of the supraclinoid internal carotid arteries likely reflecting developing moyamoya syndrome. An MRI of his brain showed multifocal areas of acute ischemia within bilateral frontal lobes as well as multifocal arterial narrowing, most pronounced involving the supraclinoid segments of bilateral internal carotid arteries. The patient underwent an exchange transfusion as well as encephaloduroarteriosynangiosis (EDAS) procedure and was started on a chronic transfusion protocol. Thirteen months after his initial presentation, the patient presented with progression of the left carotid stenosis leading to left EDAS procedure. He is currently being evaluated by our departments bone marrow transplant team for curative options.

Conclusion: Although Moya Moya has been reported in patients with sickle cell disease, it does not usually present in patients this young. Because of the rarity of Moya Moya disease and stroke in this age group, there is no clear consensus on treatment for these patients. Because chronic transfusion protocols can lead to severe complications, it is important to consider curative options in these patients. Furthermore, more research is needed on how severity of disease contributes to development of Moya Moya or stroke at an early age.

POSTER # 385 | ALTERED MENTAL STATUS IN A PATIENT WITH SICKLE CELL DISEASE AND SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Sickle cell disease (SCD) and systemic lupus erythematosus (SLE) are uncommon disorders that can both cause vascular disease. When encountered in the same patient, identifying the etiology of a complication can be challenging, yet crucial, as the treatments differ significantly. Stroke in children with SCD is unfortunately quite common, with 18.1% suffering ischemic stroke by age 18. Altered mental status (AMS) in SCD is secondary to stroke until proven otherwise. Evaluation and management of AMS in a patient with both SCD and SLE requires careful consideration as these disease processes can mimic one another.

Objectives: To highlight clinical features that may distinguish SCD from SLE in a patient with AMS.

Design/Method: Case report

Results: A 19-year-old female with SCD on chronic transfusions and recent diagnosis of SLE presented with AMS complicated by status epilepticus, ultimately requiring intubation for neuro-protection. Initial MRI stroke protocol was negative for a CNS process. Complete MRI was acquired on day four of admission which demonstrated small infarcts in the MCA-ACA and MCA-PCA watershed territories in addition to more pronounced vascular narrowing. Despite initial hemoglobin S percentage of 65% at time of admission, she underwent exchange transfusion given the severity of her presentation.

She was extubated with subsequent neurologic examination notable for waxing-and-waning mental status. Repeat MRI stroke protocol was obtained in a period of increased confusion which showed interval development of abnormal foci of hyperintensity in the bilateral basal ganglia. Despite initial workup that was suggestive of adequate control of her SLE, steroids and anticoagulation were initiated as empiric management of neurovasculitis without return to neurologic baseline. Anti-neuronal antibodies sent from the serum and CSF returned as positive. She received rituximab as treatment for CNS SLE with swift resolution of AMS.

Conclusion: Patients with SCD and SLE are exceedingly uncommon with only a dozen patients with SCD and CNS SLE. This case demonstrates the challenge of identifying the etiology of AMS in a patient with both SCD and SLE. In a patient with both SCD and SLE, both diseases can predispose one to CNS manifestations. Diagnosis can be complicated by the fact that 40% of patients with CNS SLE will have a normal MRI. This case is a reminder that SCD stroke is not always the cause of AMS in SCD. Multidisciplinary consultation and careful laboratory and radiologic assessments are crucial for arriving at the right treatment plan.

POSTER # 386 | A VASO-OCCLUSIVE CRISIS IN DISGUISE—A RARE PRESENTATION OF PAINLESS SICKLE CELL ORBITOPATHY

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Background: Sickle Cell Orbitopathy (SCO) is a rare orbital manifestation resulting in orbital bone infarction seen in patients with sickle cell disease (SCD) due to vaso-occlusive crisis. SCO is more commonly seen in the pediatric population due to greater amounts of marrow space in orbital bones compared to adults. This diagnosis is challenging as its presentation can be similar to clinical and radiologic signs of periorbital and orbital cellulitis. Early detection, diagnosis, and management of SCO is crucial to prevent ocular complications secondary to orbital nerve compression.

Objectives: To describe the rare and difficult diagnosis of acute, painless vaso-occlusive crisis leading to orbital bone infarction that can occur in pediatric patients with SCD.

Design/Method: Single subject case report

Results: A 4 year-old with HbSS presented to the emergency department (ED) with non-traumatic, painless left eye swelling for two days without systemic signs of infection. ED workup revealed leukocytosis (20.11), elevated C-reactive Protein (3.6), and elevated total bilirubin (3.4). Hemoglobin was at baseline (8.6) with an elevated reticulocyte count (21.6%). A computed tomography (CT) of orbits was performed, which showed extensive left periorbital soft tissue swelling with inflammatory changes extending into the inferior left orbit. This was initially thought to reflect a phlegmon or early abscess formation. The patient was treated for orbital cellulitis with vancomycin and ceftriaxone; however, the patient had no improvement after 24 hours. Ophthalmologic exam was unremarkable for diplopia, ophthalmoplegia, pain with extraocular movements, and optic neuropathy, making orbital cellulitis less likely. MRI was performed and was notable for T2 hyperintensity of the orbital bone, most consistent with infarction, and a subperiosteal hematoma. These imaging findings in the setting of the patient's clinical presentation were consistent with SCO, and antibiotics were discontinued. The patient was administered IV hydration and one unit of packed red blood cells. The left periorbital edema subsequently decreased without any impairment to visual acuity.

Conclusion: This case is unique due to the painless nature of presentation and the development of a subperiosteal hematoma, which is a rare complication of SCO. This highlights the importance of considering SCO in patients with SCD who present with painless or painful eye swelling, without typical clinical features or CT findings consistent with periorbital or orbital cellulitis, and in patients not improving with antibiotics. We also highlight the importance of obtaining an MRI to visualize orbital infarction and hematoma formation in patients with suspected SCO, as this is not best appreciated with CT.

POSTER # 387 | HYPERHEMOLYSIS SYNDROME—A RARE COMPLICATION IN A PATIENT WITH SICKLE DISEASE

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Background: A 19-year-old male with sickle cell disease (Hg-SS) initially presented to the emergency department with a sickle cell pain crisis in his lower extremities.

Objectives: We describe a case of a 19-year-old patient with sickle cell disease (hemoglobin SS) who developed multifactorial hyperhemolysis syndrome.

Design/Method: Chart Review

Results: Complete blood count showed Hemoglobin 10.4 g/dL, hematocrit 29.4%, platelet count 556 k/uL, reticulocyte count 12.9%. The pain was typical compared to previous sickle cell pain crisis admissions. The patient's blood type was A positive. On admission, direct antiglobulin test was positive (anti-IgG, 3+; anti-C3b/d negative) secondary to underlying warm autoantibody. The patient developed significant abdominal pain which prompted a work-up. Total bilirubin was significantly elevated at 23.8 mg/dL with a direct bilirubin of 7.1 mg/dL, AST 77 U/L, ALT 51 U/L. Imaging showed cholelithiasis without evidence of acute cholecystitis. MRCP showed biliary dilatation, which lead to ERCP to be completed. The patient's conjugated hyperbilirubinemia worsened so MRCP was repeated and showed notable improvement in hepatic biliary dilatation. However, complete blood count had an acute drop in hemoglobin levels following the MRCP, from 8.8 g/dL two days prior to 5.1 g/dL. He was also found to have acute onset coagulopathy with PT 39.3 seconds and PTT 44.7 seconds. He quickly developed acute liver failure secondary to hepatic sequestration and intrahepatic cholestasis from hemolysis: total bilirubin 60.6 mg/dL, AST 890 U/L, ALT 265 U/L. Patient subsequently required intubation and was started on methylprednisolone, IVIG, and 3 days plasma exchange with minimal improvement. The patient continued to have severe hemolysis despite having well-matched packed-red blood cell transfusion. Hemoglobin continued to drop and at its lowest was 3.4 g/dL. Tocilizumab started in an attempt to modulate his immune system response prior to transfusions. Hyperhemolysis was difficult to get ahead of despite aggressive support and patient ultimately succumbed to his death.

Conclusion: Hyperhemolysis syndrome in patients with sickle cell disease carries a very poor prognosis. Hyperhemolysis syndrome should be included in the differential diagnosis in patients with sickle cell disease who are clinically deteriorating and have received a significant amount of blood products during previous hospitalizations.

POSTER # 388 | A PILOT TO INVESTIGATE RESTING STATE IN PATIENTS WITH SICKLE CELL DISEASE POST STEM CELL TRANSPLANT

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Background: Functional MRI (fMRI) can be used to study the connectivity of the brain's resting state, including a highly replicable neural connection pattern called the default mode network, which is active in the absence of external stimuli. Studies of patients with sickle cell disease (SCD) have demonstrated an increased or decreased connectivity of the default mode network to pain processing centers of the brain, analogous to findings observed in other chronic pain cohorts. To date, it is unknown if resting state aberrancies in patients with SCD are altered by therapies such as allogeneic or autologous (gene therapy; GT) hematopoietic stem cell transplants (HSCT). As HSCT and GT treatments are available or imminent, it is increasingly important to understand the reversibility of neurocognitive effects. Persistence of aberrancies post-amelioration of SCD would add to a growing body of evidence suggesting that HSCT be offered at younger ages to avoid permanent injury to brain function resulting from the disease.

Objectives: To investigate resting state fMRI patterns of patients with SCD and patients with SCD post-HSCT.

Design/Method: Two subjects were included in this preliminary qualitative analysis; a 21-year-old female with a history of Hgb SS post HSCT (quant Hb S 60% prior to HSCT 10/2020 and post- sibling allogeneic HSCT quant Hb S 41%) and a 29-year-old female with Hgb SS on monthly apheresis for a distant history of silent infarcts and abnormal transcranial doppler screen (baseline quant Hb S 61% and apheresis goal Hgb S <30%; the study was completed two days prior to scheduled monthly apheresis). Neither patient reported acute pain exacerbation on the day of their scan. 3T MRI magnet was used to collect anatomic scans, diffusion-weighted imaging, executive functioning testing (Go/No Go task), and resting state scans for each patient. Resting state data were normalized to MNI, preprocessed, and first-level analysis of each subject was completed using CONN functional connectivity toolbox (Whitfield-Gabrieli and Nieto-Castanon, 2012).

Results: Based on the first-level analysis, qualitative observation suggests lower connectivity between the default mode network to regions of the somatosensory network, central executive network, language network, and visual processing network observed in the subject with SCD post-HSCT relative to the subject with SCD.

Conclusion: Qualitative analysis of these data (n = 2) demonstrate different patterns of default mode network connectivity. This preliminary study is ongoing and additional data must be collected to allow for group-level analyses to strengthen the understanding of resting state connectivity in relation to HSCT status.

POSTER # 389 | DELAYED HEMOLYTIC REACTIONS IN SICKLE CELL DISEASE; A CASE SERIES

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Background: Delayed hemolytic transfusion reactions (DHTR) are a well-known complication of blood transfusions, which are theoretically minimized by measures such as leukoreduction, extensive typing and matching process. This is a rare but severe complication of allo-immunization that occurs in patients who receive multiple RBC transfusions throughout their lifetime. It is characterized by severe anemia, specifically a hemoglobin that is below the patient's pre-transfusion levels from their past, as well as pain, fever, and clinical signs of hemolysis. Signs and symptoms of DHTR reactions can typically be seen after 7-10 days, but have been reported up to 28 days post transfusion.

Objectives: This case series will explore the hematological and clinical course for three patients with known HgbSS Sickle Cell Disease (SCD) that experienced DHTR within the same six-month period. Exploration of similarities and differences in patient demographics, clinical course, complications and seeking to understand potential triggers can benefit all patients requiring multiple blood transfusions over a lifetime, especially the SCD population. Early recognition is associated with improved outcomes, this case study hopes to raise the index of suspicion and improve patient care for this vulnerable population.

Design/Method: This case series is a retrospective study completed via chart review of three patients with previously diagnosed SCD that required blood transfusions and subsequently developed life-threatening DHTRs within the same six-month period.

Results: All three patients in this case series had previously received blood transfusions without complications. Each case required readmission for a long-term hospital stay, up to 26 days, for severe anemia, with one case requiring PICU management for respiratory failure.The lowest hemoglobin recorded for each patient was 2.7, 2.9, and 4.1 respectively. Furthermore, each patient underwent similar treatment plans which included steroids, epoetin alfa, IVIG, and one case required rituximab.

Conclusion: Given the magnitude of complications associated with blood transfusions and the frequency at which they are indicated for our sickle cell population, strategies to avoid hemolytic transfusion reactions need to be concrete. DHTRs are particularly insidious, as they typically occur after a resolution of the offending illness, such as acute chest syndrome, vaso-occlusive crisis, or symptomatic anemia related to stresses on the body, such as illness or dehydration. Due to similarities in presentation of these previous illnesses, they can easily be missed by the unsuspecting clinician and lead to dire consequences. Prevention is preferred, but if unavoidable, management can be complex and require close monitoring of the patient's clinical status and response to interventions.

POSTER # 390 | A BRIDGE TO BREATHING BETTER: BIPAP FOR PERSISTENT HYPOXEMIA IN A CHILD WITH SICKLE CELL DISEASE

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Background: The pathophysiology of hypoxemia in patients with sickle cell disease (SCD) remains poorly understood. Hypoventilation, ventilation-perfusion mismatch, and reduced oxygen affinity from sickled hemoglobin are implicated. Because persistent hypoxemia increases risk of SCD-related cardiopulmonary complications, early recognition and treatment are crucial. We present a patient with SCD with persistent hypoxemia who was treated with a novel regimen of bi-level positive airway pressure (BiPAP) and respiratory physical therapy (PT).

Objectives: N/A

Design/Method: Case Presentation: A 9-year-old female with SCD on hydroxyurea, asthma, history of acute chest syndrome (ACS), vaso-occlusive crises (VOC) and baseline oxygen saturations (SpO2) above 94% presented to the emergency room with fever, abdominal pain, and hypoxemia (SpO2 of 89%). Pain medications and antibiotics initiated for possible cholangitis. She then developed hypoxemic respiratory failure with SpO2 55% on FiO2 0.4. Physical exam revealed decreased air movement and chest X-ray showed opacities consistent with ARDS. She was intubated, started on mechanical ventilation, and admitted to the PICU. She was extubated on hospital day 15 but failed room air trials with intermittent desaturations to high 80s, was discharged on room air. During subsequent ED and clinic visits, SpO2 values were 88-91% on room air. Five months later, she was readmitted with VOC, hypoxemia (SpO2 88%) and grunting and gasping during sleep. Chest CT, venous blood gas and pulmonary function testing were normal. The pulmonology team recommended BiPAP initiation for persistent hypoxemia alongside diaphragmatic breathing exercises with physical therapy (PT) as she was primarily chest breathing, exhibiting diaphragmatic weakness. Outpatient polysomnography (PSG) showed sleep-related hypoxemia without apneas. She was compliant with outpatient PT and BiPAP use. Three months later, her daytime baseline SpO2 improved to 98-100% on room air. Her exam demonstrated improved rib cage excursion and diaphragm strength with chest expansion increasing from 1 to 2 inches. Sleep-related noisy breathing resolved, and she reported improvement of pain and energy. BiPAP was weaned off after a total of five months of use. Repeat PSG showed resolution of sleep-related hypoxemia.

Results: N/A

Conclusion: Discussion: For this patient, we found treating day and nighttime hypoxemia with nocturnal BiPAP and respiratory PT corrected mechanical breathing deficits that were likely contributing to persistent hypoxemia incited by ARDS. We hypothesize that in conjunction, these measures lead to improved tidal volumes and corrected hypoventilation induced hypoxemia. Prospective studies are needed to establish the efficacy of this novel and non-invasive approach for patients with SCD with persistent hypoxemia and suboptimal breathing mechanics.

POSTER # 391 | USING A REAL-TIME RISK-PREDICTION MODEL TO IDENTIFY PATIENTS AT RISK FOR THROMBOSIS: THE CLOT TRIAL

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Background: Hospital-associated venous thromboembolism (HA-VTE) is an increasing cause of morbidity and mortality among pediatric patients and identifying patients at risk for developing HA-VTE remains challenging. We previously developed and validated a HA-VTE risk prediction tool that is integrated into the electronic medical record (EMR),

automatically updates daily, and requires no provider input for score calculation.

Objectives: To determine whether a novel HA-VTE risk prediction tool, used together with pediatric hematology review, could reduce pediatric inpatient rates of HA-VTE.

Design/Method: The Children's Likelihood Of Thrombosis (CLOT) trial was a randomized, pragmatic, clinical trial was performed from November 2, 2020 through January 31, 2022, at the Monroe Carell Jr. Children's Hospital at Vanderbilt. The HA-VTE risk prediction too was incorporated into the Epic EMR system to identify patients with an elevated HA-VTE risk probability ($\geq$ 2.5%). All inpatient admissions of patients $\leq$21 years of age were included. EMR-based patient-level randomization, which occurred following admission, was performed using an Epic Best Practice Alert. Patients identified as being at elevated risk underwent additional pediatric hematology review, which included recommendations regarding prophylaxis with anticoagulation.

Results: A total of 17,427 patients met the eligibility criteria, were randomized, and included in the analyses. The two groups were evenly balanced (8717 in the intervention group and 8710 in the control group). In the intervention group, 490 patients were reviewed, and the hematology team recommended thromboprophylaxis for 287 patients; this was initiated in 74 patients (25.7%). A total of 58 patients (0.7%) in the control group and 77 (0.9%) in the intervention group developed HA-VTE ($P = 0.10$, risk difference between the two 0.0022 (95% CI −0.0004 to 0.0048). The model accurately identified patients at elevated risk, with 121 of 135 (89.6%) patients who developed HA-VTE having a risk probability of>2.5%. Three episodes of minor bleeding were observed in patients on anticoagulation.

Conclusion: The risk prediction tool correctly identified patients at elevated risk; however, there was substantial reluctance by clinical teams to prescribe prophylactic anticoagulation as recommended by the study team hematologists. In this context, the rates of HA-VTE between the control and intervention groups were not different. Future research is needed to identify improved strategies for prevention of pediatric HA-VTE and to overcome provider concerns regarding thromboprophylaxis.

POSTER # 392 | INSTITUTIONAL EXPERIENCE WITH OUTPATIENT USE OF PROPHYLACTIC ANTICOAGULATION IN PATIENTS WITH MIS-C

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Background: Prophylactic anticoagulation has been a part of supportive care recommendations for patients with Multisystem Inflammatory Syndrome in Children (MIS-C). As previously published, children older than 12 years of age with MIS-C appear to be at a higher risk for thrombotic complications. There is limited data regarding managing anticoagulation in this new pathology particularly in the outpatient setting, with most information being extrapolated from adult data. The paucity of information has caused reluctance to use prophylactic anticoagulation, citing safety concerns.

Objectives: Our aim was to analyze the effectiveness and safety of outpatient use of prophylactic anticoagulation in pediatric patients hospitalized with COVID-19-related illnesses. Our goal was to evaluate the feasibility and safety of this approach.

Design/Method: Our institution used a risk stratification algorithm previously established in other tertiary centers to determine those who would benefit from use of prophylactic anticoagulation. A retrospective analysis was conducted to compare clinical outcomes in patients with MIS-C patients who received prophylactic anticoagulation compared to those who did not, between May 2020 and June 2021 when our institution experienced two surges of COVID-19 related illness. We looked at thrombotic and bleeding complications in both groups. Wilcoxon signed rank test was used to evaluate statistical significance.

Results: Of 122 patients identified with MIS-C at our institution, 30 received prophylactic anticoagulation. Of those, 29 received Enoxaparin and one received Rivaroxaban. None of these patients developed major bleeding events requiring intervention. Two patients experienced epistaxis and gastrointestinal bleeding respectively, which was confounded by concurrent administration of high dose aspirin. Two of the 44 MIS-C patients who qualified but did not receive anticoagulation developed thromboembolic complications, specifically pulmonary embolism and superficial cephalic vein thrombosis.

Patients who met criteria to start prophylaxis were discharged on a two-week course of anticoagulation and followed by Hematology. End points established to discontinue medication were normalization of D-dimer levels and improvement/resolution of additional risk factors. We did not observe any bleeding complications nor breakthrough thrombotic complications in the treated group.

Conclusion: Our institutional experience demonstrates prophylactic anticoagulation can be safely used in the outpatient setting in patients with COVID-19 related illnesses, particularly MIS-C, if proper follow-up and specific metrics for discontinuation of anticoagulation are established. Thrombotic complications, although rare, could be life-threatening and would necessitate therapeutic anticoagulation for longer periods of time. Proper use of prophylactic anticoagulation could safely reduce such risk even further.

Whitworth, Blood, 2021. Goldenberg, J Thromb Haemost, 2020.

POSTER # 393 | A POST-HOC ANALYSIS OF THE SAFETY AND EFFICACY OF RIX-FP IN ADOLESCENT PATIENTS WITH HAEMOPHILIA B

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Background: rIX-FP is a recombinant fusion protein that links factor IX (FIX) with recombinant human albumin. rIX-FP has demonstrated effective bleed control and an excellent safety profile in adults and

children with severe haemophilia B (SHB). In clinical trials, data for adolescent patients were combined with adult patients per protocol.

Objectives: To assess the efficacy and safety of rIX-FP prophylaxis in previously treated adolescent patients with hemophilia B through a post-hoc analysis of Phase III clinical trial results.

Design/Method: Patients aged ≥12– <18 years with SHB (FIX ≤2%) who participated in the Phase III PROLONG-9FP clinical trial were included. Patients were treated on a 7-day rIX-FP prophylaxis regimen (35–50 IU/kg); patients who were well-controlled on that regimen could extend to a 10-day and then a 14-day regimen (50–75 IU/kg) at any 6-month follow-up. Efficacy, pharmacokinetic (PK), and safety data were collected.

Results: Seven patients were treated for at least 12 weeks on a 7-day regimen. The median (range) annualised bleed rate (ABR) on the 7-day regimen was 0.0 (0.0—2.9), the annualised spontaneous bleed rate (AsBR) was 0.0 (0.0—1.8) and the annualised joint bleed rate was 0.0 (0.0—2.3). Three patients switched from a 7-day regimen to a 10-day and then to a 14-day regimen. On the 10-day regimen, the median ABR was 1.78 (0.0—3.0) and the AsBR was 0.0 (0.0—0.0). On the 14-day regimen, the median ABR was 0.0 (0.0—4.0) and the AsBR was 0.0 (0.0—1.0). PK data were available in 6/7 patients; the mean (SD) incremental recovery rate was 1.11 (0.307) (IU/dL)/(IU/kg), terminal half-life was 87.25 (31.127) hours and maximum concentration (C_{max}) was 57.02 (16.158) IU/dL. The mean (SD) trough levels were 18.05 (7.654) IU/dL for the 7-day regimen (n = 6), 14.67 (4.250) IU/dL for the 10-day regimen (n = 3) and 8.11 (3.022) IU/dL for the 14-day regimen (n = 3). Overall, 58 adverse events (AE) were reported in 6 patients; 52/58 (71.4%) were mild, 3/58 (28.6%) were moderate and 3/58 (28.6%) were severe. No AE resulted in withdrawal of rIX-FP. One AE was considered related to rIX-FP, an injection site haematoma that resolved with no further treatment. One serious AE (a muscle bleed) was reported but was not considered related to rIX-FP. No inhibitors, anaphylactic reactions, or thromboembolic events were reported.

Conclusion: rIX-FP is an effective treatment option with a favourable safety profile for adolescent patients with haemophilia B.

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POSTER # 394 | ASSOCIATION OF ELEVATED FACTORS VIII, IX AND XI WITH RECURRENT VENOUS THROMBOSIS IN CHILDREN

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Background: The role of coagulation factor VIII (FVIII), FIX, and FXI for the prediction of recurrent venous thrombotic events (VTE) in children after a first non-central venous catheter (non-CVC) related deep vein thrombosis (DVT) remains unclear.

Objectives: The association between FVIII, FIX, FXI and recurrent VTE in children with non-CVC related DVT was investigated.

Design/Method: Children aged 0-18 years who experienced a first non-CVC related DVT between 1993-2014 were included in this single-center retrospective cohort study. The primary outcome was recurrent VTE per ISTH definitions. First FVIII/FIX/FXI were measured ≥30 days after the acute VTE diagnosis. In multivariable logistic regression, the association between FVIII/FIX/FXI as continuous variables and VTE recurrence was investigated, adjusting for underlying conditions with chronic inflammation (lupus, antiphospholipid syndrome, vasculitis, and inflammatory bowel disease). The role of thrombophilia (minor/major/none) and of persistent/transient/no FVIII elevation were investigated in exploratory analyses. Ethics approval was obtained.

Results: A total of 98 patients were included; median age at first DVT was 15.2 years (25^{th}-75^{th} percentile 12.6-16.6 years), 45% were male patients; 63% had lower extremity DVT; 23.5% patients had minor, 25.5% had major thrombophilia.

The median follow-up time of the cohort was 2.2 years (25^{th}-75^{th} percentile 1.1-4.3 years). In total, 24/98 (24.5%) patients had ≥1 recurrent VTE at a median of 203 days (25^{th}-75^{th} percentile 53-559 days). The incidence rate of first recurrent VTE was 7.71/100 patient-years. The most common type of recurrence was ipsilateral DVT (67%), 33% VTEs recurred at a new site.

There was no significant difference in FVIII/FIX/FXI levels according to VTE recurrence: FVIII was 1.59U/mL (25^{th}-75^{th} percentile 1.14-2.16) and 1.69U/mL (25^{th}-75^{th} percentile 1.30-2.07; p = 0.95) in patients with/without recurrent VTE, respectively. Similarly, FIX was 0.97U/mL (25^{th}-75^{th} percentile 0.88-1.23) and 0.88 U/mL (25^{th}-75^{th} percentile 0.77-1.06; p = 0.11) and FXI was 1.21U/mL (25^{th}-75^{th} percentile 1.06-1.33) and 1.06 U/mL (25^{th}-75^{th} percentile 0.88-1.31; p = 0.12), respectively.

There was no significant association between FVIII/FIX/FXI and VTE recurrence, adjusted for underlying conditions with chronic inflammation. Adjusted odds ratios (OR) for VTE recurrence were as follows: for FVIII OR 0.83 (95% Confidence Interval (CI) 0.37-1.91); FIX OR 3.80 (95% CI 0.73-19.60), FXI OR 1.70 (95% CI 0.22-12.96). However, presence of chronic inflammation was a statistically significant predictor for recurrence in all three models. Exploratory analyses did not change the results.

Conclusion: The results suggest that testing FVIII/FIX/FXI may not be helpful to predict paediatric recurrent VTE. In contrast, having an underlying condition with a chronic inflammation suggested recurrence in this patient cohort.

POSTER # 395 | MENTAL HEALTH IN PERSONS WITH VON WILLEBRAND DISEASE

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Background: Mental health disorders are often underrecognized and undertreated. While there are several studies focused on mental health

in persons with hemophilia, there are very few large population based studies in in persons with von Willebrand disease (PwvWD).

Objectives: We aim to assess prevalence of depression, ADHD and anxiety in PwvWD over a period of 20 years.

Design/Method: This is a retrospective cohort study using Epic Cosmos research platform, a deidentified dataset from 1,118 hospitals with 176 million patients. Cases were defined as patients, ages 0-110 years, both male and female, with von Willebrand disease, without Hemophilia A/Hemophilia B/ Hemophilia A carrier/ Hemophilia B carrier. Controls were defined as patients, ages 0-110 years, both male and female, without von Willebrand disease, Hemophilia A/Hemophilia B/ Hemophilia A carrier/ Hemophilia B carrier. We compared rates of depression, anxiety and ADHD in cases and controls, and by age, sex, type of vWD and type of bleeding symptoms and pain from 2003-2023.

Results: We identified 64,672 PwvWD, with 74.6% females and 25.4% males. 88.1% of females and 70% of males were ≥18 years-old. The control group consisted of 176,240,321 patients with 53.2% females and 46.7% males. 80.6% of cases were white compared to only 61.9% in the control group. For patients with documented epistaxis, the prevalence of anxiety (30.3% vs 27.1%, p = <0.0001) and ADHD (12.8% vs 6.5%, p = 0.0001) was significantly higher in PwvWD, when compared to controls. Comparing cases to controls with documented abnormal uterine bleeding (AUB), the prevalence of depression (36.8% vs 27.8%, p = 0.0001), anxiety (36.7% vs 9.5%, p = <0.0001) and ADHD (9.5% vs 4.1%, p <0.0001) were also significantly higher in PwvWD. Comparing cases to controls who reported pain, the prevalence of depression (43.3% vs 30.1%, p = <0.0001), anxiety (56.3% vs 38.1%, p = <0.0001) and ADHD (9.8% vs 3.8%, p <0.0001) were again significantly higher in PwvWD.

Conclusion: Our study shows that mental health disorders in PwvWD is a significant health burden. It is important that primary care physicians and hematologists caring for this population recognize this increased risk, and appropriately screen and refer to mental health professionals.

POSTER # 396 | HOSPITAL ACQUIRED VENOUS THROMBOEMBOLISM IN FLOOR LEVEL PATIENTS: A DESCRIPTIVE STUDY

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Background: Venous Thromboembolisms (VTEs) are a leading cause of morbidity and mortality among hospitalized pediatric patients. Despite increasing understanding of the clinical factors contributing to VTEs among a variety of populations (such as oncology, trauma, critical care), patients receiving acute care have been significantly less studied. As acute care providers continue to manage patients of increasing medical complexity and technology dependence, an understanding of the clinical context of hospital acquired complications requires further investigation. This need has been heightened during the COVID-19 pandemic given the prominent role of COVID-related illnesses (Multisystem Inflammatory Syndrome in Children and pneumonia), which have been shown to increase VTE risk.

Objectives: To describe the demographic and clinical factors present in patients diagnosed with hospital-acquired VTEs receiving acute care.

Design/Method: A retrospective chart review was performed on patients who received acute care during admission to Phoenix Children's Hospital from January 1, 2019 to December 31, 2021. Patients aged 0-18 years old who were diagnosed with a VTE after 48 hours of admission were included. Oncology patients were excluded. ICD-10 codes and an institutional database of patients with VTEs was utilized to identify qualifying patients. A manual chart review of demographics, admission characteristics, and associated diagnoses was completed.

Results: A total of 119 patients initially met inclusion for our study. After further stratifying the patients, 32 post-operative cardiology patients were excluded, with 87 patients remaining for further analysis. Eight patients (9.2%) received exclusive acute care during admission, with 79 patients (90.8%) receiving both critical and acute care. Forty-six hospital-acquired VTEs (52.9%) were diagnosed while receiving acute care, while 41 (47.1%) occurred while receiving critical care. Sixty patients (68.9%) had one or more diagnoses of a condition associated with increased VTE risk (obesity, bloodstream infection, trauma, surgical procedure, nephrotic syndrome, lupus, inflammatory bowel disease, mechanical ventilation, altered mobility, or a pre-existing clotting condition). 27 patients (31.1%) did not have any of the aforementioned diagnoses. There were 65 catheter-associated VTEs (74.7%) and 22 non-catheter-associated VTEs (25.3%). There were no VTEs (0%) as a result of COVID-related illnesses.

Conclusion: Although most patients diagnosed with hospital-acquired VTEs required critical care during admission, more VTEs were diagnosed while receiving acute care. Medical conditions previously described as risk factors for VTE and indwelling catheters continue to commonly accompany hospital-acquired VTEs. COVID-related illnesses were not found in any cases, potentially reflecting vigilant management in the setting of increased awareness of VTE risk in this population.

POSTER # 397 | PROPHYLACTIC ANTICOAGULATION IN CHILDREN UNDERGOING HEMODIALYSIS: A 10-YEAR SINGLE-CENTER EXPERIENCE

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Background: Patients with end-stage kidney disease (ESKD) undergoing hemodialysis (HD) are at an increased risk of vascular thrombotic events (TE). TE in children with ESKD are associated with higher morbidity and mortality for which the use of prophylactic anticoagulation (AC) is often required. Currently, there is limited data regarding the

use, safety and efficacy of AC in pediatric ESKD with no standardized protocols.

Objectives: This single-center retrospective study was focused on investigating the safety and efficacy of prophylactic AC in pediatric and young adult patients with ESKD undergoing HD.

Design/Method: Eligible patients were those <22 years of age with ESKD and hemodialyzed for more than 3 months receiving prophylactic AC, between 2011 and 2021. Data was collected from start of HD until either transplantation or transition/transfer of care. Captured data included demographics, clinical characteristics, anticoagulation management, and treatment outcomes (bleeding and recurrent thrombosis).

Results: Of 83 subjects with ESKD undergoing HD, 34 (41%) of them required prophylactic AC. These subjects were more likely to be female, non-Hispanic, and to have a longer dialysis vintage. The main reasons for starting prophylactic AC were recent acute TE (44.1%, n = 15), presence of thrombophilia (41.2%, n = 14) and past history of multiple TE (35.3%, n = 12). The most commonly identified thrombophilias were persistently positive lupus anticoagulant (35.3%, n = 12), followed by antithrombin deficiency (11.8%, n = 4). The most commonly used anticoagulants were low-molecular-weight heparins (47.1%, n = 16) with 12 subjects using enoxaparin and 4 others using dalteparin. Acetylsalicylic acid and apixaban use was reported in 41.2% (n = 14), and 20.6% (n = 7) of subjects, respectively.

Three (8.8%) subjects reported bleeding complications. Two of these bleeding events were classified as clinically relevant non-major bleeding (CRNMB), the other one was a minor bleeding. Bleeding sites included fistula exit site, menorrhagia and gingival bleeding. No reversal AC agent use was required. Recurrent TE rate despite AC, was 11.8% (n = 4). All patients with recurrent TE were non-compliant with their AC regimen at the time of recurrence.

Conclusion: Pediatric patients with ESKD and undergoing dialysis seem to benefit from AC prophylaxis in order to prevent thrombosis and/or thrombosis recurrences with a low rate of bleeding complications. Furthermore, AC plays an important role in securing and maintaining adequate vascular access for these patients which has implications for future dialysis and transplant candidacy. Future studies should focus on the development of specific AC protocols for pediatric ESKD patients.

POSTER # 398 | HOW DOES COVID ASSOCIATED COAGULOPATHY RELATE TO SEVERITY OF ILLNESS?

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Background: Acute COVID-19 infection and Multisystem Inflammatory Syndrome in Children (MIS-C) associated with previous COVID-19 infection were found to increase patient's risk of thrombosis because of an immune-thrombotic phenotype called COVID-19-associated coagulopathy (CAC). CAC typically presents with extremely elevated D-dimer, modest decrease in platelet count, mild prolongation of prothrombin time and elevation of fibrinogen.

No clear recommendations exist to stratify thrombosis risk in pediatric patients with COVID-19 or MIS-C to determine need for prophylactic anticoagulation. Some experts recommend an assessment of severity of illness while others advise following laboratory markers (such as c-reactive protein or CRP) or a combination of the two. The lack of consensus demonstrates clearly that persistent gaps exist in understanding coagulopathy severity in children with acute COVID-19 or MIS-C.

Objectives: Evaluation coagulopathy severity using laboratory markers and severity of illness in patients with Acute COVID-19 and MIS-C.

Design/Method: Data was collected through a retrospective chart review of all Acute COVID-19 and MIS-C patients admitted to our institution from April 2020 to April 2022. Patients were excluded if they had been receiving anticoagulation therapy for any reason prior to admission. If they did not receive any lab-work during their admission, they were excluded from the laboratory analysis.

Results: Two hundred and nine patients were included in the study, one hundred and twenty-eight with Acute COVID-19 and eighty-one with MIS-C. Seventy-two Acute COVID-19 patients had mild disease (they were admitted with COVID-19), twenty-three had moderate disease (they had an O2 requirement without an ICU stay), and thirty-two had severe disease (they required an ICU stay). Sixty-four MIS-C patients had moderate disease (they were admitted with MIS-C), and seventeen had severe disease (they required an ICU stay). Mean difference between d-dimer values between mild, moderate, and severe Acute COVID-19 patients was not statistically significant with a $p = 0.109$ using an ANOVA test. Mean difference between d-dimer values between moderate and severe MIS-C patients was statistically significant with a two sided $p < 0.001$ using an independent t-test. D-dimer and CRP values in Acute COVID-19 had a correlation of $r = 0.453$ with a $p < 0.001$; in MIS-C, they had a correlation of $r = 0.210$ with a $p = 0.062$.

Conclusion: We found a statistically significant difference in degree of coagulopathy using our definition of severity of illness in MIS-C patients, but not in Acute COVID-19. CRP was significantly correlated with severity of coagulopathy in Acute COVID-19 patients but not MIS-C patients.

POSTER # 399 | EXTENSION STUDY WITH RVIII-SINGLECHAIN FOR TREATMENT OF PUPS WITH SEVERE HEMOPHILIA A

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Background: B-domain truncated recombinant factor VIII (rVIII-SingleChain) is approved for the prevention and treatment of bleeding in hemophilia A.

Objectives: To investigate the efficacy and safety of rVIII-SingleChain in previously untreated patients (PUPs).

Design/Method: In an open-label phase III extension study, PUPs with severe hemophilia A (FVIII <1%) received either prophylactic or on-demand treatment with rVIII-SingleChain. PUPs developing FVIII inhibitors were eligible to continue receiving rVIII-SingleChain therapy, with the aim of eradicating the inhibitor.

Results: Twenty-four PUPs (median age 1 [range 0–5] year) were treated with rVIII-SingleChain. Median time on study was 35.0 (range 2.4–54.0) months. Treatment was rated as successful (hemostatic efficacy excellent or good) in 290/315 bleeding events (92.1%). During prophylactic therapy, inhibitor-negative PUPs had a median annualized bleeding rate (ABR) of 1.98 (range 0.0–23.6) and a median annualized spontaneous bleeding rate (AsBR) of 0.52 (range 0.0–19.7). The most frequent treatment-emergent adverse events were pyrexia (n = 44; 15 PUPs), upper respiratory tract infection (n = 18; 7 PUPs) and nasopharyngitis (n = 15; 9 PUPs), consistent with expectations for this population. Twelve PUPs (50.0%, CI 29.1—70.9) developed an inhibitor to FVIII, of whom six had a high titer (peak>5 BU/mL) and six had a low titer (≤5 BU/mL). The median number of exposure days at inhibitor development was 10 (range 4–23). Eleven inhibitor-positive PUPs continued treatment with rVIII-SingleChain, of whom nine (81.8%) achieved inhibitor eradication. The median time to eradication was 14.3 (range 7.7–64.4) weeks.

Conclusion: Overall, rVIII-SingleChain demonstrated favorable efficacy in PUPs, with a high treatment success rate and a low AsBR during prophylaxis. The incidence of high-titer inhibitors was similar to rates observed with other rFVIII products, and continued treatment with rVIII-SingleChain achieved eradication in most inhibitor-positive PUPs.

Funded by CSL Behring.

POSTER # 400 | HEREDITARY BLEEDING DISORDERS IN ADOLESCENT GIRLS: MANAGEMENT DILEMMAS AND SOCIAL CONSIDERATIONS

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Background: Hereditary bleeding disorders should be included in the differential diagnosis of menorrhagia in adolescent girls, even without any prior history of bleeding tendency. Despite being an integral part of management, hormonal therapy is not widely accepted in developing countries due to cultural beliefs.

Objectives: The aim of this study is to assess the acceptance of different therapeutic options of menorrhagia by teenagers with known diagnoses of hereditary bleeding disorders and their families.

Design/Method: A cross-sectional study using a structured questionnaire (repeated twice, with a 6-month interval). Patients and at least one guardian have been interviewed. Exclusion criteria included patients with a platelet count less than 100x109/L, those younger than 10 years and patients on anticoagulant, antithrombotic or factor replacement prophylactic therapy. In cases of disagreement between the girl and guardians, the whole response is discarded and the family is counseled to reach into a consensus. Patients are recruited from hemostasis clinic. Consent and ethical approval have been obatianed.

Results: Out of 221 girls diagnosed with hereditary bleeding disorders in our center, 149 cases met the inclusion criteria. One hundred and two cases with von Willebrand Disease (VWD), 21 with rare coagulation disorders (FVII, FX, FV, FXIII deficiencies and hypofibrinogenemia) and 26 with a platelet function defect. In response to our questionnaire on the preferred therapy to control menorrhagia, 137 cases (92%) opted for hemostatic therapy (oral tranexamic acid, vitamin K and desmopressin for VWD type 1) and 12 cases (only 8%) agreed for hormonal therapy. On demand replacement therapy (coagulation factors, cryoprecipitate, plasma or platelet transfusion) were not included in the questionnaire and reserved as hospital-based therapy for severe cases.

Reasons of refusing hormonal therapy were uncertainty about the ability to conceive in the future (40%), anxiety about withdrawal bleeding (25%) and fear of side effects (20%). Fifteen percent of the participants selected (prefer not say). Strikingly, repeating the questionnaire after 6 months yielded a nearly similar result; only 13 out of 149 (8.7%) patients accepted hormonal therapy. Throughout the duration of follow-up, breakthrough bleeding episodes necessitating therapy was significantly lower in hormonal therapy group compared to other patients (1/12 vs. 55/137) (P-value = 0.031).

Conclusion: Hormonal therapy is an effective and readily available intervention to prevent excessive menstrual bleeding in adolescents with bleeding disorders. In developing countries, counseling, health education and effective collaboration with gynecologists are still needed to convince families in order to avoid unnecessary transfusions and undue burden on healthcare system.

POSTER # 401 | SAFETY AND EFFICACY OF RECOMBINANT FACTOR IX FUSION PROTEIN (RIX-FP) IN PUPS WITH HEMOPHILIA B

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Background: Recombinant fusion protein linking coagulation factor IX (FIX) with albumin (rIX-FP) has been shown to be efficacious and well tolerated with prolonged dosing intervals of up to 21 days in previously treated patients.

Objectives: To evaluate the safety and efficacy of prophylaxis with rIX-FP in previously untreated patients (PUPs).

Design/Method: PUPs with severe/moderately severe hemophilia B (FIX ≤2%) who had never been treated with FIX products received weekly rIX-FP prophylaxis (25–50 IU/kg, up to a maximum of 75 IU/kg) over ≥ 50 exposure days (EDs). Primary outcomes were the safety of rIX-FP, including the development of FIX inhibitors, and pharmacokinetic (PK) parameters. Secondary outcomes included total annualized and spontaneous bleeding rates (ABR and AsBR).

Results: Twelve PUPs with a mean (range) age of 1.3 (0-11) years received routine prophylaxis. Mean (SD) exposure to rIX-FP was 68.3 (38.0) EDs. One 11-year-old PUP (8.3%, 95% CI 1.5—35.4) developed an inhibitor against FIX after eight EDs which was recorded as a related serious adverse event (AE) and the patient was discontinued from the study. Most treatment-emergent AEs were unrelated to rIX-FP and mild or moderate in intensity (Table 1) .

PK parameters were evaluated in 8 PUPs after a single infusion of 50 IU/kg rIX-FP (Table 2). The mean steady-state FIX activity trough was>10%.

In the 12 PUPs on the routine prophylaxis regimen, total ABR ranged from 0 to 3.89. Nine PUPs had an AsBR of 0. Six PUPs reported a total of 23 joint bleeding episodes; 13 episodes were reported in the PUP that had developed an inhibitor to FIX. Across all treatments, 93.8% of spontaneous bleeding events were successfully controlled with 1 or 2 rIX-FP infusions.

Conclusion: This study confirmed the safety and efficacy of rIX-FP when used for routine prophylaxis and on-demand treatment in pediatric PUPs.

Funded by CSL Behring.

POSTER # 402 | SAFETY AND EFFICACY OF RECOMBINANT FACTOR IX FUSION PROTEIN IN PEDIATRIC PATIENTS WITH HEMOPHILIA B

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Background: Recombinant fusion protein linking coagulation factor IX (FIX) with albumin (rIX-FP) has been shown to be efficacious and well tolerated in both adults and children with hemophilia B, with the potential for prolonged dosing intervals. Clinical trials have previously combined adolescent data with the adult population, per protocol.

Objectives: This review aims to demonstrate the safety and efficacy of rIX-FP for routine clinical use in pediatric and adolescent patients, including previously untreated patients (PUPs).

Design/Method: Previously treated patients (PTPs) and PUPs with severe hemophilia B (FIX ≤2%) aged ≤18 years who participated in the PROLONG-9FP clinical trial program, were included. PTPs received weekly rIX-FP prophylaxis (35–50 IU/kg); if patients were well-controlled, they could extend to a 10-day then a 14-day regimen (50–75 IU/kg) at any 6-month follow-up. PUPs received weekly rIX-FP prophylaxis (25–50 IU/kg) for ≥50 exposure days. Efficacy, pharmacokinetic (PK), and safety data were collected.

Results: The analysis included 7 adolescent (≥12 to ≤18 years) and 24 pediatric (0– <12 years) PTPs, and 12 PUPs (0—11 years). Mean (standard deviation) annual spontaneous bleeding rates (AsBR) reported for 7-day regimens for the pediatric, adolescent and PUP datasets were 0.6 (1.3), 0.3 (0.7), and 0.1 (0.3), respectively. The AsBR for 10-day regimens was 0.0 (0.0) for adolescents and PUPs, and 1.6 (2.5) for the pediatric cohort. Reported AsBR for the 14-day regimen was 1.7 (2.0) and 0.3 (0.6) for the pediatric and adolescent cohorts, respectively. Annual joint bleeding rates reported for the 7-, 10-, and 14-day regimens in the pediatric cohort were 1.8 (2.9), 2.5 (2.8), and 2.0 (1.7), respectively, and 0.3 (0.9), 0.5 (0.9), and 1.3 (2.3), respectively, in the adolescent cohort. The mean incremental recovery rates following a single 50 IU/kg rIX-FP dose were>1.0 across all cohorts, with mean steady-state trough FIX levels of>10 IU/dL on a 7-day prophylaxis regimen. Mean (SD) terminal half-life values reported for the pediatric and adolescent cohorts were 91.4 (17.5) and 70.5 (23.8), respectively. Overall, 319 adverse events were reported, of which 3 were considered related to

rIX-FP; one inhibitor development in a PUP, resulting in discontinuation from the study, and an injection site hematoma and mild rash, both resolved.

Conclusion: rIX-FP is an effective treatment option with a favorable safety profile for patients 0– <18 years, with hemophilia B.

Funded by CSL Behring.

POSTER # 403 | THROMBOLYSIS/THROMBECTOMY IN MASSIVE ILEO-FEMORAL DEEP VEIN THROMBOSIS AND MAY-THURNER SYNDROME

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Background: May-Thurner syndrome (MTS) occurs when the left common iliac vein is compressed by the overriding right common iliac artery, leading to venous obstruction and predisposing to massive ileo-femoral deep vein thrombosis (IF DVT). Current guidelines do not offer specific management recommendations for patients with massive IF DVT.

Objectives: To highlight 3 cases of massive IF DVT and successful outcomes with thrombolysis and/or thrombectomy.

Design/Method: Three subject case report series

Results: Case 1

A 14-year-old female taking oral contraceptives presented with an extensive left lower extremity (LLE) DVT. Physical exam showed left lower extremity edema. Enoxaparin was begun. Venogram showed extensive thrombosis of the left lower extremity venous circulation. Mechanical thrombectomy was performed; repeat venogram showed occlusion in the proximal left common iliac vein with flow via lumbar collaterals. An endovascular stent was placed. She did well and was found to have heterozygous FVL mutation.

Case 2

A 15-year-old male presented with acute left leg swelling and was incidentally found to have an abnormal CBC. He was diagnosed with B-cell precursor ALL complicated by extensive LLE DVT. Enoxaparin was started but his thrombus persisted. Once in remission, he underwent mechanical thrombectomy and angioplasty and he subsequently did well. Thrombophilia work-up was negative.

Case 3

A 15-year-old previously healthy male presented with painful left leg swelling. Doppler ultrasound showed extensive LLE DVT. He received tPA and heparin for 24 hours. Follow-up venogram showed decreased deep venous clot burden and segmental stenosis of the proximal left external iliac vein, treated with angioplasty with good result. He was transitioned to rivaroxaban therapy and did well. Thrombophilia work-up showed heterozygous FVL mutation.

Conclusion: Current pediatric DVT guidelines suggest thrombolysis for cases of life-, limb-, or organ-threatening events. The high risk of post-thrombotic syndrome in patients with massive ileo-femoral DVT suggests that aggressive intervention, beyond simple anticoagulation, may be indicated to improve outcomes. Furthermore, venography and clot lysis/removal are necessary to definitively diagnose and manage the compressive effects seen in MTS. Systematic reviews of pediatric patients with MTS suggest that interventional therapy improves vessel patency; lack of patency predicts DVT recurrence. Thrombolysis has been reported to be safe in children, when performed in the context of an experienced multidisciplinary team. We recommend aggressive management be pursued whenever possible, in order to improve long term outcomes in massive IF DVT and MTS.

POSTER # 404 | A CASE OF LUPUS ANTICOAGULANT HYPOPROTHROMBINEMIA SYNDROME IN AN 8 YEAR OLD CHILD

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Background: Lupus anticoagulant hypoprothrombinemia (LAHPS) is a rare disorder due to the presence of antibodies against Factor II (prothrombin). LAHPS is most commonly associated with systemic lupus erythematosus (SLE), viral infections, and primary antiphospholipid antibody syndrome and is characterized by the presence of lupus anticoagulant and hypoprothrombinemia. Lupus anticoagulant has a prothrombotic effect, but hypoprothrombinemia can counterbalance this and significantly increase the risk of bleeding. Treatment of LAPHS may require corticosteroids and immune modulating agents.

Objectives: To report a case of pediatric LAHPS as the presenting manifestation of SLE and highlight her disease refractoriness.

Design/Method: Case report and review of the literature.

Results: An 8-year-old female presented with prolonged bleeding following a left ear abrasion. Lab work revealed a prolonged PT (41.6s) and PTT (111.5s). She subsequently developed hematuria and a hematoma of the calf muscles. Further lab work revealed elevated anti-nuclear, anti-dsDNA, and anti-Smith antibodies, hypocomplementemia, and hypoprothrombinemia. Despite lacking other SLE clinical manifestations, she was diagnosed with LAHPS likely secondary to SLE and corticosteroids and hydroxychloroquine were initiated. She had a refractory disease course consisting of epistaxis and cutaneous bleeding along with low prothrombin activity (nadir of <1%) requiring mycophenolate mofetil (MMF), rituximab, and a two-year course of cyclophosphamide in addition to near-continuous corticosteroids. She currently remains on MMF, hydroxychloroquine, and a prednisone taper, with normal prothrombin levels. A literature review revealed that older adolescents and adults were more likely to have LAHPS as a presentation of SLE while children were more likely to have LAHPS secondary to an underlying viral infection. Children were more likely to have spontaneously resolving disease, while older patients were more likely to require steroids plus immune modulating agents.

Conclusion: Our case demonstrates that LAHPS can be a serious disease resistant to multiple treatments prior to achieving remission, with the risk of severe bleeding due to hypoprothrombinemia. Our patient presented at a young age with significant bleeding and required several lines of therapy over the subsequent years to achieve remission. In addition, unlike many other young children in which LAHPS is secondary to viral infections, our patient had serologic evidence of SLE at the time of presentation. This case highlights the need for further research into optimal treatment regimens for LAHPS and development of management guidelines.

POSTER # 405 | QUESTIONABLE CLINICAL PRACTICE? THE UTILITY OF A CLOTTING SCREEN BEFORE RENAL BIOPSY

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Background: The most common coagulation tests used to estimate the risk of bleeding are partial thromboplastin time (PTT) and prothrombin time (PT), where elevations can signify factor deficiencies or inhibitors of the coagulation cascade. When considering the low prevalence of bleeding disorders, PT and PTT produce a high number of false positives and false negatives [1]. Reports in the literature show that changes in PTT have limited sensitivity and specificity. In the context of nephrotic syndrome, PTT has a low positive predictive value for bleeding prior to kidney biopsy as loss of coagulation factors can falsely elevate PTT.

Objectives: To explore the role of pre-procedure coagulation testing in a child with idiopathic nephrotic syndrome.

Design/Method: Case report.

Results: We report a 3-year-old male who presented with a recurrence of facial edema and oliguria. The urinalysis had nephrotic range proteinuria and he was hospitalized to restart steroids. With the potential for steroid-resistant nephrotic syndrome, nephrology

recommended a renal biopsy. A pre-procedure clotting screen demonstrated an elevated PTT and elevated fibrinogen. INR and PT were within normal limits. The patient had no personal or family history of abnormal bleeding. Two days after the clotting screen, further workup by pediatric hematology revealed an elevated Factor VIII and a low Factor XII (11%, normal 50-139%). Factors IX and XI were within normal limits. Lupus anticoagulant, anticardiolipin antibody, and B-2-glycoprotein antibodies were not detected. Antithrombin III was decreased, prompting treatment with prophylactic enoxaparin 0.5 mg/kg BID. Following clearance by hematology, the biopsy was completed without abnormal bleeding and demonstrated mild to moderate segmental podocyte foot process effacement with no glomerulosclerosis.

Conclusion: The patient's coagulation screen revealed a prolonged PTT, a result associated with an increased risk of bleeding. The patient was actually in a hypercoagulable state secondary to Antithrombin III deficiency. Literature supports that factor XII deficiency is a common cause of PTT prolongation in individuals without a history of bleeding. Importantly, neither congenital nor acquired FXII deficiency is associated with impaired hemostasis. This case illustrates the potential pitfall of screening coagulation tests in a patient without a personal or family history of bleeding: the prevalence of false positives using these assays can lead to delays in diagnostic or therapeutic procedures, further costly and painful blood tests, and potential anxiety for patient and families. Instead, a thorough history is likely to be a more effective and efficient screening test in patients with protein-losing disease states.

[1] Chee&Greaves, The Hematology Journal, 2003

POSTER # 406 | SIBLINGS WITH MAY-THURNER SYNDROME: COINCIDENCE OR GENETICS?

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Background: May-Thurner syndrome (MTS) is an anatomic abnormality that can result in venous outflow obstruction in the lower extremity. There are variations of pathology, but it results most commonly from compression of the left common iliac vein between the lumbar spine and the right common iliac artery. MTS has been estimated to be the cause of 2% to 5% of deep vein thromboses (DVT). The exact prevalence of MTS is unknown and likely underestimated, as most individuals with this anatomy are asymptomatic. MTS is found most commonly in women in their 3rd to 5th decade of life. It is important to note that no genetic cause has been associated with MTS.

Objectives: Our case highlights two siblings diagnosed with MTS, a condition that is not known to be hereditary.

Design/Method: We reviewed the medical records of the two patients presented.

Results: A thirteen-year-old male with no significant past medical history presented to the pediatric emergency department with three weeks of left lower extremity pain. He underwent an extensive evaluation for what was initially thought to be an orthopedic problem. An MRI was obtained and revealed findings concerning for extensive thrombosis in the left lower extremity. Doppler studies showed extensive occlusive deep vein thrombosis of the left distal popliteal vein, left femoral vein, left peroneal vein, and left posterior tibial vein. The patient was started on low molecular weight heparin and due to the extensive nature of thromboses in the left lower extremity, a CT abdomen/pelvis was obtained to assess for MTS. CT showed compression of the left common iliac vein by the right common iliac artery, confirming a diagnosis of MTS. It was subsequently discovered that this patient's younger brother had been diagnosed with MTS three years earlier after presenting with extensive thromboses throughout his left lower extremity. He was also diagnosed with protein S deficiency.

Conclusion: It is well understood that many inherited thrombophilias can lead to DVT in the lower extremities and that MTS is associated with inherited thrombophilias. However, there has been no genetic mutation associated with MTS. It is reasonable to hypothesize that inherited thrombophilias and MTS are not genetically linked, but that MTS is more prevalent than previously thought and those with inherited thrombophilias are more likely to become symptomatic. We could find no reports of siblings or relatives diagnosed with MTS. Further investigation is needed to determine if such a link exists.

POSTER # 407 | A COAGULOPATHY CONUNDRUM: A NEW CASE OF FV-ATLANTA

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Background: Factor V(FV) and tissue factor pathway inhibitor alpha (TFPIα) have recently been shown to regulate the initiation of coagulation. Genetic mutations in Factor V can result in a moderate to severe bleeding diathesis. We report the second patient with the novel qualitative factor V deficiency characterized by severe bleeding. FV East Texas causes a splicing mutation that enhances the isoform, FV-short. FV-short inhibits Factor Xa by TFPIα/protein S ten-fold more potent that FV. Upregulation of FV short increases both TPFIα antigen and its anti-Xa activity causing moderate bleeding. FV Amsterdam has a FV isoform with a similar mechanism causing moderate bleeding. FV Atlanta produces a FV-short binding with high affinity to TFPIα.

Objectives: We report a 10-year-old girl with a history of an unknown coagulopathy presenting with hemorrhagic ovarian cysts.

Design/Method: Case Report/Literature Review

Results: We report a 10-year-old female with a history of prolonged bleeding from umbilicus at birth, post-surgical bleeding, bleeding after loss of teeth, and prolonged menses presenting with hemorrhagic ovarian cysts who underwent laboratory investigation to

identify the coagulopathy. Patient has a family history of an estranged father who is now deceased but reportedly had an 'unknown bleeding disorder' since childhood. Patient clinically responded to fresh frozen plasma, Vitamin K, and antifibrinolytics. Laboratory testing revealed a prolonged PT and aPTT that failed to correct with mixing studies and normal factor activity levels of II,V,VII,VIII,IX,X,XI,XII,XIII. Total fibrinogen level and activity were normal. A lupus anticoagulant was not detected. Von willebrand factor profile and platelet aggregation studies were normal. Thromboelastography was inconclusive. Alpha 2-antitrypsin, euglobulin lysis time, PAI-1 activity and plasminogen antigen level were all normal. Hereditary bleeding disorder panel was negative due to the type of mutation, this diagnosis could only be determined by whole exome sequencing. Whole exome detected a 0.830 kb deletion within FV heterozygous, called FV-Atlanta.

Conclusion: This is the second report of a patient with FV Atlanta with severe bleeding. In cases like these, where there is a clear clinical bleeding phenotype and a negative bleeding evaluation there is a utility to use whole exome sequencing. This diagnosis can not be made in standard clinical laboratories because phenotypic confirmation is not currently possible and even many genetic panels are limited in the types of mutation able to be identified.

POSTER # 408 | VENOUS THROMBOEMBOLISM IN TRANSGENDER ADOLESCENTS

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Background: A person's biological sex has a significant influence on their health, including their risk, presentation, prognosis, and management of hematologic diseases. The coagulation system is largely influenced by sex due to variations in estrogen. Estrogen is considered a prothrombotic hormone through multiple mechanisms: increasing factor (F) II, FVII, FVIII, FIX, FX, protein C and fibrinogen, decreasing antithrombin and protein S, and promoting resistance to activated protein C1-4. Moreover, estrogen increases von Willebrand Factor (vWF) and pro-inflammatory cytokines, further perpetuating a prothrombotic state5. As a result, patients prescribed exogenous estrogens, both for contraception and hormone replacement, are at increased risk of thrombosis. In addition to contraception and hormone replacement, exogenous estrogen is used for gender-affirming hormone therapy (GAHT) in transgender individuals. While the risks of VTE among patients receiving exogenous estrogen for contraception and hormone replacement have been thoroughly studied, there is a lack of information on the thrombotic risks involved with GAHT1,6

Objectives: This case report describes two pediatric transgender patients with unprovoked extensive venous thromboembolisms, and the consideration for diagnostic and therapeutic approach.

Design/Method: Multiple subject case report.

Results: MM, a trans man, was taking an oral contraceptive for menorrhagia for one month when he developed a VTE of the left common iliac, external iliac and common femoral veins with bilateral pulmonary embolism. Extensive thrombophilia workup was negative. He received intravenous unfractionated heparin during hospitalization with thrombectomy. He was then transitioned to rivaroxaban and has been free from recurrence.

AA, a trans woman, was not taking exogenous estrogen, however expressed interest in GAHT. She developed right lower extremity VTE requiring hospitalization with intravenous heparin followed by a 3-month course of enoxaparin. Within 1 week after discontinuation, she had recurrent VTE and was subsequently started on rivaroxaban, with subsequent non-occlusive thrombosis of the right distal femoral vein despite reported compliance. She underwent stent placement and remains on rivaroxaban. Extensive thrombophilia work-up has been negative.

Both patients were advised against use of exogenous hormone replacement.

Conclusion: Guidelines for GAHT, including VTE risk is necessary for patients and providers to make informed decisions when considering its use. This is especially true for patients with an underlying increased risk of VTE, highlighted in this case series.

POSTER # 501 | CREATING AN INTRANET SEARCHABLE DATABASE TO IMPROVE ACCESS TO MANAGEMENT GUIDELINES: A QI INITIATIVE

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Background: Guidelines for management of pediatric hematology, oncology, and bone marrow transplant (BMT) patients are frequently evolving because of new literature, regulatory updates, and institution-specific infectious pathogen prevalence. In a large tertiary care pediatric hematology/oncology/BMT program with a high volume and acuity of patients, multiple providers and trainees provide initial care and cross coverage of these complex patients. In our institution, accessing the most updated management guidelines for common clinical questions was inefficient with multiple versions of a single guideline being available in several locations and no designated content expert responsible for the content.

Objectives: To utilize Microsoft SharePoint™, a secure and user-friendly platform, to create a searchable, comprehensive database containing the most updated management guidelines for our patients.

Design/Method: Between February and July 2022, we conducted a quality improvement initiative to curate SharePoint™ for use by our frontline providers. First, we identified topics and clinical questions that were relevant to include. We then gathered existing documents for each topic and designated a content expert responsible for revising, updating and combining the information for that topic into a single document. Each updated document was then uploaded into the

appropriate folder on SharePoint™—categories include hematology, oncology, supportive care and other SOPs. A reminder message will be automatically generated annually via SharePoint™ to alert the content expert to make any needed changes or updates to each document. The platform was introduced at the start of the new academic year as a pilot period. After 6 months we sent an anonymous survey to all hematology/oncology fellows to gauge the utility of SharePoint.™

Results: All pediatric hematology/oncology fellows in our program responded to the survey. 91% (11/12) noted that they were able to find the answer to a clinical question on SharePoint™ when caring for patients on the inpatient unit or while on call. 100% of fellows noted that they were able to find the guideline they were looking for in between 1 to 5 minutes. When commenting on the advantages of SharePoint,™ providers felt that the platform was easily searchable, organized and increased their confidence while caring for complex patients.

Conclusion: By organizing clinical practice guidelines into a searchable database using SharePoint,™ we were able to create a comprehensive and efficient platform for frontline providers to use to access up-to-date guidelines within our field.

POSTER # 502 | SARS-COV2 SEROPREVALENCE IN PEDIATRIC HEMATOLOGY-ONCOLOGY PATIENTS

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Background: Many pediatric hematology-oncology patients are immunocompromised with presumed altered vulnerability and immune response to COVID-19.

Objectives: To compare SARS-CoV2 infection frequencies and antibody response to infection and vaccination in pediatric hematology-oncology patients.

Design/Method: Semi-quantitative anti-Spike Ig (S) and qualitative anti-Nucleocapsid Ig (N) were measured by Roche commercial immunoassays in routine clinical blood samples among 3 cohorts: 1. on-therapy oncology patients receiving ≥ 6 months chemotherapy (cancer), 2. patients with sickle cell disease (SCD), and 3. benign hematology consults and patients off-therapy for cancer>2 years (control). Anti-Spike level > 10 OD units is considered positive, and ≥ 2500 is considered high; anti-Nucleocapsid is positive if ≥ 1.0. Infection was defined by anti-Nucleocapsid positivity or history of positive PCR/antigen COVID testing. Vaccination is completion of primary series. ANOVA and t-tests were performed.

Results: From February to July 2022, 356 samples were studied including 55 cancer, 150 SCD, and 151 controls, age ≥ 6 months to <19 years.

COVID infection frequency was similar in cancer (63%) and controls (50%), but higher in SCD patients (71%) ($p = 0.0003$). Failure to mount anti-Nucleocapsid or anti-Spike to COVID infection was high in cancer: ($COVID^+N^-$) rates were: cancer 39% (13/33), SCD 0% (0/32), controls 2% (1/41) ($p = 0.0001$); ($COVID^+S^-$) rates were: cancer 24% (4/17), SCD 2% (1/42), controls 3% (1/32) ($p = 0.02$-0.008). COVID infection led to high anti-Spike ($COVID^+vac^-S\geq2500$) only in 12% (2/17) cancer, 14% (6/41) SCD, and 16% (5/32) controls.

Vaccination rates (vac+) were similar: cancer 73.2% (30/41), SCD 78.4% (87/111), and controls 78.9% (101/128). Anti-Spike responses (vac^+S^+) were 100% in SCD and controls, 90% in cancer ($p = 0.001$-0.002). Vaccination led to high anti-Spike ($vac^+COVID^-N^-S\geq2500$) in 20% (2/10) cancer, 47% (8/17) SCD, and 41% (15/37) controls. COVID infection augmented vaccination in eliciting high anti-Spike ($vac^+COVID^+orN^+S>2500$) in SCD 87% (48/55) and controls 85% (29/34) but not in cancer 23% (3/13) ($p = 0.0001$). Of vaccinated and boosted patients without previous infection ($vac^+boost^+COVID^-N^-S\geq2500$), 1/2 cancer, 6/6 SCD and 19/19 controls had high anti-Spike, which persisted > 90 days.

Conclusion: In pediatric hematology-oncology patients, cancer patients had similar COVID infection frequency as controls but diminished anti-Nucleocapsid and anti-Spike responses to infection and vaccination compared to SCD and controls. SCD had higher infection frequency and similarly high antibody responses to infection and vaccination as controls. COVID infection was ineffective in eliciting high anti-Spike. In SCD and controls but not cancer patients, vaccination was more effective than infection, and vaccination plus booster was most effective in eliciting high anti-Spike.

POSTER # 503 | IMPLEMENTATION OF UNIVERSAL MENTAL HEALTH SCREENING IN THE PEDIATRIC HEMATOLOGY AND ONCOLOGY SETTING

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Background: Chronic illness, such as cancer or a blood disorder, is a risk factor depression and anxiety in adolescents. Universal mental health screening is recommended during pediatric well child visits. However, there are no recommendations for screening during subspecialty visits. In our institution, a mental health screening process in the Pediatric Hematology and Oncology (PHO) clinic was implemented.

Objectives: We sought to implement universal mental health screening for patients being seen at a PHO clinic in order to improve quality of care.

Design/Method: A Plan, Do, Study, Act (PDSA) quality improvement model was utilized. Patients greater than 12 years old were screened with PHQ-2 and GAD-2. If a patient's score was ≥ 3 on the PHQ-2 or GAD-2, they were required to complete the PHQ-9 or GAD-7, respectively. To study this process, a retrospective chart review was conducted to analyze screening over the first seven weeks of initiation. All patients over age 12 seen in the PHO clinic were included. Data was collected regarding screening scores, diagnosis type, suicidality, and social work intervention with the goal of identifying gaps in the screening process for the next PDSA cycle

Results: There were 334 patient encounters during this 7-week period. Of these, 50 patients were not screened, resulting in a 15% miss rate. Bone marrow transplant appointments had a high miss rate (33.3%.) Among those screened, 8.6% and 8.9% had PHQ-2 and GAD-2 scores that were high enough to require completion of the PHQ-9 and GAD-7, respectively. By diagnosis category patients with bleeding disorders had the highest rate of requiring PHQ-9 completion at 31%. There were 10 encounters where patients expressed suicidal thoughts. Among the 334 patient encounters, 46.4% met with a social worker. In particular, 82.7% and 76.6% of patients requiring completion of the PHQ-9 and GAD-7, respectively, were seen by social workers.

Conclusion: Universal mental health screening is feasible in a subspecialty setting. Next steps are to understand the staffing requirements needed to offer social work assistance in a consistent manner and to better understand the workflow in certain areas, such as bone marrow transplant, to improve screening rates. Further PDSA cycles are needed to improve the process and increase resources for this patient population.

POSTER # 504 | ESTABLISHING HEALTH EQUITY RESEARCH INFRASTRUCTURE: FEASIBILITY OF A SOCIODEMOGRAPHIC BANKING STUDY

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Background: Adverse social determinants of health (SDOH) are associated with inferior disease- and patient-reported outcomes in pediatric hematology/oncology. Research to elucidate mechanisms underlying these disparities and develop interventions to mitigate them has been limited by inadequate data. Specifically, standard practice includes medical record-derived collection of race, ethnicity, insurance and zip code—non-modifiable data elements prone to misclassification bias. Systematic collection of patient-reported SDOH has the potential to contribute essential data, including modifiable exposures such as household material hardship ([HMH] housing, utility, food, and transportation insecurity), to inform health equity research and enable improved annotation of patient outcomes and biospecimens.

Objectives: To report the preliminary feasibility of a sociodemographic data banking protocol in children with cancer or blood disorders designed to complement existing biobanking and clinical data through the systematic collection of family-reported SDOH.

Design/Method: Design of a single-center, prospective banking protocol at Dana-Farber/Boston Children's Cancer and Blood Disorders Center that launched in February 2022. Parents of patients <18 years identified within 6-weeks of treatment initiation for a diagnosis of *de novo* malignancy, relapsed/refractory malignancy, or cellular therapy for a malignant or non-malignant disease were systematically invited to participate. Consenting parents complete a brief, single-timepoint survey at enrollment and study personnel abstract vital status and disease-directed therapy annually. Paper/pencil or REDCap surveys available in English and Spanish are self-completed or read aloud by study personnel in any language with an appropriate interpreter. Survey domains include demographics, HMH, household income, social support, resilience, anxiety/depression, and experiences of discrimination. Data are banked for future research with appropriate IRB approval.

Results: As of December 30, 2022, 159/189 (84%) eligible participants were consecutively approached in-person, and 145/159 (91%) consented to enrollment. Among enrolled participants, 133 surveys (92%) were successfully completed (n = 6 pending within protocol-specified window, n = 6 parents declined survey completion after initial consent). Missing data for HMH, a key SDOH of interest, was 0.1%. Surveys were successfully completed by participants with primary languages of English, Spanish, French, Mandarin, Portuguese, and Haitian Creole.

Conclusion: Systematic collection of parent-reported SDOH for research purposes in the context of a sociodemographic banking protocol is feasible and acceptable as demonstrated by high willingness to participate and minimal missed data. This banking study will be expanded to include non-malignant hematology and opened at 2 additional US institutions in 2023. Expansion of sociodemographic banking alongside biobanking as a standard research practice is essential to advance impactful health equity research in pediatric hematology/oncology.

POSTER # 505 | REINVENTING THE PEDIATRIC PATIENT EXPERIENCE: THE USE OF BEHAVIORAL ECONOMICS

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Background: Healthcare settings can be frightening and intimidating for anyone, especially children. Fear and anxiety can lead to trauma and disruption to their medical care, increasing risks for the patients and inefficiencies and costs for the healthcare providers. Our global aim is to improve patient safety by reducing these risks.

Objectives: Our smart aims are to analyze and improve the efficacy of behavioral economics, an approach to understanding decision-making and behavior that integrates behavioral science with economic principles, specifically in the form of Hope for Henry's Super Rewards for Super Kids (SRSK) program, in improving pediatric patient anxiety, coping skills, adherence, and overall patient experience—our key drivers—as a means of improving safety before and during 17 medical procedures.

Design/Method: In advance of, during, or following a medical procedure, hospital staff trained in the implementation of Super Rewards for Super Kids program present the patient with a colorful gameboard with removable stickers that feature superheroes undergoing each step of a procedure. The program maps out their procedural pathway step-by-step, which educates them about the procedure and helps them

develop a coping plan. After completing each step of the procedure, the patient adds an "I Did It" sticker to the gameboard. Once a procedure is complete, the patient chooses a reward from a selection of popular toys and games to recognize their achievement.

Certified Child Life Specialists (CCLS), employed by 25 participating healthcare facilities, and trained in Hope for Henry's Super Rewards for Super Kids, entered deidentified data from 1,877 patient encounters into a password-protected online database based on their observations course of eight months (January 1, 2022 – August 31, 2022). CCLS assessed each child receiving support for the included procedures based on age, past experiences in the hospital, understanding of why they are there and what's going to happen to them, and expressions of fear and anxiety. CCLS offered the program to every child they believed would benefit based on that assessment.

Results: The reported outcomes indicate that procedure adherence was improved in 88% of patients, with an overall patient experience improvement in 95% of patients. Anxiety reduction was observed in 86% of patients, and an improvement in coping skills was observed in 87%. For patients undergoing sedation for MRI, avoidance of sedation was attributed to SRSK intervention in 68% of patients.

Conclusion: Findings suggest that behavioral economics can effectively improve health outcomes for pediatric patients undergoing medical procedures.

POSTER # 506 | A PRELIMINARY EVALUATION OF MYCARE APP IN YOUTH WITH HEMATOLOGY/ONCOLOGY DISORDERS

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Background: Oral medications are a critical part of treatment, yet many do not take their oral chemotherapy as prescribed. Additional methods for promoting medication adherence are needed. The rapid growth in portable technology has led to numerous healthcare-related apps. A review of medication adherence apps showed a positive impact on adherence, but few had healthcare providers involved in development or utilized gamification as a strategy for improving adherence. We developed the MyCare App (MyCare) to improve medication adherence visualization and provide reminder notifications and gamification enhancements to patients for logging medications. MyCare provides a centralized location for patients/caregivers to track side effects such as pain scores, nausea, and vomiting.

Objectives: To examine feasibility and acceptability of MyCare among youth with Hematology/Oncology (HO) Disorders. To examine the effect of MyCare on treatment adherence, self-efficacy, and communication within the HO Clinic among youth and caregivers of children with HO Disorders.

Design/Method: Patients 12-21 years and caregivers of patients <12 years with confirmed HO disorders requiring daily oral medications were eligible. We assessed baseline medication adherence using standard monthly clinic assessments for 3 months, followed by a 6-month study period utilizing app medication reminders (months 4-9). Subjects also completed monthly simplified medication adherence questionnaire (SMAQ) and System Usability Survey (SUS) and Patient/Caregiver Survey at months 4 and 9 to assess patient/caregiver perceptions of MyCare and impact on disease management. Surveys were scored using Likert scales 1-4 with 4 being most favorable unless otherwise indicated.

Results: To date, eighteen subjects have reached study completion. Adherence via standard clinic assessments ranged from 58% to 84% reporting no missed doses. Adherence via SMAQ survey trended higher, ranging 92% to 100% adherence. Compliance with documenting medications via MyCare varied widely from 1-89%, making medication adherence difficult to interpret. SUS scores were positive at study completion (n = 6, range 70-97.5%). Overall, subjects were very satisfied with MyCare (3.2 $\pm$ .837), felt medications were easier to remember/track with MyCare (2.8 $\pm$ 1.3), and noted somewhat reduced stress/worry about disease management (1.20 $\pm$ 1.304). Subjects felt the logs for medication, nausea/vomiting and mood/energy were helpful, while the logs for pain, sleep, stool, diet, and fever were not frequently used. Seven patients have continued to use MyCare past study completion.

Conclusion: MyCare is feasible and perceived as useful in remembering and tracking medications for some patients and may help with chronic illness management in HO patients. Feedback will guide future app development.

POSTER # 507 | SUFFICIENT IMMUNE RESPONSE TO SARS-COV-2 IMMUNIZATION IN IMMUNOSUPPRESSED PEDIATRIC PATIENTS

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Background: Immunosuppressed pediatric oncology patients have increased risk of morbidity and mortality compared to immunocompetent children when infected with SARS-CoV-2. Previous works showed SARS-CoV-2 vaccines have a weaker immune response in adult immunosuppressed patients with solid tumors (ST) or hematologic malignancies (HM). The immunogenicity of the SARS-CoV-2 vaccines, in pediatric oncology patients, needs to be evaluated.

Objectives: The Pediatric Oncology Patient SARS-CoV-2 Immunization on a Cellular Level Examination (POPSICLE) trial will measure antibody and T cell response to SARS-CoV-2 vaccines and phenotype the peripheral blood mononuclear cells (PBMCs) to characterize the immune status in immunosuppressed children compared to pediatric healthy controls (HC) throughout vaccination to evaluate adequate immune response against SARS-CoV-2, to optimize vaccine protocols, and to improve patient care.

Design/Method: Eligibility: 6 months – 24 years; diagnosis of HM or ST; actively receiving or within 6 months of therapy. HC were 6 months-24 years. Blood samples were drawn at baseline and throughout vaccination.

Antibody response was evaluated with a multiplex-bead assay (MBA) to discriminate between the immune response to the vaccine (spike protein) or to a SARS-CoV-2 infection. T cell response to Spike protein was analyzed by TruCulture Assay to measure IL-2 and IFN-gamma response. An activation induced marker (AIM) assay was utilized for phenotyping and quantification of SARS-CoV-2-specific T cells using markers such as $Ox40^+$, $CD137^+$ for $CD4^+$ T cells and $CD69^+$, $CD137^+$ for $CD8^+$ T cells.

Results: Enrollment: HM = 13; ST = 5; bone marrow transplant (BMT) = 4; median age 9.82 years. HC = 6.

We detected a significant antibody response for IgG specific for spike proteins in HC ($p = 0.0004$), HM ($p = 0.0043$), and ST ($p = 0.0066$) measured by MBA after the second vaccine. BMT and HM patients had reduced, non-significant immune responses compared to ST and HC.

The Spike-specific IFN-gamma response showed significant increase for HC ($p = 0.0124$) and HM patients ($p = 0.0217$) after 2 vaccines. IL-2 response showed significant increase for HC ($p = 0.0051$) and ST patients ($p = 0.0434$) after 2 vaccines. HC IFN-gamma and IL-2 were non-significantly higher than other groups. AIM analysis is ongoing and preliminary data will be presented.

Conclusion: HC, HM, and ST patients had significant immune responses to the SARS-CoV-2 vaccine after the second SARS-CoV-2 vaccine.

The immune response in our study demonstrates SARS-CoV-2 vaccines are immunogenic in immunosuppressed children, are effective, and should be encouraged in pediatric patients undergoing immunosuppressive therapy.

POSTER # 508 | TIME TO POSITIVITY OF BLOOD CULTURES AND CORRELATION WITH CLINICAL OUTCOMES IN PEDIATRIC PATIENTS

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Background: Blood cultures(BCx) are the gold standard to determine source of infection in immunocompromised(IC) children with fever. Children are monitored inpatient for at least 48 hours, while awaiting BCx results to determine treatment course. Many BCx are negative, even if they remain febrile and neutropenic(FN). Children with immunodeficiency and/or FN may be hospitalized for weeks on antibiotics despite persistent BCx negativity. Multiple studies have shown near universal time to positivity (TTP) of BCx within 24 hours, yet practices remain conservative regarding discontinuation of antibiotics.

Objectives: The purpose of this study was to investigate TTP of BCx and correlate with clinical outcomes.

Design/Method: IRB-approved retrospective study obtained data through chart review of 52 IC patients(ages 0—20 years) from July 1, 2019 through August 31, 2022. Data included demographics, clinical characteristics, and laboratory values.

Results: From 52 patients, a total of 146 BCx became positive. Of these, 138 were considered pathogenic with 9 contaminants by lab standards. During this time, a total of 2,605 blood cultures were negative. Preliminary data analysis was done at 12, 24, 36, 48, 60, and 72 hours from collection and compared with final result at 120 hours. At 12 hours, BCx positivity was 25% sensitive and 99.9% specific with a positive predictive value (PPV) of 94.7% and a negative predictive value (NPV) of 96%. At 24 hours, BCx positivity was 68% sensitive and 99.8% specific with a PPV of 95% and a NPV of 98.3%. At 36 hours, BCx positivity was 81.9% sensitive and 99.7% specific with a PPV of 93.4% and a NPV of 99%. At 48 hours, BCx positivity was 85.5% sensitive and 99.7% specific with a PPV of 93.7% and a NPV of 99.2%. At 60 h, BCx positivity was 92.7% sensitive and 99.7% specific with a PPV of 93.4% and a NPV of 99.6%. At 72 hours, BCx was 96.3% sensitive and 99.7% specific with a PPV of 93.6% and a NPV of 99.8%.

Conclusion: Most IC patients including those with FN will remain inpatient for weeks on broad spectrum antibiotics, and many will have complications from antibiotic therapy such as Clostridium difficile infection and emergence of drug-resistant organisms. Our data suggests that antibiotics could potentially be stopped while continuing to monitor the patient clinically. More studies are needed to evaluate earlier discontinuation of antibiotics in these patients.

POSTER # 509 | IMPROVING THE QUALITY OF PEDIATRIC BONE MARROW BIOPSIES: A QUALITY IMPROVEMENT INITIATIVE

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Background: Bone Marrow (BM) examination is integral for thorough hematological evaluation for many indications. In Pediatric Hematology Oncology (PHO), Bone Marrow Biopsy (BMB) and Aspiration (BMA) procedures are performed for the diagnosis and prognostication of many malignant and non-malignant conditions. Inadequate sampling may result in delayed or misdiagnoses, which can impact therapeutic decisions and patient outcome. Obtaining high-quality specimens in a safe manner is paramount to deliver expedited and appropriate patient care. Aspirate is considered adequate and evaluable if spicules are present, the slide is evenly prepared, and clots are absent. Pediatric BM core specimens require a sample of at least 5-10 mm in length, whereas, in adults, cores>2 cm are considered adequate. We identified two main challenges at our institution: 1) hemodilute, aspicular aspirate preparations and 2) inadequate core length.

Objectives: To improve the quality of BM aspirate and core specimens in PHO patients.

Design/Method: We collaborated with hematopathology, flow cytometry, adult oncology proceduralists, and procedure center staff to modify our BMA and BMB techniques to improve specimen quality. Beginning in November 2020, we implemented several procedural process changes including 1) obtaining the biopsy specimen prior to the aspirate, 2) preparing aspirate slides by trained/experienced laboratory technicians rather than at the bedside, 3) utilizing heparin washes between each aspirate pull, and 4) standardizing the order of aspirate collection. A core group of BM proceduralists was identified who received specialized training of the interventions and education on intentional communication verifying needed samples before and after the procedure. Adequacy of specimens before and after interventions were compared with Chi Square analysis with each patient contributing only one data point.

Results: Direct feedback was provided to proceduralists using audit and feedback on a regular basis. Over a 2-year period, 386 BMA and 387 BMB procedures were performed on 169 unique patients. In 2020, 66.7% (70/105) aspirates and 53.3% (56/105) cores were adequate. In 2021, following implementation of interventions, adequacy of cores improved to 70.3% (45/64) (c^2 (1, n = 169) = 4.77, p = 0.03). Aspirate quality did not improve significantly (c^2 (1, n = 168) = 2.35, p = 0.13).

Conclusion: Through this QI initiative, we identified and implemented practice and workflow changes that directly resulted in improved BM specimen quality in PHO patients. Future efforts will include consideration of alternative biopsy needles, to further improve upon our success

POSTER # 510 | AN ONLINE PLATFORM TO GENERATE EFFECTIVE INDIVIDUALIZED DEVELOPMENT PLANS

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Background: Beginning in 2019, the Accreditation Council for Graduate Medical Education (ACGME) has required trainees complete individualized development plans (IDPs) at least twice annually. When done well, IDPs are detailed tools to outline both long-term and short-term goals as well as the strategy to achieve them and serve as a blueprint for the trainee's career development. While most fellows have had exposure to IDPs during residency, prior research has shown that most residents do not have a good understanding of their purpose and are not confident in their ability to write one. We therefore set out to develop an online platform to assist trainees with an evidence based approach for completion of effective IDPs.

Objectives: To design a large-scale online platform to assist pediatric hematology-oncology fellows with the development of effective IDPs.

Design/Method: We built a custom web application from scratch, using Java, Spring Boot, and Spring Data for the business layer, Keycloak for the authentication and authorization layers, PostgreSQL for the data layer, and Fomantic-UI for the presentation layer. The web application provided roles for trainees, mentors, and administrators, and modeled IDPs as compositions of goals (classified as either short-term or long-term) and sub-goals.

Each trainee received an individual login that directed them to an IDP template, which walked the user through the main sections of an effective IDP, including a mission statement, long-term goals and short-term goals. Prompts exist for completion of each section, including the necessary components of SMART goals (specific, measurable, achievable, relevant and time-bound). Additionally, this evidence-based framework for goal-setting included concrete subgoals and specific strategies. Goals are tagged with the associated category, to ensure a diverse set of domains are addressed.

Results: The website went live in January 2021, and underwent several rounds of beta testing by program directors and trainees at several institutions. Initial feedback included that the platform was user friendly with clear instructions and helpful prompts and was quicker to complete than when done on paper. Subsequent iterations were notable for the ease of updating an IDP after the initial one. After completion of the beta testing, eight fellowship programs nationally began participation in a study to compare the use of this portal to the prior institutional standard.

Conclusion: We developed an online platform to assist trainees with the generation of evidence based IDPs. Future directions include further study of the user experience of the platform, as well as its impact on self-regulated learning.

POSTER # 511 | IMPACT OF A CLINICAL PHARMACIST IN AN OUTPATIENT PEDIATRIC ONCOLOGY CLINIC/INFUSION CENTER

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Background: With the rapid expansion of knowledge and complexity of disease states, oncology pharmacy specialists have become increasingly utilized in both inpatient and outpatient settings. Their background in pharmacology, pharmacokinetics, and oncolytic toxicities allows for effective identification of drug therapy problems in oncology patients. Previous research has indicated that clinical pharmacists in pediatric oncology can play a vital role in patient care.[1] This study aimed to investigate the impact of a clinical pharmacy specialist in an outpatient pediatric oncology clinic and infusion center at WVU Medicine Children's.

Objectives: Primary: to characterize the patient encounters and interventions associated with clinical pharmacist visits at WVU Medicine Children's Blood Disorders and Cancer Center.

Secondary: to analyze the distribution of clinical and non-clinical activities within the role of the clinical pharmacist.

Design/Method: A retrospective study was conducted via Tableau data visualization software collected from January 1, 2021 to December 31, 2021. Data surrounding the encounter type, pharmacist interventions, patient care services, and medication reviews were

collected. Data was inputted by the clinical pharmacist using SmartForms via EPIC during patient encounters in the electronic medical record (EMR). Descriptive statistics were used in interpretation of results.

Results: There were 657 unique patient encounters identified during the data collection period. The most common reasons for pharmacist encounters were for medication interventions (35%) and medication reviews (30%). The majority of medication therapy management sessions were related to IV oncolytics. There was a total of 321 medication interventions reported, with dose modifications and oncolytic monitoring being the most common (19% and 36% respectively). Non-clinical interventions were also apparent, accounting for 13% of reported pharmacist encounters, the most common intervention being coordination with specialty pharmacies.

Conclusion: The clinical pharmacy specialist was responsible for an extensive number of patient interventions, both clinical and non-clinical. This study was limited by its retrospective nature and reliability of data input by the user. Further research opportunities include investigating impact of the clinical pharmacist on patient outcomes related to medication safety in this practice setting.

1. Hyun, Journal of Oncology Pharmacy Practice, 2021.

POSTER # 512 | FIRGUN: USING MEANINGFUL RECOGNITION TO IMPROVE THE WORK ENVIRONMENT AMONG A PEDIATRIC ONCOLOGY TEAM

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Background: Pediatric oncology staff are at risk for work-related stress and burnout. Meaningful recognition is inversely associated with burnout and compassion fatigue and fosters a healthy work environment. Firgun is a Hebrew word that describes genuine, unselfish delight or pride in the accomplishment of another, without expectation of reciprocity.

Objectives: We hypothesized that if pediatric oncology team members gave and received Firgun, it could decrease perceived stress and improve the work environment.

Design/Method: Clinicians, trainees, and interdisciplinary staff at The University of Texas MD Anderson Cancer Center were consented and invited to participate in the study. After viewing an on-line 15-minute educational module, participants logged acts of Firgun into a Qualtrics form. Electronic administration of validated measures occurred at baseline and after 3 months (follow-up), including the Maslach Burnout Inventory, The Areas of Work-Life Survey, Clark Workplace Civility Index, WHO-5 Wellbeing Index, Professional Quality of Life Scale, and the Perceived Stress Scale, and a COVID-19 related distress thermometer question. Model-adjusted estimates of the change in scale score were calculated from baseline to post-Firgun period. The count of Firgun given or received was used as a covariate.

Results: 112 participants enrolled; 64 participants completed the post surveys. 24 were physicians, 27 were registered nurses, 29 were administrative staff and 32 were other support staff. The mean Firgun given was 4 with a standard deviation (SD) of 5.4, and mean Firgun received was 1.8 with a SD of 3.2. The Clark Workplace Civility Index was significantly improved from baseline to follow up (71.9 v. 75.5; $p = .035$). Moreover, Firgun given and received were significant predictors of improvement in the The Clark Workplace Civility Index baseline to follow-up ($p = 0.0007$) and ($p = 0.012$), respectively. Compared to baseline, participants reported less anger for things out of their control ($p = 0.001$) and this was also significantly related to frequency of Firgun given ($p = 0.04$). Firgun given was a predictor of improvement in the frequency reported of these additional items: felt nervous/stressed ($p = 0.002$), felt able to overcome difficulties ($p < 0.001$); felt frustrated with their job ($p = 0.026$), could easily create a relaxed environment ($p = 0.023$) and felt accomplished ($p = 0.027$). Firgun given and received predicted these items: felt they could cope with all necessary things (Firgun given: $p = 0.0001$, Firgun received: $p = 0.01$), and felt they dealt with problems effectively (Firgun given: $p = 0.005$, Firgun received: $p = 0.038$).

Conclusion: Firgun is a meaningful recognition tool that can be used to improve civility in the pediatric oncology workplace and decrease perceived stress.

POSTER # 513 | UTILIZING "TUCK-IN ROUNDS" TO IMPROVE TEAM COMMUNICATION IN PEDIATRIC HEMATOLOGY/ONCOLOGY

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Background: A high level of surveillance is required on pediatric hematology/oncology services due to patients' severity of illness. This can lead to patient safety concerns during shift changes and extended hospital stays due to frequent changes regarding patient updates, contingency plans, and discharge preparations. Furthermore, there may be unanswered questions overnight leading to extra pages and miscommunication among the interprofessional workforce. An ongoing quality improvement (QI) project initiative aiming to achieve and sustain improved communication was piloted at the Cleveland Clinic in 2022.

Objectives: The overall goal of this QI project is to improve communication among the interprofessional team by utilizing "tuck-in rounds" to (1) expedite discharges to $\geq$ 80% before noon and (2) reduce the quantity of pages overnight.

Design/Method: Using a Plan-Do-Study-Act (PDSA) quality improvement methodology, a daily "tuck-in rounds" was implemented that requires the presence of a hematologist/oncologist, nurse, intern, and senior resident at approximately 10 PM daily. Standardized questions

were utilized to maintain consistency including: (1) Are there any labs to follow up? (2) Are lab draws needed as currently scheduled? (3) When will the patient be discharged and, if tomorrow, will they be ready for discharge by rounds? (4) Is the medication reconciliation completed for discharge? Data was collected in a pre-intervention period (April—May 2022) prior to implementation and for the intervention phase (June-August 2022). Three PDSA cycles were performed, each 4 weeks in duration. The proportions of pages per night and discharges before noon were compared pre- and post- intervention using a one-tailed t-test and chi-square test, respectively.

Results: In the last PDSA cycle, implementation of the "tuck-in rounds" intervention was statistically significant in decreasing the average number of pages per night by nursing staff to residents (8.02 vs. 5.83, $p = 0.05$). For our second outcome, discharges before noon significantly improved (27% vs. 58%, $p = 0.005$).

Conclusion: Although "tuck-in rounds" are not routinely done on pediatric hematology/oncology units, initial implementation was promising at our institution. We demonstrated that with improved daily communication following team handoffs at night, discharges before noon were expedited ultimately leading to decrease in hospital length of stay, and there was a significant decrease in the number of pages per night. In subsequent PDSA cycles, additional questions relating to discharge will be implemented to attempt to reach goal of 80% discharges prior to noon, and handouts will be given for nursing staff to assist with common paging concerns to further improve outcomes.

POSTER # 514 | AN INTERPROFESSIONAL VIRTUAL WELLNESS PROGRAM TO STRENGTHEN TEAM COHESION

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Background: As the COVID-19 pandemic unfolded, data emerged on the increased risk for psychological distress on healthcare staff. Work volume, personal safety, patient illness acuity, and high mortality rate contributed to distress on healthcare providers. The organizational leadership at M.D. Anderson Children's Cancer Hospital responded to a concern for the psychological safety of their healthcare workforce by encouraging wellness programming. A grassroots wellness taskforce was assembled within the pediatric department at the institution with a principal aim of promoting community, resilience, and wellness. Eventually, the primary goal evolved into the creation of an effective virtual wellness program.

Objectives: Our aim is to present the results of a 26-month long quality improvement initiative involving the establishment of a Weekly Wellness virtual program aimed to decrease psychological stress among staff members at M.D. Anderson Children's Cancer Hospital.

Design/Method: We launched a virtual program, "Weekly Wellness" for all healthcare staff which was based on the Stanford Model for Professional Fulfillment and guided by the quality improvement Plan-Do-Study-Act (PDSA) framework. Weekly Wellness was a 50-minute live-streamed program with varied thematic content promoting health and wellbeing, workplace efficiency, and community. The program was evaluated and modified based on data collected from confidential electronic surveys sent to the staff. Three PDSA cycles were completed.

Results: Ninety-seven Weekly Wellness program sessions and 3 staff surveys were conducted between March 2020 and May 2022. Of 300 total staff, 125 (41.6%) completed at least one survey and of these, 114 attended at least one wellness program (91.2%). Most participants (83-98%) found the program helpful and 69.4% (90% confidence interval of 69.0-79.4) experienced decreased distress. After attending the program, the mean decrease in distress was 1.67 (standard deviation of 2.2) on a 10-point scale. Lifted spirits and increased social connectivity were the most frequently reported benefits.

Conclusion: This virtual wellness program was favorably received by pediatric oncology healthcare staff. Participants of the program endorsed increased social connectivity and improved mood during a period of pandemic-related social isolation guidelines. This program was implemented by an interdisciplinary pediatric collaboration and sustained through the present day.

POSTER # 515 | GROUNDWORK FOR STUDYING THE IMPACT OF TEAM STRUCTURE AND FUNCTION ON CHILD QUALITY OF LIFE

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Background: Children with cancer experience significant symptoms and disruptions to daily life, placing them at risk for poor quality of life (QOL). Clinicians with complementary training collaborate to deliver childhood cancer care, yet little is understood about how care team structure and function impact child QOL.

Objectives: We sought to explore: 1. parent-reported careteam membership, teamwork quality, and parent-proxy child QOL. 2. Potential variability in clinician-reported collaboration as measured by the joint problem-solving scale (JPS) when clinicians reflected on their work in response to different prompts.

Design/Method: Cross-sectional survey of parents and clinicians. Eligible parents spoke English/Spanish and had a child age 2 years to <18 years receiving cancer care for ≤18 months at two large pediatric cancer centers. At one site, parents were referred by clinicians on their child's healthcare team who completed the JPS. At the second site, parents self-referred in response to posted flyers or emails. Eligible clinicians spent ≥20% time as a nurse (practitioner), physician, or psychosocial clinician (social worker, psychologist, chaplain, or child-life

specialist) treating children with cancer. Data presented include clinician completion of the JPS for two scenarios: A patient about whose care they felt proud and a patient about whose care they felt less proud. Parent survey items queried team membership and teamwork quality. Parent-proxy child QOL was measured by age-appropriate PedsQL 4.0 Generic Core Scales (reference values for healthy child parent-proxy: mean 81.34, SD 15.92, minimal clinically important difference 4.5).

Results: Twenty-two parents and 23 clinicians completed surveys. Children's care teams included oncologists (100%), nurse practitioners (95%), home care nurses (52%), primary nurses (outpatient 82%, inpatient 91%), child-life specialists (100%), psychologists (55%), social workers (100%), chaplains (33%), and palliative care clinicians (29%). Parent-proxy mean QOL score was 65.34 (standard deviation (SD) 17.02), 1 SD below reference values. Seventy-three percent of parents (n = 16) endorsed excellent teamwork with observed differences by child age: ages 2-4 years, 57% (n/N = 4/7); ages 5-12 years, 50% (n/N = 3/6), ages 13 to <18 years 100% (n/N = 9/9). Mean clinician JPS scores were higher for proud (4.47) than less proud (3.63) patient care.

Conclusion: Although most parents reported excellent teamwork and multi-disciplinary involvement, ratings varied across age groups. Notably, parent-proxy child QOL scores were fair-to-poor, and clinicians reported variable collaboration. Future larger studies will need to evaluate the relationships between team structure and function with child QOL and identify potential moderating factors.

POSTER # 516 | IMPLEMENTATION OF A PEDIATRIC HEMATOLOGY ONCOLOGY ACUTE CARE CLINIC

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Background: In January 2020, the Acute Care Clinic for Established Patients (ACC) at St. Jude Children's Research Hospital (SJCRH) was established to provide outpatient care services to acutely ill children with chronic illnesses during weekday business hours instead of at a patient's primary disease-based clinic. Primary clinics began referring to the ACC in a staged pattern over the course of the first several months of the opening of the ACC.

Objectives: To evaluate the utilization, common diagnoses, and disposition of patients presenting to the ACC during the first two years of operation.

Design/Method: Records from all ACC visits during weekday business hours from January 2020 through December 2021 were extracted from the electronic medical record. Data, such as demographics, primary diagnosis, and acute care diagnoses, were included or confirmed through manual review of the medical record. All clinical characteristics and patient demographics were summarized by descriptive statistics.

Results: There were 1,497 unique clinical encounters by 811 patients. The median age was 8.96 years (Range 0.10, 25.7) and 53.9% of patients were male. During the last six months of the study period, the Hematology Clinic (34.6%) referred the most patients followed by the Leukemia Clinic (23.6%), and the Solid Tumor Clinic (18.1%). The most common primary diagnosis was sickle cell disease (28.5%), followed by solid tumors (22.6%), acute lymphoblastic leukemia (ALL) (16.5%), and central nervous system tumors (14.1%). The most common acute care diagnoses were fever (with or without neutropenia and sickle cell disease) (28.5%), gastrointestinal illness (21.6%), and pain (20.6%). Of the 29.9% of encounters that resulted in inpatient admission, 9.3% of admissions were to the intensive care unit (ICU). Twenty-two percent of acute chest syndrome encounters resulted in ICU admission while only 6% of febrile neutropenia cases required ICU admission. For children with non-neutropenic fevers, 73.5% were discharged from the ACC while 35.4% of encounters for vaso-occlusive crisis resulted in floor admission.

Conclusion: In the first two years of a specialized ACC, children with a broad range of cancers and blood disorders were evaluated with fever, pain, and gastrointestinal illnesses being the most common acute diagnoses. Nearly a third of patients required inpatient admission with almost 10% being admitted to the ICU. A specialized ACC for children with chronic medical conditions allows for the evaluation of acute illness by specialty trained providers outside of an emergency department while also reducing unexpected visits to primary specialty clinics, thus improving workflow.

POSTER # 517 | IMPROVING COMMUNICATION BY STANDARDIZING PHONE TRIAGE IN AN ACUTE CARE SETTING

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Background: The St. Jude Acute Care Clinic for Established Patients (ACC) was launched in 2020 to provide around-the-clock access to specialized care in an outpatient setting. The ACC is predominantly staffed by pediatric hematology & oncology (PHO) trained physicians and advance practice providers. Incoming patient calls on nights and weekends are triaged by pediatric nurses to determine appropriate disposition. Common reasons for calls include fever, pain, and nausea/vomiting.

Objectives: In order to optimize patient care, standardized triage criteria and nurse-provider communication are necessary. Our SMART aim was to increase standardized hand-off of patient triage from nurses to ACC providers from 25% to 50% within 6 months, thus increasing provider comfort level in medical decision making.

Design/Method: Utilizing a multiple-choice survey, providers were questioned on the phone triage process. This initial data informed PDSA cycle 1 which was mandatory usage of an existing standardized triage template form. We then used follow-up surveys to measure the success of this strategy. PDSA cycle 2 was adaptation and implementation of a published standardized PHO triage toolkit. The new system uses an algorithmic approach to classify 16 common triage pathways, based on chief complaints, into color-coded severities (green,

yellow, or red). Unique patient simulation cases were developed and implemented for training providers and nurses using the phone triage process. Each of the 16 protocols were built into electronic medical record (EMR), as the institution was in the midst of transitioning EMRs.

Results: Based on our initial survey results, we noted that only 21% of phone triage encounters by nurses were communicated to providers in a standardized format, which led to 80% of providers being uncomfortable determining a patient's situational severity. Implementation of mandatory use of the standardized triage form led to 100% use of the form, which led to 50% of providers feeling more comfortable issuing medical decisions. Process measurement showed that 71% of nurses found the new triage protocols helpful, with 50% of them feeling more comfortable with the triage process, although our balancing measure showed the new protocols did take more time.

Conclusion: Standardization of after-hours phone triage for acutely ill PHO patients led to improved provider and nurse satisfaction, which we believe will lead to fewer adverse patient events. Implementation into the new EMR will allow a more streamlined approach and increased capacity to track utilization and performance of the phone triage process.

POSTER # 518 | EVALUATION OF AN UPDATED PEDIATRIC EARLY WARNING SCORE IN PEDIATRIC HEMATOLOGY-ONCOLOGY PATIENTS

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Background: The Pediatric Early Warning Score (PEWS) is an evidence-based tool providing a standardized assessment of a child's clinical status while hospitalized. It is utilized to identify patients at risk for clinical deterioration and match their illness severity with the appropriate level of care. The ideal PEWS reliably detects patients at risk for deterioration (high sensitivity) while avoiding unnecessary evaluation of stable patients (high specificity). In our large tertiary pediatric hospital, patients with elevated PEWS scores outside the intensive care units require assessment by the rapid response team (RRT).

Objectives: The aim of this project is to determine if an updated PEWS system leads to earlier pediatric intensive care (PICU) level care while decreasing late rescues within the hematology/oncology patient population.

Design/Method: A retrospective chart review was completed of all RRT responses on the hematology/oncology floor from March, 2020 to February, 2022. It was determined if the patient required PICU transfer, PICU level care (defined as care not available on acute care floors) and was classified as a late rescue (defined as needing inotropic support or mechanical ventilation within 12 hours of transfer). The data was analyzed using u-charts (RRTs and PICU transfers per patient days), p-charts (percentage of patients requiring PICU level care of all PICU transfers, percentage of late rescues of all PICU transfers) and t-charts (days from last late rescue).

Results: Following the initiation of the updated PEWS system, RRTs significantly increased leading to a centerline shift from 1.2/100 patient days to 2.6/100 patient days, however the number of PICU transfers/100 patient days remained stable with a center line 0.68/100 patient days. While there may be a trend to fewer transferred patients requiring PICU level care, this was not significant enough to lead to a centerline shift (0.74). Days between late rescues showed a trend to increasing but not significant to lead to a centerline shift, however the percentage of late rescues of all PICU transfers significantly decreased leading to a centerline shift from 25.68% to 9.57% demonstrating that the updated PEWS system is leading to earlier identification of patients at risk for significant deterioration thus avoiding late rescues.

Conclusion: An updated PEWS system has increased safety in pediatric hematology/oncology patients by reducing the percentage of late rescues in patients requiring PICU transfer even though it has increased resource use with more frequent RRTs. Ongoing data collection will determine whether this high sensitivity PEWS system has sufficient specificity to be sustainable.

POSTER # 519 | REVAMPING THE PEDIATRIC HEMATOLOGY ONCOLOGY LEARNING EXPERIENCE

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Background: The Pediatric Hematology Oncology (PHO) rotation is a challenging part of resident education. Evidence suggests that inpatient medical oncology rotations fail to increase resident interest in oncology. This could be due to the perceived difficulty in caring for complex patients with high acuity. While many studies in internal medicine and radiation oncology are geared towards improving resident education, few of these studies exist in the pediatric literature. By implementing a standardized curriculum, we plan to improve resident confidence and learning on this rotation.

Objectives: Our project aims to improve resident satisfaction and knowledge within the PHO rotation by implementing a standardized curriculum using succinct and practical learning tools. Increasing interest in PHO as a specialty as a key driver to generate enthusiasm in our field is the ultimate goal.

Design/Method: A 9-question survey was distributed via email to 2nd and 3rd year residents (30) who completed the PHO rotation over the previous academic year. Multiple choice questions assessed their satisfaction with and use of the current curriculum. Additionally, our survey included open-ended questions evaluating their requested topics of interest and use of alternative resources.

Results: We obtained 23 responses. Seven residents (30%) did not use the curriculum; 8 residents (35%) reported it was not helpful for their learning. Four residents (17%) reported that they relied on external

online resources. Out of the 16 residents who opted to use the curriculum, 13 (81%) read 3 articles or less. Articles on tumor lysis syndrome, neutropenic fever, and acute chest syndrome were the most read. Residents frequently requested additional resources on transfusion reactions, components of blood products, and anemia management. Fourteen residents (61%) requested an electronic resource in addition to written materials for their learning.

Conclusion: Our survey highlights gaps in the current PHO curriculum. A portion of our residents are not satisfied with the current curriculum. This may be due to difficulty in accessing a written handbook and the time constraints of reading full articles. Our curriculum does not include hematology topics like transfusion reactions, blood products, and anemia management. This survey creates opportunities to improve the learning experience through an easily accessible online curriculum that covers key PHO concepts. Our next step will be a collaboration with PHO faculty and residents to create an online curriculum. Implementing a curriculum like ours may promote interest in the field of PHO and could be replicated among other pediatric subspecialties to improve pediatric resident education overall.

POSTER # 520 | IMPROVING TEAM EFFICIENCY AND SATISFACTION: BEDSIDE RN ROUNDING INCLUSION

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Background: Effective communication between all members of a patient's healthcare team is essential to providing excellent patient care. Interdisciplinary bedside rounds are known to improve the quality of family centered rounds, communication between healthcare team members, and coordination of patient care. Bedside nurses are a vital part of the healthcare team, with important insight into the patient's care and concerns. Consistent interdisciplinary rounds including bedside nursing, would promote a more collaborative culture and increase satisfaction of team members.

Objectives: We designed a quality improvement project aimed at enhancing the culture and communication between medical providers and bedside nurses through increased inclusion of bedside nursing perspectives into daily rounds.

Design/Method: We first analyzed how often bedside nurses are present and included during rounds on both our pediatric hematology oncology (PHO) and stem cell transplant (SCT) floors. Additionally, we conducted a pre-intervention qualitative survey regarding satisfaction with rounds. We then reviewed the same metrics after a series of interventions were implemented. Interventions included calling bedside nurses prior to rounding on each patient's room, creating a guide for nursing presentations to be delivered at the start of rounds for each patient, and nursing education on presentations.

Results: During our pre-intervention analysis, we found that 77% of the time nurses were actively included during rounds on our PHO and SCT floors. After interventions, we found that 91% of the time nurses were present and actively involved during rounds on both PHO and SCT floors.

A satisfaction survey found that 51% of physicians and nurses ranked neutral—strongly disagree, on a Likert scale, that inpatient rounds were effective. This decreased to 37% of physicians and nursing responding as Neutral—Disagree compared to 63% of respondents stating Agree—Strongly Agree that inpatient rounds are effective, after interventions were implemented.

Conclusion: An increase in the inclusion of bedside nurses was noted after our interventions. The intentional inclusion of bedside nursing in daily patient-centered rounds improved communication and satisfaction with rounds from all members of the care team. It also allowed for improved coordination of care and patient-centered shared decision-making.

POSTER # 521 | USE OF FAILURE MODES AND EFFECT ANALYSIS FOR CONSENT AND ENROLLMENT IN PEDIATRIC CLINICAL TRIALS

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Background: In a pediatric oncology clinical trials program, obtaining informed consent and enrolling a patient on study is a critical component. This is complicated by the fact that pediatric cancer patients are a vulnerable research population, by nature of their age, diagnosis, and inability to consent for themselves. There are multiple steps in this process and an error in any one of them could affect a patient's ability to participate in a clinical trial. Furthermore, errors in this process can jeopardize a clinical trials program.

Objectives: Through failure modes and effects analysis (FMEA), we sought to prospectively evaluate the process of identifying, consenting, and enrolling patients on clinical trials to identify steps at risk for failure.

Design/Method: We formed a representative multidisciplinary team of physicians, advanced practice nurses, nursing leadership, bedside nurses, clinical research staff, and nurse coordinators, to create a process map. All failure modes were identified for each step and scored for severity, likelihood of occurrence, and detectability. Failure modes were categorized using a Risk Product Number (RPN) where RPN 3-49, 50-89, and 90 or greater equaled low, moderate and high risk, respectively. For comprehensive evaluation, each failure mode was also assessed with a risk matrix based on severity and likelihood of occurrence.

Results: We identified a total of 23 steps from the time of identifying an eligible patient through enrolling the patient on study. A total of 94 failure modes were identified. 13 of the 94 failure modes, from 6 total steps, were categorized as high risk by at least one method

of categorization. The six steps most at risk of failure were provider emails clinical research associate (CRA) for initial screening, provider obtains and documents consent, provider documents eligibility, CRA and provider sign eligibility packet, CRA sends green light email for treatment, and provider places "ok to treat" order for therapy. Six of the 13 high risk failure modes (46%) occurred within the single step of provider obtains and documents consent. As a result, we have focused our efforts on implementing safeguards to improve the process to decrease the likelihood of failure mode occurrences.

Conclusion: Through proactive FMEA process mapping, we identified crucial steps within clinical trial conduct that represent potential points of failure. Future efforts will focus on sustainment of implementation and continued education to further improve the consent and clinical trial enrollment processes.

POSTER # 522 | EFFICACY OF COMMUNICATION USING INTERPRETATION SERVICES: A SURVEY OF PARENTS WITH LEP AND STAFF

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Background: With an increasing number of Latinx patients receiving oncologic care, more parents report limited English proficiency (LEP.) This can lead to communication barriers with the healthcare team. In addition, during the COVID-19 pandemic, most institutions moved to providing virtual rather than in-person interpretation services.

Objectives: Describe the efficacy of communication between the healthcare team and parents with LEP using the different interpretation modalities at our institution.

Design/Method: As part of an institutional quality improvement initiative to address communication barriers with Spanish speaking families with LEP, we surveyed one parent of patients 0-21 years of age with an oncologic diagnosis receiving care between January and October of 2022, who declared Spanish as their preferred language. Clinic staff, including nurses, providers, social workers, child life specialists and chaplains were also surveyed. Respondents were asked to rate the efficacy of communication on a scale of 1-10 (with 10 being the most effective) when using an in-person vs video vs phone interpretation modality.

Results: A total of 14 patients were identified whose parents reported LEP. Parents reported a mean efficacy score of 9.3 for in person, 6.2 for video, and 5.8 for audio only services. Thirty-two clinic staff members were surveyed, and results for all 3 communication modalities were essentially identical to that of the parent responses (scores 9.0. 6.5 and 5.8, respectively).

Conclusion: Our results confirm our assumption that communication barriers exist for Spanish speaking parents with LEP, and that in-person interpretation services are most effective in overcoming these barriers. While virtual interpretation services were a necessary resource during the global pandemic, they should not be a permanent primary modality for interpretation in the pediatric oncology patient care setting. With the expected continued increase of patients and families with LEP, our health care system should invest more in onsite specialized interpretation services for patients with complex health care needs. We are using the information from this ongoing QI initiative to further inform how our institution faces these challenges in the future.

POSTER # 523 | INTERFERON DRIVES GRAFT FAILURE AFTER HEMATOPOIETIC STEM CELL TRANSPLANT

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Background: Graft failure (GF) is a dreaded complication of hematopoietic stem cell transplant (HSCT) and there is no available therapy. We've shown that interferon and complement contribute to GF in HSCT for bone marrow failure (BMF) syndromes, but these GF pathways have not been studied in HSCT recipients with primary immune deficiencies (PIDs) or hematologic malignancies (HMs). Based on the data in BMF patients, interferon and complement blockers may have a role in GF treatment.

Objectives: We hypothesized that interferon drives GF and interferon-gamma blockade may prevent impending GF. Our objectives were to validate our published biomarkers in HSCT recipients with PIDs and HMs and study the tolerability and efficacy of interferon-gamma blockade for the prevention of GF.

Design/Method: Stored patient samples were used for biomarker studies on GF patients (all were febrile during GF) and febrile controls. CXCL9, sC5b-9 and BAFF were measured prior to conditioning and at the time of fever/GF. Mononuclear cells from GF patients and controls were used to study differences in interferon-related genes (Nanostring nCounter). Based on these findings, we began pre-emptively treating patients with clinical signs of GF with emapalumab (EMA) +/- eculizumab (ECU).

Results: In our biomarker analysis, HM patients with GF ($n = 3$) had higher CXCL9s at the time of GF compared to controls ($n = 5$; $p = 0.0003$). Higher baseline CXCL9s in GF patients with HMs were also seen ($p = 0.07$). PID patients with GF ($n = 4$) had higher CXCL9s at the time of GF compared to controls ($p = 0.09$). BAFF and sC5b-9 levels were not different at any time point. Nanostring analysis showed increased expression of interferon-alpha, gamma and NF-κB related genes in GF patients compared to controls.

EMA was then used in 21 HSCTs with signs of impending GF. ECU was given concurrently in 14 HSCTs. All treated patients were febrile and commonly had mismatched donors (85.7%, 18/21). Eighty percent (17/21) of CXCL9s were elevated prior to EMA dosing. GF occurred in 42.8% (9/21) of HSCTs. Responders had resolution of GF concerns, with improvement in fevers and neutrophil counts

with sustained engraftment. No complications from EMA or ECU were seen.

Conclusion: CXCL9 is a marker of interferon production and is significantly more elevated in GF compared to other febrile complications. We successfully identified subjects at high risk for GF and EMA +/-ECU therapy was well tolerated with promising responses. Efficacy conclusion are limited in this study, however these data support a formal clinical trial of EMA for the prevention of GF.

POSTER # 524 | NONMYELOABLATIVE CONDITIONING REDUCES TOXICITY OF MATCHED SIBLING TRANSPLANT FOR SICKLE CELL DISEASE

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Background: Pediatric hematopoietic stem cell transplant (HSCT) using an HLA-matched sibling donor (MSD) for sickle cell disease (SCD) has traditionally used myeloablative conditioning. Recently, the use of reduced-intensity conditioning (RIC) regimens has increased. Such chemotherapy-based approaches have serious toxicities and a risk of graft-versus-host disease (GVHD). Nonmyeloablative conditioning using alemtuzumab, low dose total body irradiation (TBI), and sirolimus, has shown promising outcomes in adults with SCD, but this approach has not been well studied in children and adolescents.

Objectives:

To compare outcomes, specifically markers of toxicity, between myeloablative and RIC MSD HSCT with nonmyeloablative HSCT in pediatric patients with SCD.

Design/Method: Data was retrospectively collected on patients with SCD who underwent an MSD HSCT using myeloablative or RIC conditioning at our institution since 2012. Data was prospectively collected on patients with SCD who underwent MSD HSCT using nonmyeloablative conditioning (alemtuzumab 1 mg/kg, TBI 300 cGY, sirolimus x 1 year) at our institution on a phase II clinical trial (NCT03587272). Patients with <1-year follow-up were excluded.

Results: Study cohort included 47 patients who received chemotherapy-based conditioning (40/47 myeloablative, 7/47 RIC) and 14 patients who received nonmyeloablative conditioning. Median age at transplant for the entire cohort was 9 years (IQR 5.5, 15.4). Median total hospital days in first year post-HSCT was significantly greater for patients who received chemotherapy-based conditioning (46 days) compared to nonmyeloablative conditioning (19.5 days), $p < 0.0001$. In the chemotherapy-based conditioning group 12 patients (25.5%) were admitted to the intensive care unit (ICU) for a median of 5 days, vs. 1 patient (7.1%) for 1 day who had no ICU intervention in the nonmyeloablative group. The overall incidence of grade 2-4 acute GVHD and chronic GVHD in the chemotherapy-based group was 7/47 (14.9%) and 6/47 (12.8%), whereas no GVHD was observed in the nonmyeloablative group. One-year overall survival (OS) for the chemotherapy-based conditioning group was 97.9% (46/47, one death related to GVHD) compared to 100% and 85.7% (12/14) in the nonmyeloablative group (one secondary graft failure with autologous recovery and one patient with low donor chimerism had HbS%>50%). One-year sickle-free, chronic GVHD-free survival was similar for the two groups (87.2% vs. 85.7%).

Conclusion: Compared to established myeloablative and RIC conditioning, the studied nonmyeloablative regimen decreased transplant-related toxicities for children and adolescents with SCD undergoing MSD HSCT. While secondary graft failure is a problem with the studied nonmyeloablative approach, its other benefits make it an appealing option for providers and families considering curative therapy for SCD.

POSTER # 525 | FOLLOW-UP OF MIXED CHIMERISM IN HEMATOPOIETIC CELL TRANSPLANTS (HCT) FOR SICKLE CELL DISEASE (SCD)

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Background: SCD symptoms are ameliorated following HCT and establishment of donor hematopoiesis. A long-term goal is to control hemolysis, endothelial damage, and vasculopathy progression. A myeloablative HCT has been standard practice due to concern for graft rejection (GR) or mixed chimerism. The development of mixed chimerism/rejection has been considered a risk factor for hematologic malignancy in adult SCD. Recently, reduced-intensity (RIC) and non-ablative (NMA) conditioning has been used to offset myeloablation toxicities. We analyzed long-term outcomes in patients with mixed myeloid chimerism (MMC) in the first year post-HCT.

Objectives: Evaluate (1) adequacy of MMC in controlling SCD symptoms (2) risk of eventual GR with MMC at 1-year and (3) incidence of clonal hematopoietic disorders in the presence of MMC. *Hypothesis*: Despite RIC/NMA, MMC>20% at 1-year can provide long-term disease control without hematologic malignancy in children.

Design/Method: Long-term follow-up was extracted for SCD patients with MMC (<95% donor myeloid chimerism) at 1-year post-HCT and follow-up ^{3} 2-years post-HCT. Data included health status beyond 1-year—severe infections, graft-versus-host disease, SCD complications, hemolytic parameters/hemoglobin analysis, other complications/hospitalizations, and most recent chimerism status.

Results: Twenty-six patients have met inclusion criteria to date. Eleven HLA-matched sibling, 8 matched unrelated, 2 umbilical cord blood, and one haploidentical donor HCT. Median age was 9.5 years (range, 4-22 years). Median duration of follow-up was 36 months (range 24-123 months). Myeloid donor chimerism (DC) was>51% in 18 (1 myeloablative, 15 RIC, 2 NMA) and <50% in 8 (3 RIC, 5 NMA). Fourteen were off immune suppression at 1-year and 21 at 2-years. There were 8 hospitalizations beyond the first year—fever (3), infection (2), migraine (1), vasculopathy associated CNS event (1) and vaso-occlusive crisis (1). Median myeloid chimerism at 1-year was 70% (25-93). At last follow-up, median myeloid chimerism was 55% (13-99). Two patients (3 and 10 years post-HCT), with <15% donor myeloid chimerism developed disease manifestations. The others were hemolysis-free, had donor-derived erythropoiesis, and had no vasculopathy progression. No patient has developed a hematologic malignancy or defective hematopoiesis to date.

Conclusion: Ninety-two percent of recipients with MMC at 1-year post-HCT maintained donor-derived erythropoiesis and SCD control long-term. GR and symptom recurrence was noted in only 2 patients. We have previously described successful salvage with purified donor stem cells in this setting. These data also emphasize the need for continued follow-up long-term with registries that describe long-term outcomes enhancing transplant data collection by the CIBMTR.

POSTER # 526 | ROUTINE BONE HEALTH SCREENING IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS

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Background: Abnormal bone density and fragility fractures frequently complicate recovery from hematopoietic stem cell transplant (HSCT). We have previously shown that this is particularly true in pediatric HSCT recipients and observed higher rates of fragility fractures in children who underwent HSCT compared to published literature in adult HSCT recipients.

Objectives: We hypothesized that routine bone health screenings in pediatric HSCT candidates would identify asymptomatic bone disease and facilitate treatment and disease monitoring in these patients. Our objective was to perform spine X-rays and dual-energy X-ray absorptiometry (DXA) scans prior to HSCT and at 1 year after HSCT in allogeneic HSCT recipients without radiation sensitivity syndromes.

Design/Method: All allogeneic HSCT recipients without radiation sensitivity syndromes were included. Abnormal DXA studies were defined as those with a bone mineral density (BMD) Z-score <−2. Abnormal spine X-rays were defined as those with vertebral compression fractures, wedging or vertebral height loss. Screening began in subjects who were 1-year post-HSCT in March 2021 and pre-HSCT screening began in February 2021.

Results: A total of 175 transplants were eligible for pre and/or post-HSCT screening. Sixteen percent (12/74) of pre-HSCT DXAs were abnormal. Spinal compression fractures were found in 5.6% (4/72) of pre-HSCT studies and vertebral height loss or wedging was found in 7.1% (5/70) of pre-HSCT studies. Twenty one percent (11/52) of post-HSCT DXAs were abnormal. Spinal compression fractures were found in 19% (4/21) of post-HSCT studies and vertebral height loss or wedging was found in 35% (7/20) of post-HSCT studies. We then looked at bone health screening data across different diagnostic categories. Primary immune deficiency (PID) patients had the highest incidence of abnormal DXAs prior to HSCT (27%, 3/11), whereas patients with leukemia or myelodysplastic syndrome (MDS) had the highest incidence after HSCT (29%, 7/24). PID patients also had the highest incidence of spinal compression fracture on both pre and post-HSCT assessments (19%, 3/19 and 50%, 3/6).

Conclusion: Routine DXA and spine film studies are feasible pediatric HSCT recipients and can identify patients with asymptomatic bone disease. The observed abnormal bone health findings in PID patients are consistent with prior work by our group and confirm this population is likely at higher risk for adverse bone health outcomes. These findings suggest a potential role for prophylactic or early-intervention bisphosphonate therapy in HSCT recipients at highest risk for adverse bone health events.

POSTER # 527 | HAPLOIDENTICAL STEM CELL TRANSPLANTATION IN SEVERE APLASTIC ANEMIA IN CHILDREN

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Background: Severe aplastic anemia (SAA) is a rare multi-lineage bone marrow failure disorder, the majority of SAA diagnoses (over 80%) are thought to be caused by autoimmune destruction of hematopoietic stem cells. SAA can be treated and often cured by immunosuppressive therapy (IST) or hematopoietic stem cell transplantation (HSCT). HSCT from a human leukocyte antigen (HLA) matched sibling donor (MSD) has become standard initial therapy for younger, newly diagnosed patients with long-term survival up to 95—100% in patients under 20.

Objectives: To describe the outcome of Haploidentical HSCT in SAA as a feasible option in countries with limited access to unrelated donor register.

Design/Method: We describe 11 pediatric patients, mean age 12 years (8-19) with a diagnosis of severe acquired aplastic anemia, all without an identical family donor available for which they received immunosuppressive therapy with ATG and cyclosporine without response 1 or 2 cycles. They were taken to a related haploidentical transplant.

Results: The preparative regimen was fludarabine 150 mg/m2/ASC-Cy30 mg kilo- melphalan 120 mg/m2/ASC- rabbit ATG. Acute-GVHD

prophylaxis with Cy post/ methotrexate and cyclosporine. All grafted and reached 100% chimerism at day +30. Six patients developed acute II-IV GVHD. The dose of CD34 infused was 16.49 x 10e6 x kilogram of recipient weight (range 2.4 to 57). Two patients died because refractory grade IV acute GVHD. Nine patients are alive in a mean follow-up of 520 days (range 97-796 days). Two patients developed severe chronic GVHD.

Conclusion: Haploidentical transplantation is a promising alternative for pediatric patients unresponsive to immunosuppressive therapy. Additionally, the conditioning regimen used without total body irradiation is motivating in the pediatric population where long-term effects are a major concern. In developing countries, there are not many options for the management of graft-versus-host disease refractory to steroids and this represents a limitation for the use of alternative donors; however, it is important to compare with the responses to immunosuppressive therapy when patients do not have an eligible identical family donor but have the option of multiple haploidentical donors to select from.

POSTER # 528 | THE INTEGRATION OF AN ORAL HEALTH EDUCATOR ENHANCES MBI-CLABSI PREVENTION FOR PEDIATRIC BMT PATIENTS

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Background: Eighty percent of pediatric cancer patients experience chemotherapy-induced oral toxicities. These toxicities can potentially cause delays in treatment, chemotherapy dose reductions, decreased quality of life, and a higher risk of oral infections. In some cases, these toxicities can include life-threatening mucosal barrier injury central line associated bloodstream infections (MBI-CLABSIs). MBI-CLABSIs are an especially dangerous complication of inadequate oral healthcare and are associated with a 7% 30-day mortality rate. Treatment-induced side effects, limited access to dental care, non-adherence to oral care guidelines, and variations in oral health practices within a cancer treatment team can contribute to the oral complications that predispose to MBI-CLABSIs. Addressing these barriers requires novel solutions to better integrate specialties.

Objectives: Our aim is to decrease MBI-CLABSIs and healthcare-associated costs in the Bone Marrow Transplant (BMT) unit by hiring a dental hygienist who will function within a newly developed Oral Health Educator (OHE) role. The OHE educates patients, families, and staff on the importance of the oral-systemic link in cancer care, ensures optimal oral healthcare maintenance, liaises with dental services to coordinate dental care, and functions as a member of the cancer care team.

Design/Method: The OHE role was implemented in March 2022 for a 15-bed BMT unit. CLABSIs were captured in real time six months before and six months after implementation between October 2021 and September 2022 (n = 20). Other measures captured included oral hygiene bundle compliance.

Results: Post implementation, oral care hygiene compliance improved by 10.5%, MBI-CLABSI rates decreased by 59%, and MBI-CLABSI cases decreased by 56% with an estimated cost savings of $230,000 in a six-month period.

Conclusion: The OHE contributed to standardizing oral hygiene protocols, improving patient education, reinforcing compliance with oral care protocols, and facilitating dental referrals. This has contributed to reduced MBI-CLABSI rates and associated healthcare cost savings for high-risk pediatric BMT patients. Future efforts will focus on expanding the role of the OHE to the broader population of hematology/oncology patients, and further sustained reduction of our MBI-CLABSI rates.

POSTER # 529 | ENGRAFTMENT, IMMUNE RECONSTITUTION AND CHIMERISM AFTER CD34+ ENRICHED WITH T-CELL ADDBACK TRANSPLANT

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Background: Allogeneic hematopoietic stem cell transplantation (HCT) is a curative modality for high risk malignant and non-malignant disease. Given that the majority of patients are lacking an HLA-matched stem cell donor, an alternative donor source is urgently required. We previously reported rapid engraftment, donor chimerism, and low incidence of Grade II-IV aGVHD in pediatric MUD recipients of $CD34^+$enriched grafts with T-cell addback.[1] A similar approach using haploidentical parental donors for children and adolescent with high-risk sickle cell disease also reported favorable outcomes.[2-3] Here we investigate outcomes for $CD34^+$ enriched grafts with T-cell addback in both pediatric and adult patients with malignant and non-malignant disease.

Objectives: To determine the safety, engraftment, immune reconstitution, chimerism, and cumulative incidence of Grade II-IV aGVHD and cGVHD following a $CD34^+$ enriched graft with a fixed dose of T-cell addback in patients with malignant or non-malignant diseases.

Design/Method: $CD34^+$ cells were enriched using automated CliniMACS ® Plus System device with target dose of $5x10^6$ $CD34^+$ cells/kg with T-cell addback dose of $2x10^5$ $CD3^+$/kg in the final product. Hematologic engraftment, immune reconstitution, chimerism, cumulative incidence of Grade II-IV aGVHD and cGVHD and survival was monitored.

Results: After enrichment the product had 76.1% (± 2.7%) $CD34^+$ cells with a 96% (± 0.3%) viability and a mean ±SEM log T cell depletion of 4.0 (±0.2). The median $CD34^+$/kg dose infused was 6.1 x10^6 $CD34^+$/kg (0.4—13.8 x 10^6/kg) with T-cell add back of 2.0 x 10^5 $CD3^+$/kg (n = 37). Thirty-eight patients with malignant (n = 32) and non-malignant (n = 6), with median age 35.2 years (21mth- 71yrs) in CR1,>CR1, PR or SD (n = 14,14, 7 respectively) underwent HCT. Median engraftment of myeloid (n = 37, 100%) and platelet (n = 32, 88%) engraftment was 11 and 17 days, respectively. At 14 days, donor chimerism was>95%. By day 100 all recipients demonstrated evidence of immune reconstitution with average absolute counts: $CD4^+$ T cells 58 (±12); B cells 183 (±36) and NK cells 215 (±21). The cumulative incidence of Grade II-IV aGVHD was 28.1% (CI95: 9.3-50.7). The probability of cGVHD was 4% (CI95: 0-63.5). The probability of OS at 1 year was 45.7% (CI95: 26.0-63.5). Thirteen patients had disease progression. Six had organ failure; three of which also had significant viral infection.

Conclusion: $CD34^+$ enrichment HCT with fixed T-cell addback achieved rapid engraftment, sustained donor chimerism and adequate immune reconstitution with a low incidence of aGVHD and cGVHD in patients with high risk malignant and non-malignant disease.

POSTER # 530 | USING MHEALTH TO UNDERSTAND SYMPTOM SEVERITY AND DISTRESS IN PEDIATRIC BLOOD AND MARROW TRANSPLANT

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Background: Patients undergoing blood and marrow transplant (BMT) require intense chemotherapy associated with significant symptom burden. Ultimately, pediatric patients have difficulty in managing their symptoms and communicating with their providers. The Nanbar Health mobile application has been previously used as an effective mHealth tool to collect data in this population. Few methods exist, however, to accurately measure symptom occurrence, intensity, and distress. Understanding these specific aspects of symptoms can lead to an improved understanding of symptom burden and improve management decisions.

Objectives: Evaluate patterns and compare reported differences in symptom intensity and distress via mHealth (Nanbar Health).

Design/Method: Following IRB approval, patients were approached and consented within the Pediatric BMT unit at Duke University Health System. Patients were given an Apple iPhone and Apple Watch preloaded with the Nanbar Health application. Participants were instructed to wear the watch as often as possible, as well as submit the intensity and distress of 15 cancer-related symptoms, at least once daily in the application. Participants used the tool for 60 days or until discharge from the hospital. Data was preprocessed in RStudio and analyzed for differences in reported intensity and distress.

Results: We collected data from a convenience sample (n = 4; 2 male, 2 female) with an age range of 11-14 years. 233 individual reports were collected from this cohort over the 60 days for the 15 symptoms. Shapiro-Wilk assessment showed data deviated from normal distribution; therefore, a nonparametric Wilcoxon signed-rank test was performed to assess for significant differences in symptom intensity and distress (Table 1). Of the compared values, nausea, tired, sore throat, vomiting, mouth pain, and pain showed highly significant differences between reported intensity and distress ($p < .001$). Headache and diarrhea were also significant ($p = .002$ and .033 respectively). Rash, fever, difficulty breathing, and trouble peeing showed similar reports for levels of intensity and distress.

Conclusion: The results were unexpected. We hypothesized that symptom distress would be equal to or greater than symptom intensity. Most often, however, patients reported distress for symptoms as far less than intensity. This finding raises questions regarding a possible dulling effect of symptom distress due to persistence in this population, as well as the utility of assessing distress in this way. Further research is merited to determine why reported distress was vastly different than symptom intensity and additional methods to be used to accurately assess distress.

POSTER # 531 | COMPASSIONATE USE OF NARSOPLIMAB IN A CHILD WITH HIGH-RISK NEUROBLASTOMA AND SEVERE HSCT-TMA

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Background: Hematopoietic stem-cell transplantation associated thrombotic microangiopathy (HSCT-TMA) is a severe complication with significant morbidity and mortality. HSCT-TMA results from endothelial injury, which activates the lectin pathway of complement. Narsoplimab (OMS721), an inhibitor of mannan binding lectin-associated serine protease-2, has been evaluated for safety and efficacy in adults with HSCT-TMA yielding high response rates. Currently there is no approved therapy and data on pediatrics is scarce.

Objectives: We report a child with relapsed high-risk neuroblastoma complicated by HSCT-TMA after her second tandem autologous HSCT who was successfully treated with narsoplimab via a compassionate use program

Design/Method: Pubmed search performed for terminology including "high grade neuroblastoma" "TMA" "Narsoplimab". Relevant papers were selected for literature review.

Results: A three-year-old female initially diagnosed at 12 months of age with low-risk neuroblastoma, underwent radical nephrectomy for tumor resection, and continued surveillance with urine catecholamines relapsed 3 years later. Abdominal MRI showed recurrence of a left posterior paraspinal mass with epidural extension, and positive bilateral bone marrow biopsies. She was classified as high risk. Completed 5

cycles of induction chemotherapy as per ANBL1531 (complicated by food aversion, poor weight gain requiring GT placement, and episodes of acute kidney injury) followed by tandem autologous stem cell transplants (ASCT). Her first ASCT was complicated by an acute symptomatic COVID infection during conditioning (requiring omission of 50% of cyclophosphamide dose) treated with remdesivir and grade 2 mucositis. Second ASCT was complicated by refractory TA-TMA (hypertension, elevated LDH, refractory thrombocytopenia, elevated sC5b9, proteinuria, pulmonary HTN). She was initially treated with Eculizumab (600 mg every 72 hours for 4 weeks) and defibrotide (6.25 mg/kg every 6 hours for 3 weeks) with minimal improvement in symptoms and laboratory markers. Compassionate use of narsoplimab was requested. She received a total of 12 doses of narsoplimab (4 mg/kg administered twice weekly), initiated in hospital and continued outpatient. No infusional reactions were noted. Peripheral counts, LDH, anemia, thrombocytopenia and sC5b-9 improved with reduction in proteinuria, reduction in anti-hypertensive medication and resolution of pulmonary HTN, reflecting resolution of HSCT-TMA. Narsoplimab was discontinued prior to initiation of planned immunotherapy with Dinutixumab.

Conclusion: Treatment with narsoplimab resulted in improvement in TMA laboratory markers and clinical symptoms. Narsoplimab use was effective and safe in this patient. Additional data is needed to support concomitant use of Narsoplimab and Dinutixumab.

POSTER # 532 | SUSTAINED REMISSION OF IPEX-LIKE SYNDROME FOLLOWING FAILED UMBILICAL CORD BLOOD TRANSPLANTATION

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Background: Immunodysregulation, polyendocrinopathy, enteropathy, and X-linked (IPEX) syndrome is a systemic autoimmune disorder caused by a hemizygous *FOXP3* mutation resulting in regulatory T-cell defects. Patients present with enteropathy/diarrhea, eczema, and endocrinopathies triad; cases without a *FOXP3* mutation are classified as IPEX-like syndrome some of which can be associated with various genetic mutations. Treatment options for both include immunosuppression with improved long-term life expectancy in those who undergo hematopoietic stem cell transplantation (HSCT).

Objectives: To report on a IPEX-like syndrome patient with sustained remission of symptoms following a failed umbilical cord blood transplantation (UCBT).

Design/Method: Electronic medical reports are reviewed to collect data.

Results: An African American male with appropriate growth at 2 months was diagnosed with atopic dermatitis. By 6 months, he developed persistent diarrhea, weight loss and growth failure on exclusive breast milk. He was found to have eosinophilia, low albumin, low total protein, elevated thyroid-stimulating hormone, low free T4, high anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin antibodies, high IgE and low IgG. No *FOXP3* mutation was detected leading to IPEX-like syndrome diagnosis. He was placed on levothyroxine and monthly intravenous immunoglobulin (IVIG). Despite oral steroids, there was minimal weight gain or improvement in eczema and diarrhea. Addition of tacrolimus led to marked improvement. Disappearance of anti-TPO and anti-thyroglobulin antibodies and improvement in eosinophil count were observed after six months of therapy. Due to improved outcomes with early HSCT, the patient underwent HLA-B antigen-mismatched (5/6-matched) UCBT with a total nucleated and CD34+ cell dose of $16.4x10^7$/kg and $12.1x10^5$/kg, respectively, after prednisone and tacrolimus discontinuation. Conditioning regimen comprised of busulfan, fludarabine and rabbit anti-thymocyte globulin. Tacrolimus and mycophenolate mofetil were used for graft vs. host disease prophylaxis. The patient failed engraftment but had resolution of diarrhea and hypogammaglobulinemia, significant improvement in eczema and eosinophilia with continued elevated IgE and impaired growth 26 months following UCBT without any tacrolimus or IVIG.

Conclusion: IPEX syndrome can be variable, even in families with the same *FOXP3* mutation. Genetic background variability in IPEX-like syndrome may contribute to heterogeneity. This case shows regression/resolution of many findings after a period of immunosuppression followed by an unsuccessful UCBT in IPEX-like syndrome. It is unclear if pre-UCBT immunosuppression or conditioning regimen with autologous recovery would have led to sustained resolution/regression. Therefore, in responsive patients, we would like to propose a trial period of immunosuppression discontinuation prior to planned HSCT to assess, if continued disease control can be achieved in IPEX-like syndrome.

POSTER # 533 | BONE MARROW TRANSPLANT FOR MACROPHAGE ACTIVATION SYNDROME IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Background: The recognition of macrophage-activation-syndrome (MAS) in the setting of systemic-juvenile-idiopathic-arthritis (sJIA) is complex, but a necessary distinction given emerging treatment options. With overlapping clinical manifestations including fever, end-organ involvement and lymphadenopathy, there is a focus on laboratory values to differentiate MAS from a sJIA flare. Once parameters are met, multiple treatment modalities can be considered, as monotherapy or in combination, including steroids, immunosuppression, chemotherapy, intravenous immunoglobulin, and cytokine-directed biologics. Given the long-term morbidity and mortality associated with progressive inflammation and immune dysregulation due to MAS with sJIA, it is imperative to regain control over this complication. However, these treatments are not without their own adverse effects, and in this case presentation, those side effects overcame the benefits and led to bone-marrow-transplant (BMT).

Objectives: 1. To describe the success of BMT in the setting of severely refractory MAS in sJIA.
2. To describe a possible genetic predisposition to severe disease: PLCG2 gene and HLA haplotyping.
Design/Method: Case report.
Results: Our patient was initially diagnosed in 2018 with sJIA and quickly developed MAS, complicated further with interstitial lung disease (ILD). Experienced multiple mono- and combined therapy failures, escalating from NSAIDs, IL-1 blockade (anakinra and canakinumab), glucocorticoids, cyclosporine, IL-6 blockade, JAK inhibition, etoposide, and to emapalumab. Due to significant toxicity, most of the steroid-sparing medicines were stopped, except for anakinra and high dose steroids which were utilized for disease stabilization during the BMT process. A matched unrelated allogenic bone marrow transplant was completed in 10/2020. No evidence of graft-versus-host-disease and early ANC engraftment with stable mixed chimerism. At 2 years post BMT, patient has resolution of osteopenia, normalization of pulmonary function tests and normal inflammatory markers off medications. Genetic testing returned with a variable of unknown significance (VUS) in the PLCG2 gene that may contribute to refractory disease via PLAID/APLAID/FCAS3, an immune dysfunction syndrome spectrum including immune deficiency and autoinflammation. Also discovered an HLA haplotype associated with a hypersensitivity reaction to medications that can mimic inflammatory features of sJIA with higher relative risk for severe disease and/or lung complications, as seen with this patient.
Conclusion: In refractory cases of severe MAS in the setting of sJIA, with the possibility of genetic predispositions leading to further medication non-response and toxicity, a bone marrow transplant may be the best option for disease resolution.

POSTER # 534 | EARLY UNRELATED CORD BLOOD TRANSPLANT WITH REDUCED INTENSITY CYTOREDUCTION FOR PNP DEFICIENCY

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Background: Severe Combined Immunodeficiency (SCID) secondary to a purine nucleoside phosphorylase (PNP) deficiency is a rare, autosomal recessive, primary immunodeficiency characterized by early neurologic damage, autoimmune disorders, and recurrent infection. Enzyme deficiency results in the accumulation of toxic metabolites in lymphoid progenitors, especially to T lineage cells. Enzyme replacement is unavailable, and prompt hematopoietic stem cell transplant (HSCT) is indicated to minimize neurologic damage and other complications. Published cases of BMT for PNP/SCID are rare and usually are late (> 6 months of age) and involve myeloablative cytoreduction unless a matched sibling is available. Partial red blood cell (RBC) exchange may provide enzyme replacement.
Objectives: To describe the clinical course of an infant diagnosed with SCID secondary to PNP deficiency and her hospital course undergoing a reduced intensity cytoreduction (RIC) unrelated cord blood transplantation (UCBT).
Design/Method: Case Report
Results: A 4-week-old infant born to consanguineous parents presented following an abnormal newborn screening (NBS) result on TREC CT assay. Initial lymphocyte subsets revealed CD3 819, CD4 731, CD8 76, CD19 63, CD56 227, RA 76.9%, RO 57.1%. Work up revealed normal phytohemagglutinin (PHA). The SCID mutation panel from INVITAE showed a homozygous mutation in PNP gene c199C>T9 (p.Arg67*). PNP level was 72 (normal range 1336 +/- 441).
After initial consultation, she presented with right arm twitching; imaging showed an acute infarct in the right precentral gyrus. Weekly subsets showed a precipitous drop of lymphocytes: CD3 145, CD4 120, CD8 15, CD19 58, CD56 28 by week 8 of life. We performed partial RBC exchanges to provide enzyme replacement.
Her father was phenotypically HLA matched but had only 50% of normal PNP enzyme. A UCBT 5/8 match was readily available and was considered the best option to provide normal enzyme levels post-transplant. Cytoreduction was employed to achieve donor full chimerism. The infant received a RIC regimen consisting of Hydroxyurea, Campath, Fludarabine, Melphalan and Thiotepa.
Transplant course was complicated by clinical seizures, veno-occlusive disease, sepsis, and feeding intolerance. Engraftment occurred on day 35 with 99% donor chimerism in CD3, CD15 and whole blood. The infant still requires RBC transfusions. PNP level will be drawn 4 weeks after last red cell infusion to assess transplant outcome, neurodevelopment will also be assessed.
Conclusion: We present a patient who had early PNP deficiency/SCID diagnosis. Early diagnosis allowed her to receive a very prompt RIC UCBT ultimately leading to engraftment with full donor chimerism.

POSTER # 535 | TREATMENT PRACTICES & RESPONSE RATES IN KAPOSIFORM HEMANGIOENDOTHELIOMA: A MULTICENTER COHORT STUDY

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Background: Kaposiform hemangioendothelioma (KHE) and tufted angioma (TA) are rare vascular tumors primarily affecting infants and young children and associated with significant morbidity and mortality, especially in the setting of Kasabach-Merritt phenomenon (KMP). Due to disease rarity, prospective clinical trials have not established optimal medical management.

Objectives: The primary objective of this study is to compare response rates (at 3 and 6 months) to sirolimus vs. vincristine in KHE/TA. Secondarily, durability of response and response to other treatment modalities were evaluated.

Design/Method: We conducted a national, multicenter retrospective cohort study through the ASPHO Vascular Anomalies Special Interest Group. Centers collected data on patients diagnosed with KHE/TA between January 2005-January 2020 with at least 6 months of follow-up. Patients were divided into KMP vs. no KMP groups and by primary treatment intervention. Response to primary intervention incorporated the following endpoints: clinical response (ClinR), radiologic response (RadR), and hematologic response (HemR; in KMP subjects only). Group were compared using Fisher's exact test.

Results: 159 unique subjects with KHE or TA from 17 participating institutions were evaluated. KMP was present in 64 patients (40.3%). Sirolimus was the most common treatment (n = 51, 32.1%), followed by steroids (n = 32, 20.1%), beta-blocker or minimal/none (n = 27, 17%), vincristine (n = 25, 15.7%), surgical/interventional radiology (IR) (n = 17, 10.7%), and sirolimus + vincristine (n = 7, 4.4%). Over 60% (n = 96) demonstrated a treatment response at 3 months and over 70% (n = 114) by 6 months (no significant difference across groups). The vincristine treatment group had higher RadR at 3 months compared to sirolimus (72.7% vs 20%, p = 0.03). There was no difference in RadR (p = 0.7), HemR (p>0.9) or ClinR (p = 0.4) between these groups at 6 months and no difference in rates of progressive, recurrent, or persistent disease at 3 and 6 months. Rates of persistent disease at 3 months were higher in patients receiving beta-blocker/minimal/no treatment (p = 0.02) and recurrent disease rates at 3 months were higher in patients treated with steroids alone (p = 0.04). Of 17 patients treated with surgery or IR embolization, 100% had response by 3 and 6 months, however 5 (29.4%) had recurrent disease within 6 months requiring initiation of systemic medical therapy.

Conclusion: In this large, multicenter cohort of 159 patients with KHE/TA, 40% had KMP, which is consistent with prior published rates. Over 60% of patients had response to medical or surgical therapy by 3 months and there were no significant differences in response rates or durability of response comparing sirolimus with vincristine.

POSTER # 536 | BARRIERS TO GENETIC TESTING IN VASCULAR MALFORMATIONS

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Background: Vascular malformations (VM) are rare disorders of vasculogenesis associated with significant morbidity and requiring comprehensive, multidisciplinary care. Improved understanding of their genetic basis is increasingly guiding management. Logistical barriers to obtaining genetic testing in patients with VM may prevent optimal medical care.

Objectives: Our objective was to query institutional mechanisms for and obstacles to obtaining genetics testing for VM.

Design/Method: We sent an electronic survey to members of the American Society of Pediatric Hematology Oncology Vascular Anomalies Special Interest Group and analyzed responses with descriptive methods. We also reviewed requirements for genetic testing from several laboratories and insurance companies.

Results: We received responses from 55/81 (67.9%) ASPHO participating institutions. Most respondents (90.9%, n = 50) were pediatric hematology-oncology physicians (PHO). Results were stratified by size of center; > 100 VM patients/year (n = 27, 49.1%), 25-100 VM patients/year (n = 17, 30.9%), and <25 VM patients/year (n = 11, 20%). Multidisciplinary VM clinics or programs were more common at large and medium-sized centers (88.9% and 64.6% vs. 18.2%). More than half of centers (n = 29, 52.7%) followed patients through adulthood. Most centers reported testing between 5-50 patients per year (n = 35, 58.2%) and that their volume of genetic testing has increased 2 to 10-fold in the past 3 years (n = 38, 71.7%). Most testing is ordered by PHO (n = 35, 66%), geneticists (n = 28, 52.8%), or genetic counselors (n = 24, 45.3%). In-house testing was more common at large and medium-sized centers. Smaller centers were more likely to utilize Tempus and Foundation Medicine for testing. However, these primarily oncology-focused laboratories are less likely to detect allelic variants at frequencies <5%. Prior authorization duties were shared amongst PHO and nursing/administrative staff, but the burden of insurance denials and appeals were on PHO (n = 35, 66%). Lack of administrative support, institutional and insurance requirements for testing, and lack of provider education about best approach to genetic testing were problems at centers of all sizes. The effort to obtaining genetic testing for this population, compared with that for oncology patients, was perceived as excessive at centers of all sizes.

Conclusion: We identify barriers to genetic testing for VM across institutions, describe differences between centers based on size, and make recommendations for systems improvements. PHO respondents noted significantly more obstacles to obtaining genetic information for patient with VM compared to routine molecular testing in oncology patients. Because genetic testing for VM is rapidly becoming standard-of-care, it is critical to identify and address barriers to such testing.

POSTER # 537 | PEDIATRIC MORTALITY IN COMPLEX LYMPHATIC ANOMALIES

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Background: Vascular anomalies were considered for a long time only a cosmetic inconvenience. While the large majority of vascular anomalies can be managed with pharmacologic, surgical and endovascular interventions, even during current years, complex lymphatic anomalies have a high incidence of mortality despite advanced treatment.

Objectives: Present a case series of complex lymphatic anomalies that resulted in death in our institutional experience outside of the early infancy period (older than 6 months at time of death).

Design/Method: Chart review of complex lymphatic anomalies in the last 10 years. Describe mortality etiology and outcomes. This study excluded patients that were diagnosed at birth or prenatally and have never been discharged from the NICU.

Results: Our case series includes four patients with ages at death between 9-33 months old. All 4 were girls. During the analysis time period 2013-2023, we managed 30 outpatient children with complex lymphatic anomalies. All 4 patients were diagnosed at birth or during the first few months of life with chylothorax. Three had central conducting lymphatic anomaly (CCLA) proven via MR lymphangiogram and the 4th had all the features of CCLA, but was too sick to complete the study. Two of them had also massive extremity lymphedema, one presented with pericardial lymphatic effusion and ascites while the fourth had additional intestinal lymphangiectasia. They had all received sirolimus with good therapeutic levels before last admission. Three had low Absolute Lymphocyte Counts (ALC), one had also very low IgG level, and one had normal ALC and IgG level.

The cause of death for all 4 patients, was acute respiratory failure due to viral infection (3 due to human metapneumovirus) and one due to respiratory syncytial virus. Two of them had superimposed bacterial pneumonia (one Pseudomonas Aeruginosa, one Klebsiella pneumonia). All four passed away in the intensive care unit with last admission lasting between 13-44 days. All were breathing on room air with no chest tubes prior to last admission. During last episode they had received the entire spectrum of respiratory support from CPAP to ECMO. One patient spent almost one entire month on ECMO without improvement.

Conclusion: Despite significant advances in medical care, complex lymphatic anomalies and especially CCLA has a high mortality (~ 15%) during early childhood with the major cause of death being upper respiratory viral infections that result in acute decompensation with irreversible respiratory failure.

POSTER # 538 | DISSEMINATED PYOGENIC GRANULOMAS IN AN INFANT WITH PIK3CA RELATED OVERGROWTH SYNDROME

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Background: PIK3CA Related Overgrowth Spectrum (PROS) encompasses a variety of genetic overgrowth disorders caused by somatic mutations in the PIK3CA gene. Skin abnormalities including epidermal nevi and lipomas have been associated with PROS, pyogenic granuloma (PG) has not previously been described with this disorder.[3] Pyogenic granulomas, benign vascular tumors with a propensity for bleeding, [1] have been associated with mutations in the RAS-MAPK pathway.[2,4]

Objective: To highlight disseminated pyogenic granulomatosis as a potential feature of PROS and to emphasize the relevance of molecular testing on PG tissue.

Design/Method: Case Report.

Results: A two-week-old male presented with several skin lesions and a large left thigh mass present at birth. There was no family history of vascular anomalies. On physical examination, there were firm papules and nodules on his scalp, chin, left wrist, right upper extremity, and right anterior thigh, and a large nodule on his left anterior thigh. He had partial syndactyly of his right 2nd and 3rd toes. Biopsies at 2 weeks of age of the right and left lower extremities suggested multifocal infantile myofibromatosis. These lesions grew and bled frequently leading to anemia. At four months of age, he began chemotherapy with vinblastine and methotrexate (total of 3 cycles) due to progression. Following an excisional biopsy of his left thigh lesion, pathology was more consistent with disseminated pyogenic granuloma. Chemotherapy was stopped and excision of problematic lesions was performed.

Brain MRI at 12 months of age demonstrated two intracranial lesions, one a transcalvarial lesion of the left occiput and the other in the right mastoid. His PGs resolved and he had no new lesions. At two years of age, left lower extremity hypertrophy was noted. At 7 years of age, leg length discrepancy demonstrated the lower extremity 2.6 cm longer than the right. A biopsy from 5 months of age was sent for genetic testing and demonstrated a PIK3CA c.3139C>T (p.H1047Y) mutation (VAF 25%).

Conclusion: Increased use of genetic testing in vascular anomalies has helped to broaden our understanding of the correlation between genotype and phenotype. This patient's overgrowth and leg length discrepancy are consistent with PROS. However, a PIK3CA mutation was identified from the pyogenic granuloma lesions, which to date has not been associated with PROS. Molecular testing of unique and problematic skin lesions in patients with vascular anomalies may help guide clinicians in diagnosis and specific treatment.

References:

1. Alomari, JPeds, 2020
2. Groesser, JID, 2016
3. Keppler-Noreuil, AJMG, 2015
4. Young, JID, 2015

POSTER # 539 | USE OF VINCRISTINE IN VANISHING BONE DISEASE

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Background: Gorham-Stout syndrome or Vanishing bone disease is a rare lymphangiomatosis of unknown etiology, characterized by the proliferation of vascular structures and destruction of the osseous matrix. This entity can affect multiple bones such as the skull, spine, extremities, and pelvis, although consider benign in pathogenesis this disorder has an unpredictable prognosis, reabsorption of the bones

via osteolysis could lead to major shrinkage and loss of bone mass, with associated comorbidities such as pathologic fractures, and pain. Treatment of this condition requires a multidisciplinary approach that involves surgical procedures, pharmacological management, and potentially radiation.

Objectives: We report a case of Gorham- Stout Disease with a large kaposiform hemangioendothelioma managed with Vincristine.

Design/Method: Literature and chart review.

Results: The patient presented as a 21-year-old female with a history of Gorham-Stout disease with a Sirulimus-resistant multifocal kaposiform hemangioendothelioma of the right ear confirmed with a biopsy. Since early childhood, the affected areas involved the skull, mandible, and cervical spine. Managed her disease with Sirolimus and bisphosphonates, followed by a multidisciplinary team that included endocrinology, craniofacial, plastics, ENT, orthopedics, and Hematology Oncology. Given no response to Sirolimus/ Rapamycin patient was also started on Vincristine 2 mg IV weekly for 4 doses. Course complicated with neuropathic pain managed with decreased dosage to Vincristine 1 mg IV monthly at this time for 2 years. The patient showed clinical improvement with the resolution of skin lesion, facial swelling, drainage, and associated pain.

Conclusion: Gorham-Stout syndrome is a rare disorder with no fully clarified Etiopathogenetic. The pharmacological approach for these patients should be considered to be multi-targeted, which could include bisphosphonates, vitamin D, calcium, and corticosteroids, and in this case, we speculate that Vincristine could provide added benefit in the management of vascular malformations. The potential beneficial effect of vincristine in Gorham–Stout syndrome should be further investigated, and additional studies are necessary to clarify the future of this therapy.

PTCTC ABSTRACTS

1) Theme: Advanced Practitioners | *ASCARIS LUMBRICOIDES* INFECTION AFTER PEDIATRIC HAPLOIDENTICAL ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT)

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Background: Post-HSCT helminth infection has been well documented in the literature, primarily in adults with strongyloidiasis. As the field of HSCT advances, international patients will increasingly present for HSCT and therefore nonconventional infectious processes should be considered in patients from nations where endemic parasitic infections are common.

Case: Our patient is a 6-year-old female with relapsed CNS-negative AML who emigrated from Central America to the United States 5 months prior to her haploidentical HSCT. On day −2 her phosphorous level began to downtrend until day +2 when the level dropped below the normal limit, prompting intravenous replacement. On day +1 she developed fever. Despite supplementation her level continued to drop. She was transferred to the PICU for additional phosphorous repletion on day +4 in the setting of tachypnea and abdominal distention. On day +5 she had a single episode of emesis containing a worm-like organism, determined to be a single *Ascaris lumbricoides*. She was treated with a course of albendazole, after which her phosphorous levels normalized. She continued to have fever and was treated for engraftment syndrome with tocilizumab and methylprednisolone starting on day +8. Due to persistent fever, she was subsequently diagnosed with hemophagocytic lymphohystiocytosis (HLH) based on ferritin level, soluble IL2 receptor, NK cell activity, fever, and hypertriglyceridemia. HLH was managed with dexamethasone and tocilizumab due to elevated IL6 levels. No signs of *A. lumbricoides* infection were detected on repeated stool studies or imaging.

Discussion: We highlight this case due to a paucity of literature regarding *A. lumbricoides* infection post-HSCT in both adult and pediatric patients. While post-HSCT *A. lumbricoides* infection in the setting of hypophosphatemia and the subsequent diagnosis of HLH are not well described in the literature, there are reports of hypophosphatemia being associated with parasitic infections and febrile illness. Normalization of phosphate levels despite persistent fever after albendazole treatment led us to postulate that her hypophosphatemia was due to the helminth infection rather than fever. HLH in this case appears to have resulted from the engraftment process combined with a parasitic infection. Despite an extensive pre-transplant infectious evaluation, no signs of helminth infection were noted on imaging or laboratory testing. However, our parasitic screening included only a single stool ova and parasite test. In light of the continued increased diversity in country of origin among pediatric transplant patients, this case highlights the need to consider additional pre-HSCT testing for a broader range of infectious etiologies.

1) THEME: ALLOGENEIC HSCT | OPTIMIZING HAPLOIDENTICAL DONOR SELECTION FOR PEDIATRIC HEMATOPOIETIC CELL TRANSPLANT

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Background: There is little data to help guide pediatric physicians in identifying the optimal haploidentical donor for pediatric patients.

Methods: The Center for International Blood & Marrow Transplant Research database was used to assess our hypothesis that use of

younger age or sibling donors would be associated with less graft-versus-host-disease (GVHD). Graft failure and relapse were evaluated, stratified by donor age or relationship, compared by Gray's Test for Equality. Multivariable analysis was performed using logistic regression for aGVHD and Cox regression for the remaining outcomes, adjusting for significant patient and transplant co-variates.

Results: 1069 patients ≤18yo received haploidentical HCT in the US from 2013-2019.

Donors were stratified by age: <18 years (n = 138), 18-35y (n = 440), and>35y (n = 491). Frequency of Grade II-IV aGVHD at 100 days post-HCT was highest with older age donors: 31% for donors>35y, 23% for 18-35y, and 15% for <18y (p <0.001). The cumulative incidence of cGVHD at 2 years was also higher with older age donors: 30% (95% CI 28-32%) with>35y donors, 26% (95% CI 23-29%), and 16% (95% CI 12-20%) with <18y donors (p = 0.025). Multivariable analysis confirmed increased risk of aGVHD (grade II-IV) with donors>35y compared to donors age 18-35y (OR 1.46, p = 0.02) and donors age <18y (OR 2.24, p = 0.003) and increased risk of cGVHD with donors>18y (18-35: HR 1.78, p = 0.014) (> 35: HR 1.88, p = 0.009).

Donor relationship was analyzed as mother (n = 382, median age 36), father (n = 386, median age 39) and sibling (n = 244, median age 16) donors. Use of parental donors had an increased risk of aGVHD (II-IV) compared to sibling donors (mother: OR 1.63, p = 0.024, father: OR 1.57, p = 0.034). The use of mothers had a significantly increased risk of cGVHD compared to both father and sibling donors (HR 2.33, p = <0.001). There were no differences in aGVHD (grade III-IV), relapse, or survival by donor age or donor relationship, however, graft failure was highest when donors were ≥18y (22% with 18-35y, 13% with>35y) compared to donors <18y (10%, p = 0.0013).

Conclusions: Our data shows GVHD outcomes are correlated with haploidentical donor selection—use of donors <18y has decreased incidence of aGHVD, cGVHD, and graft failure. The use of a sibling donor confers a lower risk for acute GVHD while the use of a maternal donor increases risk of chronic GVHD. For pediatric patients receiving haploidentical HCT, the use of sibling donors should be considered to decrease the risk of acute and chronic GVHD.

2) THEME: ALLOGENEIC HSCT | PAYING A-TEN-TION: TOXIC EPIDERMAL NECROLYSIS AS A UNIQUE PRESENTATION OF AGVHD IN A PEDIATRIC PATIENT

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Background: Acute Graft Versus Host Disease (aGVHD) is a common complication of stem cell transplant (SCT). Findings of toxic epidermal necrolysis (TEN) with rapid progression and mucosal involvement are uncommonly noted in aGVHD. There are reports of patients with aGVHD and clinical characteristics mimicking TEN suggesting a possible overlap between the two. Management and outcomes of patients with this overlapping presentation have rarely been described in pediatric patients.

Objective: We aim to supplement the literature with the description of the diagnosis, management, and clinical course of a unique case of aGVHD with TEN.

Design/Method: Single subject case report.

Results: We present an 11-year-old male with refractory T-cell Acute Lymphoblastic Leukemia who received peripheral blood SCT from a matched unrelated donor. Preparative regimen included total body irradiation and cyclophosphamide. Methotrexate and cyclosporine were used for GVHD prophylaxis. Engraftment was achieved on day 21 (D+21) post SCT with 100% donor chimerism. On D+23 the patient developed lip swelling that was unresponsive to diphenhydramine. On D+26, he developed a maculopapular facial rash which rapidly progressed over 24 hours to involve 80% of his total body surface area. The progression was also notable for development of vesicles coalescing into bullae involving his face, mouth, and genital mucosa, as well as ocular involvement with injected sclera and blurry vision concerning for TEN. Broad infectious work up was negative and skin biopsy on D+27 confirmed aGVHD. Topical and systemic steroids (methylprednisolone 2 mg/kg/day) were started on D+27. When the rash continued to progress after 24 hours on steroids, intravenous immunoglobulin (IVIG) 2gm/kg divided over 5 days was given as adjunctive management for TEN. By D+29 the skin manifestations had stabilized but with concern for overlapping aggressive aGVHD and TEN, which was only partially responsive to steroids and IVIG, ruxolitinib was added at D+32. An aGVHD biomarker algorithm panel including regenerating islet-derived 3-alpha (Reg3a) and suppression of tumorgenicity2 (ST2) sent on D+7, D+27, and D+34, respectively, were all low risk for severe aGVHD and non-relapse mortality. His skin findings continued to improve with near total resolution by D+49.

Conclusion: We report a unique case of aGVHD with TEN based on rapid progression, severity, and distinctive presentation with mucosal involvement. There have been few case reports of similar presentations, most with poor outcomes. We hope to add to the paucity of literature available by reporting our successful management with steroids, IVIG, and ruxolitinib, which resulted in early resolution of symptoms in a pediatric patient.

3) THEME: ALLOGENEIC HSCT | SUCCESSFUL ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN SICKLE CELL DISEASE USING A HAPLOIDENTICAL DONOR

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Background: Despite advancements in disease-modifying therapies, severe sickle cell disease (SCD) continues to be associated with a shortened life span and decreased quality of life. Allogeneic hematopoietic

stem cell transplantation (HSCT) is the only curative therapy currently available off a clinical trial. Previous reports of transplantation with unrelated or haploidentical donors have shown unacceptable rates of graft failure and/or graft versus host disease (GVHD), causing some apprehension in transplanting those without an HLA-matched sibling; One particular concern with patients with a long history of transfusion therapy is HLA antibody mediated graft failure.

Objective: We present two cases of successful HSCT of patients with SCD using related haploidentical donors, one with known anti-HLA antibodies prior to HSCT requiring desensitization.

Method: Our patients are both females, aged 11 and 5 years old, diagnosed with Hemoglobin S Beta-0 Thalassemia and Homozygous S disease and history of ischemic stroke. Conditioning regimen utilized identical methods using Anti-thymocyte globulin, Fludarabine, Cyclophosphamide, and Total Body Irradiation (TBI) with 400cGy. The GVHD prophylaxis regimen included Post transplant Cyclophosphamide (PTCy), Sirolimus, and Cellcept. One patient underwent desensitization with rituximab and IVIG prior to conditioning for known anti-HLA antibodies.

Results: Both patients tolerated conditioning well with no significant complications. One developed grade I stage I acute GVHD of the skin which responded rapidly to topical steroids. Both are transfusion independent 1year post-transplant without evidence of chronic GVHD and stable mixed donor chimerism of CD3 75%/CD33 81% and CD3 87%/CD33 99%

Conclusion: The incorporation of PTCy as GVHD prophylaxis has greatly improved outcomes in haploidentical transplants through the destruction of alloreactive T-cells, decreasing previously high rates of GVHD; however, there is much room to improve in terms of the high rates of graft failure seen, particularly in haploidentical transplants of hemoglobinopathies. Studies have shown that when increasing the dose of TBI to 400cGy, only 6% of patients had graft failure compared to a previous 50% rate. Our patients have had similar success using this technique. Additionally, the burden of HLA-antibody mediated rejection in patients can be overcome with desensitization as demonstrated in our patient.

While transplantation using an HLA matched sibling remains the ideal standard for cure, the use of related haploidentical donors with these techniques can be a safe and effective alternative to increase the available donor pool, particularly in minority groups where unrelated matches are scarce, and promises for the continued improvement in transplantation techniques to improve outcomes.

4) THEME: ALLOGENEIC HSCT | IMPACT OF ABATACEPT IN PATIENTS WITH INHERITED BONE MARROW FAILURE SYNDROMES

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Introduction: Hematopoietic stem cell transplantation (HSCT) is a curative option for patients with inherited bone marrow failure syndromes (IBMFS). These patients often have increased sensitivity to DNA damaging agents, leading to the need for reduced intensity (RIC) or reduced toxicity myeloablative regimens to minimize morbidity. Unrelated donors (URD) are often used when patients lack an HLA-matched related donor. The combination of URD, HLA mismatch, and RIC increases the risk for acute graft-versus-host disease (aGvHD), underscoring the need to evaluate novel GvHD prophylaxis agents in this population. We studied transplant outcomes of IBMFS patients who received abatacept, a selective inhibitor of T-cell activation.

Objective: Describe the impact of abatacept on acute GvHD in IBMFS patients

Methods: We conducted a retrospective review of IBMFS patients from Cincinnati Children's Hospital Medical Center and Rady Children's Hospital who received an allogeneic transplant from September 2017–May 2022. We hypothesized that incidence of grades III-IV acute GvHD with abatacept would be less when compared to a historical cohort of IBMFS patients (October 2013-November 2017) without abatacept. We compared the overall survival (OS), GvHD free-graft failure free-overall survival (GFS), rates of infections within the first 100 days and thrombotic microangiopathy (TMA).

Results: Twenty-one were in our historical control, and 26 patients were in our abatacept cohort. Patients who received abatacept (10 mg/kg/dose) with a calcineurin inhibitor had a standard dosing schedule of Day −1, +5, +14, +28, and longer if enrolled on a trial or per clinician. Median day of neutrophil engraftment were similar in both groups at 12 days respectively. There were no significant differences between any grade aGvHD (CI 0.29 vs 0.28; $p = 0.73$) or grades II-IV GvHD (CI 0.24 vs 0.15, $p = 0.12$). None of the patients in our abatacept treated population developed grades III-IV aGvHD (CI 0.14 vs 0.0, $p = 0.05$). There were no differences in rates of any grade chronic GvHD (23.8% vs 19.2%). OS (0.95 vs 1 $p = 0.3$) and GFS (0.59 vs 0.65, $p = 0.5$) were preserved in the abatacept cohort, without significantly impacting the incidence of viremias (57.1% vs 65.3%) or bacteremias (28.6 vs 19.2%).

Conclusions: Our retrospective review demonstrates that abatacept can be safely incorporated into GvHD prophylaxis regimens without contributing significantly to worsening infections, while maintaining engraftment, high OS and GFS, in patients who lack an HLA-matched donor. Incorporation of abatacept significantly reduced incidence of grades III-IV aGvHD.

5) THEME: ALLOGENEIC HSCT | EXTENDED RELEASE (ER) TACROLIMUS FOR GRAFT-VERSUS-HOST-DISEASE (GVHD) PROPHYLAXIS IN PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT): A CASE REPORT

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Background: Tacrolimus is a calcineurin inhibitor used for GVHD prophylaxis in patients undergoing HSCT. The immediate release (IR) formulation is administered every 12 hours and titrated to therapeutic concentrations. However, an extended release (ER) formulation is available, which shares similar exposure ($AUC_{0\text{-}24}$) and C_{min}. Moreover, it has a comparable safety profile and may improve medication compliance given daily dosing. While it has been studied in adult HSCT patients, no data exists in the pediatric HSCT population.

Objectives: A 13-year-old pediatric patient with aplastic anemia underwent haploidentical HSCT following preparative regimen with rabbit thymoglobulin, fludarabine, cyclophosphamide, and total body irradiation (200cGy). She received post-transplant cyclophosphamide followed by mycophenolate and tacrolimus for GVHD prophylaxis. Tacrolimus was started IV at 0.03 mg/kg/day every 12 hours. She was converted to IR oral suspension tacrolimus on day 33 post-HSCT which was titrated to therapeutic range (goal 6-10 ng/mL) at 1.3 mg. Unfortunately, the patient had challenges with medication compliance and had consistent sub-therapeutic concentrations. She was admitted to the hospital and transitioned from suspension to IR capsule formulation, but despite consistent administration had variable concentrations requiring frequent titration in drug dosing. Thus, on day 85 post-HSCT she was switched to ER oral tacrolimus at 2 mg every 24 hours and achieved a concentration of 7.4 ng/mL. Following hospital discharge, concentrations fell despite reported compliance and dose increased to 3 mg ER tacrolimus daily. She continued through day 365 post-HSCT and tapered off.

Methods: We retrospectively reviewed a single pediatric patient who underwent haploidentical HSCT and received ER tacrolimus GVHD prophylaxis.

Results: The patient was continued on 3 mg ER daily with consistently therapeutic concentrations when compliant with medications. She did not have any adverse effects from the medication, including no change in renal function. She did not develop any evidence of graft rejection and donor chimerism at 1-year was 100%. Moreover, she had no evidence of acute or chronic GVHD.

Conclusion: ER tacrolimus was successfully administered to a pediatric patient for GVHD prophylaxis post haploidentical HSCT to reach therapeutic concentrations without adverse effects. While compliance remained a challenge, it was improved compared to prior 12-hour dosing of IR formulations. Moreover, the patient did not develop any acute or chronic GVHD. Further investigation is needed to establish pediatric dosing standards and investigate efficacy for both GVHD prophylaxis and treatment.

6) THEME: ALLOGENEIC HSCT | VORINOSTAT FOR GVHD PROPHYLAXIS IN CHILDREN, ADOLESCENT, AND YOUNG ADULTS IS WELL-TOLERATED, ASSOCIATED WITH LOW INCIDENCE OF ACUTE GVHD, AND MAY REDUCE POST-TRANSPLANT COGNITIVE DIFFICULTIES

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Background: Graft-versus-host disease (GVHD) is a major cause of morbidity and mortality following hematopoietic cell transplantation (HCT). Histone deacetylase inhibition (vorinostat) reduced proinflammatory cytokines, increased Treg number and function, and reduced GVHD in preclinical and clinical studies. Previous data suggest that vorinostat may also confer neuroprotection. We are currently evaluating vorinostat in children and adolescent/young adults (AYA) for GVHD prevention and neuroprotection.

Objective: The primary endpoint is to determine a difference in historical day 100 grade 2-4 acute GVHD incidence of 50% versus 28% with vorinostat.

Design/Methods: In an ongoing Phase 1/2 prospective, multisite study, Children and AYA patients undergoing allogeneic HCT for hematologic malignancies receive standard GVHD prophylaxis plus vorinostat (45-60 mg/m2 BID) using 3+3 design (phase 1). Subsequent patients are enrolled in a phase 2 cohort at the RP2D. All patients receive bone marrow. Neurocognitive testing is performed pre-transplant and days 100, 180, and 365 post-HCT using standard neuropsychological tests and computerized cognitive assessments. The study will accrue 37 patients in total.

Results: Fifteen patients (median age of 16 years) are enrolled and evaluable to date (MUD, N = 9; MRD, N = 2; haplo, N = 4; prior HCT, N = 1). Six patients enrolled in the phase 1 portion. The RP2D is 60 mg/m2 BID (N = 12 treated at RP2D on phase 1/2). There have been no dose-limiting toxicities from vorinostat. The median day of neutrophil engraftment was 13 and 16.5 post-HCT for HLA-matched and haploidentical recipients, respectively, with no primary graft failures. One patient (7%) developed grade 2-4 GVHD before day

100. Two patients (13%) with ALL experienced relapse of their primary disease post-HCT. One patient (7%) died from transplant-related complications. The median follow-up is 5.4 months with 4 patients completing the planned 1-year follow-up period. Limited neurocognitive data suggest that baseline expressive vocabulary and visuospatial construction skills were in the average range, while academic performance was average for reading and at the lower limit of average for math. Vocabulary and visuoconstruction may improve after transplant. Academic achievement in reading was stable and improved in math post-transplant.

Conclusion: Vorinostat for GVHD prophylaxis is well-tolerated and feasible in children and AYA patients with low incidence of grade 2-4 GVHD. Although limited by the small sample size, the neurocognitive data suggest that the addition of vorinostat to standard GVHD prophylaxis does not adversely affect neurocognitive outcomes and may mitigate some cognitive difficulties experienced shortly after transplant. These data warrant continued evaluation in the ongoing clinical trial.

7) THEME: ALLOGENEIC HSCT | TWICE DAILY INTRAVENOUS INTERMITTENT TACROLIMUS INFUSIONS FOR GRAFT VERSUS HOST DISEASE (GVHD) PROPHYLAXIS IN CHILDREN UNDERGOING HEMATOPOIETIC CELL TRANSPLANTATION (HCT)

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Background: Tacrolimus is a highly effective immunosuppressant used in the prevention of graft versus host disease (GVHD) among pediatric allogenic hematopoietic cell transplant (HCT) recipients. Tacrolimus is commonly administered as a continuous 24-hour infusion; however, this schedule is logistically difficult and requires a dedicated central line for administration. Hence, we examined the safety and efficacy of administering tacrolimus as twice daily intravenous (IV) intermittent infusion in pediatric HCT recipients.

Methods: This was a retrospective IRB approved study of pediatric allogenic HCT recipients aged ≤18 years, who received twice-daily intermittent infusions of IV tacrolimus from January 2012 through September 2022 (N = 136). Tacrolimus was started on Day −2 or −3 from HCT at 0.015 mg/kg/dose infused over 2 hours at 12-hour intervals to simulate oral dosing. Trough levels were maintained between 5 and 15 ng/mL by dose-adjustments and continued until the patient was able to tolerate oral tacrolimus. Post-transplant complications through day 100 post-HCT were collected and analyzed.

Results: Our study cohort included 78 males (54.9%). Donor source was predominantly matched unrelated donor (61.3%, n = 87). Mean age at HCT was 7.00 years (*SD* ± 5.69, range 42 days- 18 years). Most patients received methotrexate (66.9%) in combination with IV tacrolimus as GVHD prophylaxis. Median trough tacrolimus level was 16.3 ng/mL (IQR: 13.7-18.5 ng/mL). Nephrotoxicity (≥2 x baseline creatinine) occurred in 31 (23.8%) patients with 16 patients (11.3%) needing renal replacement therapy (RRT). Five patients (3.5%) had seizures and PRES, and 19 (13.4%) developed transplant associated thrombotic microangiopathy (TA-TMA). Hypo-magnesia was recorded in 85.9 % cases (N = 122). Majority of patients (68.3%; N = 97) were hypertensive requiring treatment with anti-hypertensives. Acute GVHD (aGVHD) was observed in 30.3% (n = 43) of the study cohort.

Conclusions: When compared to previous studies assessing efficacy of twice-daily intermittent tacrolimus infusions reports, we observed lower incidence of nephrotoxicity (23.8% vs 42%[1]), PRES (3.5% vs 5.9%[2]), seizures (3.5% vs 3.9%[2]) and risk of aGVHD (30.3% vs 37%[1]). However, due to the lack of historical reports on TA-TMA in the allogenic HCT pediatric population[1-4], we were unable to compare TA-TMA rates from our cohort. Our study shows no decrease in efficacy of intermittent infusions and because central venous line access in children is challenging, our findings suggest that intermittent infusions could be administered as a safe and effective alternative in the allogenic HCT pediatric population. However, prospective studies examining the safety and efficacy of twice-daily intermittent infusions of IV tacrolimus administration are needed.

References:

1. Hashmi H, Bhandari S, Kumar R, et al. Twice-daily intravenous bolus tacrolimus infusion: A safe and effective regimen for graft-versus-host disease prophylaxis. *Hematology/Oncology and Stem Cell Therapy*. 2020;13(4):232-237.

2. Bacopoulos AJ, Ho L, Yang A, et al. Safety of two-hour intermittent intravenous infusions of tacrolimus in the allogeneic hematopoietic stem cell transplantation unit. *Journal of Oncology Pharmacy Practice*. 2021-01-01 2021;27(1):33-39. doi:10.1177/1078155220908948

3. Hirano Y, Sugimoto S, Mano T, et al. Prolonged administration of twice-daily bolus intravenous tacrolimus in the early phase after lung transplantation. *Annals of Transplantation*. 2017;22:484-492.

4. Skeens M, Pai V, Garee A, et al. Twice daily iv bolus tacrolimus infusion for GVHD prophylaxis in children undergoing stem cell transplantation. *Bone marrow transplantation*. 2012;47(11):1415-1418.

8) THEME: ALLOGENEIC HSCT | AUTOIMMUNE ENDOCRINOPATHIES IN PEDIATRIC NON-MALIGNANT HEMATOPOIETIC STEM CELL TRANSPLANTATION: A CASE SERIES

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Background: Autoimmune complications are reported in about 5% of pediatric patients following hematopoietic stem cell transplantation (HCT). Non-hematologic autoimmune complications are less common than autoimmune cytopenias and previous reports have included autoimmune thyroid, liver, skin and CNS disease. Risk factors for autoimmune complications post-HCT include non-malignant disease indication, use of T-cell depleted grafts, serotherapy during conditioning, and presence of GVHD. It is unclear whether these are truly autoimmune or alloimmune complications. The incidence and diversity of autoimmune endocrinopathies post-HCT have not been well described.

Objective: We describe a series of 5 patients who received a bone marrow transplant for nonmalignant disorders and developed 6 autoimmune endocrinopathies.

Method: Retrospective chart review was performed for all nonmalignant transplants from 2008 – 2022 (N = 199). Five patients were identified who subsequently were diagnosed with autoimmune endocrinopathies (AE) and confirmed auto-antibodies.

Results: Identified autoimmune endocrinopathies included Type 1 diabetes mellitus (N = 2), Hashimoto's thyroiditis (N = 2), and Graves' disease (N = 2). Incidence of autoimmune endocrinopathies in our nonmalignant population during this period was 2.5%. Median age at time of transplant was 14 years (range 4 months to 27 years). Indications for transplant were severe Hb SS disease (n = 3), X-linked CGD (n = 1), and RAG1 deficiency SCID (n = 1). Median time from transplant to the diagnosis of autoimmune endocrinopathy was 3.3 years (range: 11 months to 4 years post HSCT). All patients received reduced intensity conditioning regimen for matched sibling donor transplant and 1 received a haploidentical graft, 4 received serotherapy (n = 3 Alemtuzumab, n = 1 ATG), and 1 patient received TBI 200cGy. Both patients who developed type 1 DM were transplanted for Hb SS disease and presented with diabetic ketoacidosis, elevated HbA1c, and positive IA-2 and GADA antibodies. Two patients developed Graves' disease more than 2 years after HCT, with positive thyrotropin receptor antibodies and symptoms of weight loss, anorexia, diarrhea, and goiter. Two patients developed Hashimoto's disease; one patient after second transplant for sickle cell disease (SCD) and was found to have elevated TSH, low T4 and positive TPO antibodies during screening. The second Hashimoto's patient was symptomatic with dry skin, increase weight and fatigue and was found to have abnormal thyroid function and positive TPO antibodies. Three patients developed chronic limited GVHD. The patient with CGD had mixed CD3 compartment chimerism (72% donor at 9 months post HCT) and the SCID patient had full donor CD3 and CD19 chimerism but low CD33 (16%). The patients with thyroid autoimmunity responded to treatment. The patients with type 1 diabetes continue treatment with insulin.

Conclusion: The mechanism behind autoimmunity after HCT remains poorly understood; in part due to the rarity of these cases. We observed a 2.5% incidence of AE in nonmalignant HCT patients over a period of 14 years; specifically highlighting 2 cases with type 1 DM, which has not previously been reported in the literature. The paucity of literature in post-HSCT autoimmune endocranopathies supports the need for future studies to better understand the biology behind these cases.

9) THEME: ALLOGENEIC HSCT | CLINICAL RESPONSE OF PATIENTS ON TOPICAL RUXOLITINIB FOR ACUTE AND CHRONIC GVHD

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Introduction: Ruxolitinib 1.5% cream is approved for atopic dermatitis and psoriasis, with one study demonstrating efficacy in patients ≥12 years with chronic skin GVHD (Markova et. al).

Objective: We describe our experience of Ruxolitinib cream in children and young adults with acute or chronic skin GvHD.

Methods: Ruxolitinib cream was applied twice daily limited to ≤20% body surface area, to areas of erythematous skin rash of acute and chronic GVHD. Complete response (CR) was resolution of skin GVHD while partial response (PR) was a reduction of symptoms. Adverse reactions including skin infections, allergy, worsening pruritis and topical site changes were monitored.

Results: We treated 8 patients, median age 18 years (range 2-40) with Ruxolitinib 1.5% cream for median duration of 118 days (range 27- 334 days + ongoing)

Acute skin GVHD: Five patients had acute skin GVHD (Stage 2 n = 1; Stage 3 n = 4). One patient had additional GI and liver involvement. Median number of prior systemic treatments was 2 (Range 1-5). Two patients were on oral ruxolitinib when topical ruxolitinib was initiated. Two patients were previously on topical steroids and one patient was on topical tacrolimus without response. Four patients had a CR, while one patient did not respond.

Chronic skin GVHD: Three patients had chronic skin GVHD with an erythematous maculopapular rash. Two of the patients had underlying deep sclerotic features (Score 3). Additional organs involved were oral (n = 3), GI (n = 1), GU (n = 1), eyes (n = 2). All three patients had failed ≥2 prior systemic treatments and two had progressed on topical steroids prior to topical ruxolitinib. All patients were on concurrent systemic agents at time of topical ruxolitinib initiation, but no patients were on oral ruxolitinib. All three patients had a CR.

All patients: Responses have remained durable after discontinuing ruxolitinib cream. Resolution of symptoms persist in all CR patients at their last follow-up. One patient had pruritis following topical ruxolitinib use leading to discontinuation. No patients had skin infections or allergic reactions at sites of application. One patient had perineal HSV+ cellulitis where topical ruxolitinib was not applied. One patient had bacteremia and one patient had a bacterial urinary tract infection leading to pause in treatment out of caution. One patient developed BK

hemorrhagic cystitis which was likely related to underlying GvHD and systemic immune suppression.

Conclusions: Topical ruxolitinib demonstrates promise in treating children and young adults with acute and chronic skin graft versus host disease.

10) THEME: ALLOGENEIC HSCT | GUT IMMUNOMODULATION WITH VEDOLIZUMAB PRIOR TO ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION IN PEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Background: Inflammatory bowel manifestations can be seen in patients with immunodeficiency/dysregulatory disorders that are increasingly being treated with hematopoietic stem cell transplantation (HSCT); with varying ability to control gut inflammation prior to transplant. There is concern that peritransplant intestinal inflammation will result in a greater risk of intestinal graft-versus-host disease (GVHD). Vedolizumab is a monoclonal antibody that inhibits the interaction between a4b7 integrin and mucosal vascular addressin cell adhesion molecule-1 (MAdCAM-1) which is important in homing of lymphocytes to the gut and may be tool to prevent gut GVHD in these patients.

Objective: To describe the clinical course of a cohort of patients with inflammatory bowel disease treated with vedolizumab prior to and peri-allogeneic HSCT.

Design/Method: Retrospective chart review of patients with primary immunodeficiencies and IBD who underwent HSCT between 2018 to 2022 and who received vedolizumab pretransplant. At least 3 doses of vedolizumab were given at 6, 4, and 1 week(s) prior to the start of preparative regimen. Dose was 100 mg (<10 kg), 150 mg (10-25 kg), 300 mg (> 25 kg). Conditioning regimen for HSCT consisted of treosulfan, fludarabine and cyclophosphamide with ATG, with tacrolimus and methotrexate/steroids as GVHD prophylaxis.

Results: Six patients (5 female) with a median age of 5.8 years (range: 5 m-12 y) with inflammatory bowel manifestations received pretransplant vedolizumab. Their underlying diseases were chronic granulomatous disease (n = 4), IL-10 deficiency (n = 1) and gain function of SYK mutation (n = 1). Graft sources were unrelated donor cord (n = 4), peripheral blood stem cells (n = 1) and bone marrow (n = 1). Median number of doses pre-HSCT was 3.8 (range: 3-6), 4 patients received concurrent systemic corticosteroids, average of post HSCT infusions was 1.3 (range:1-3). Infusions and peritransplant courses were uneventful. All patients engrafted. GVHD was limited to grade 1 skin only (one limited skin cGVHD) and no gut GVHD. Two patients had CMV viremia. All 6 patients remain alive with no evidence of disease or GI symptoms at median follow up of 9 m (range 2-30 m).

Conclusion: In this patient cohort where we were concerned of peritransplant GI-related inflammatory complications including GVHD, the addition of pretransplant vedolizumab was both well tolerated and associated with a lower GI toxicity than expected. These findings provide a platform for study and use of vedolizumab for GVHD prophylaxis in patients with GI intestinal comorbidity pretransplant—and possibly for a wider range of patients.

1) THEME: CELLULAR THERAPIES | SUCCESSFUL INFUSION OF EXG34217 - AUTOLOGOUS CD34+ CELLS TREATED WITH EXG-001- FOR EX VIVO TELOMERE ELONGATION IN A PATIENT WITH A DYSKERATOSIS CONGENITA

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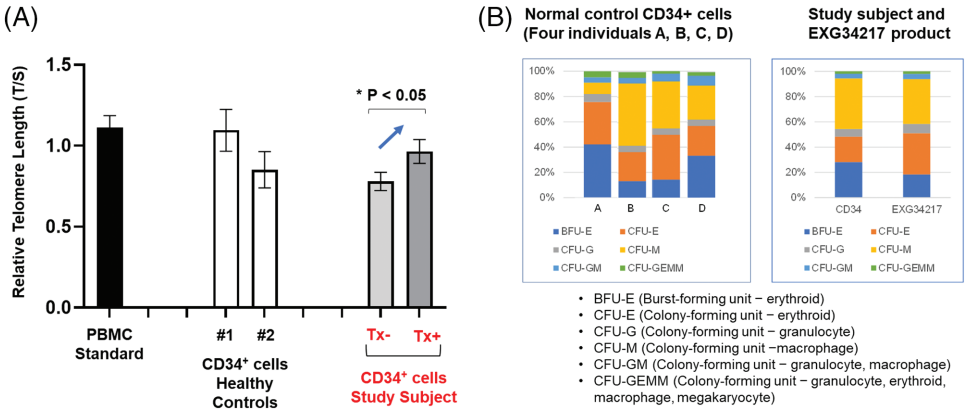
Background: We report a first-in-human cell therapy strategy for patients with telomere biology disorders to extend telomere length. Extremely short telomeres in patients with telomere biology disorders, including dyskeratosis congenita, lead to premature cellular senescence and increased risk of bone marrow failure. Zinc Finger and SCAN Domain Containing 4 (ZSCAN4) is a protein expressed transiently in preimplantation embryos, germ cells during meiosis, embryonic stem cells, and rare adult tissue stem cells that regulates telomere elongation and enhances genome stability.

EXG-001 is a non-integrating non-transmissible temperature-sensitive Sendai virus vector encoding for human ZSCAN4. We showed that transient exposure to ZSCAN4 via EXG-001 extended telomeres of primary fibroblast cells derived from patients with dyskeratosis congenita as well as healthy human CD34+ cells. However, whether EXG-001



can extend short telomeres in CD34+ cells of dyskeratosis congenita patients remained unclear.

Objectives: Based on this work, we translated this approach into a first-in-human clinical trial (NCT04211714), in which autologous CD34+ hematopoietic stem cells (HSC) were collected by pheresis over two days from an adult subject with dyskeratosis congenita after mobilization with filgrastim and plerixafor after IRB approval and consent.

Methods: We collected 2.8x10^6 CD34/kg and treated with EXG-001 ex vivo in a functionally closed tubing system using the CliniMACS Prodigy (Miltenyi Biotec).

Results: Telomere length of the subject's CD34+ cells was increased by 1.24-fold by treatment with EXG-001, bringing them into the healthy control range of CD34+ cell telomere length (Figure 1A). Maintenance of normal differentiation potential after treatment was demonstrated by colony forming unit studies to address the concern of effects on terminal differentiation (Figure 1B; EXG34217). 0.85x10^6 CD34/kg autologous treated HSC (EXG34217) were reinfused into the subject in February 2022 without conditioning regimen and further in vivo studies are in progress.

Conclusion: This novel approach uses modified autologous stem cells in the absence of conditioning regimen or immunosuppression and is genotype and mutation independent which is highly desirable in this chemotherapy and radiation sensitive population. These data support further investigation and translation of telomere elongation via ZSCAN4 exposure by EXG-001 in patients with telomere biology disorders as a potential therapeutic intervention for the prevention or treatment of bone marrow failure.

2) THEME: CELLULAR THERAPIES | TARGETING EWING SARCOMA WITH ANTI-IL1RAP CHIMERIC ANTIGEN RECEPTOR MODIFIED EX-VIVO EXPANDED NATURAL KILLER CELLS (IL1RAP-CAR NK) AND TGF-BETA IMPRINTED NK CELLS (CAR TGFBI-NK) IN COMBINATION WITH DINUTUXIMAB AND NKTR-255

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Background: Metastatic Ewing sarcoma (ES) has a dismal prognosis, largely secondary to therapy resistance within the tumor microenvironment. NK cell resistance in solid tumors is largely due to the small number and lack of specific tumor targeting of NK cells [1]. Our group has developed a novel approach to expanding NK cells [2] and demonstrated significantly enhanced cytotoxicity of CAR engineered expanded NK cells against various targets compared to mock NK cells against sarcomas [3,4]. IL1RAP (IL-1 receptor accessory protein) is a novel immunotherapy target highly expressed on ES cells but not in normal tissues as we previously reported[5]. TGFβ is a major mechanism of NK cell resistance. We found that TGFb-imprinted NK (TGFbi-NK) cells have enhanced NK-specific lysis of tumor cells[6]. Dinutuximab is an FDA approved mAb against GD2 which is overexpressed on ES. NKTR-255 is a recombinant hIL-15 agonist that boost NK cells, improve NK persistency and enhance response to ADCC-mediated therapy.

Objective: Here we aim to develop IL1RAP-CAR NK and TGFbi-NK cells and investigate their efficacy alone and in combination with dinutuximab and NKTR-255 in promoting cytotoxicity against ES.

Design/Method: PBMCs were expanded into NK cells using K562-mbIL21-41BBL feeder cells, or into TGFbi-NK cells by TGFb selection. The IL1RAP-CAR NK cells were generated by non-viral electroporation of CAR mRNA into expanded NK cells. NK cell cytotoxicity was evaluated by luciferase based cytotoxicity assay. IFN-γ and perforin secretion were analyzed by ELISA. CRISPR-Cas9 approach was utilized to knockout IL1RAP in ES cells.

Results: We found a significantly increased cytotoxicity of IL1RAP-CAR NK cells compared to mock NK cells against ES A673 and SKNMC cells at various effector to target ratios ($p < 0.01$ and $p < 0.05$). IL1RAP-CAR NK cells secreted significantly higher levels of IFN-γ and perforin than mock NK cells ($p < 0.01$ and $p < 0.05$). The enhanced cytotoxicity of CAR NK cells is due to specific targeting of IL1RAP because no significant increase in cytotoxicity with CAR NK compared to mock NK was observed in the IL1RAP knockout cells as we did in the wildtype cells. TGFb imprinting and IL1RAP-CAR expression in TGFbi-NK cells further enhanced NK cell cytotoxicity in-vitro against ES cells. Furthermore, we found that NKTR-255 and dinutuximab synergistically enhanced in-vitro cytotoxicity of CAR NK cells against ES cells.

Conclusion: Our data provide a rationale for a preclinical evaluation of IL1RAP-CAR NK/TGFbi-NK combined with NKTR-255 and dinutuximab in limiting ES xenograft tumor growth and/or metastasis and prolonging animal survival in-vivo.

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References

[1] Nayyar G, Chu Y, Cairo MS: Overcoming Resistance to Natural Killer Cell Based Immunotherapies for Solid Tumors. Front Oncol. 2019; 9:51. PMC6378304, https://www.ncbi.nlm.nih.gov/pubmed/30805309

[2] Chu Y, Flower A, Cairo MS: Modification of expanded NK cells with chimeric antigen receptor mRNA for adoptive cellular therapy, in Somanchi S (ed): Methods in Molecular Biology. Natural Killer Cells: Methods and Protocols. New York, Humana Press, Springer, 2016, pp 215-230

[3] Chu Y, Hochberg J, Yahr A, Ayello J, van de Ven C, Barth M, Czuczman M, Cairo MS: Targeting CD20+ Aggressive B-cell Non-Hodgkin Lymphoma by Anti-CD20 CAR mRNA-Modified Expanded Natural Killer Cells In Vitro and in NSG Mice. Cancer Immunol Res. 2015; 3:333-344. http://www.ncbi.nlm.nih.gov/pubmed/25492700

[4] Gardenswartz A, Luo W, Rosenblum JM, Ayello J, and Cairo MS. Targeting Ewing sarcoma and osteosarcoma with anti-MCAM chimeric antigen receptor modified NK cells. Cancer Research 2020;80.

[5] Zhang HF, Hughes CS, Li W, He JZ, Surdez D, El-Naggar AM, Cheng H, Prudova A, Delaidelli A, Negri GL, Li X, Orum-Madsen MS, Lizardo MM, Oo HZ, Colborne S, Shyp T, Scopim-Ribeiro R, Hammond CA, Dhez AC, Langman S, Lim JKM, Kung SHY, Li A, Steino A, Daugaard M, Parker SJ, Geltink RIK, Orentas RJ, Xu LY, Morin GB, Delattre O, Dimitrov DS, Sorensen PH. Proteomic Screens for Suppressors of Anoikis Identify IL1RAP as a Promising Surface Target in Ewing Sarcoma. Cancer Discov. 2021;11(11): 2884-2903.

[6] Foltz JA, Moseman JE, Thakkar A, Chakravarti N, and Lee DA. TGFb imprinting during activation promotes natural killer cell cytokine hypersecretion. Cancer. 2018; 10: 423.

3) THEME: CELLULAR THERAPIES | TARGETING PEDIATRIC NEUROBLASTOMA AND GLIOBLASTOMA WITH THE COMBINATORIAL THERAPY OF IL-21 SECRETION ONCOLYTIC VIRUS AND ANTI-ROR1 CAR NK CELLS

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Background: Children with recurrent and/or metastatic neuroblastoma (NB) and glioblastoma multiforme (GBM) have a dismal event-free survival (<25%) (1). Novel therapies are desperately needed for these poor risk patients. ROR1 is highly expressed on the majority of NB and GBM. Our group has successfully expanded functional and active peripheral blood NK cells (exPBNK) with irradiated feeder cells and electroporated CAR mRNA to exPBNK (2). Oncolytic herpes simplex viruses (oHSVs) are a promising experimental therapy. C134 is a selective replication competent oHSV with enhanced viral gene expression (3).

Objective: To determine if C134-based human IL21 expression combined with anti-ROR1 CAR engineered exPBNK cells can efficiently target ROR1$^+$ NB and GBM.

Methods: ExPBNK cells were expanded with lethally irradiated K562-mbIL21cells as we previously described (1). ExPBNK cells were electroporated with anti-ROR1-CAR mRNA using maxcyte electroporator as we previously described (2). C021 was generated by modifying C134 to express human *IL-21* gene. The supernatants of C134 and C021 were generated as previously described (3). in vitro cytotoxicity of anti-ROR1 CAR NK against NB and GBM cell lines were examined at different E:T ratios. IFN-g, granzyme and perforin levels were evaluated by ELISA assays (1). In vivo anti-tumor effect was examined utilizing human NB tumor xenografted NSG mice (1,2).

Results: C021 infected NB cells (MOI 0.025) generated hIL-21 in cell supernatants at 24 hours post infection (hpi) and peaked at 72hpi. Combinations of C021(C134+IL21) and anti-ROR1 CAR exPBNK cells had the greatest anti-tumor effect significantly enhancing NB and GBM cell death when compared to C134 + anti-ROR1 CAR exPBNK cell combinations ($p < 0.05$, $p < 0.05$). C021 addition to enhanced anti-ROR1 CAR exPBNK killing significantly increases IFN-g ($p < 0.05$),

granzyme B ($p < 0.05$) and perforin ($p < 0.05$) secretion and significantly upregulated the NK activating marker CD25 ($p < 0.05$). Our in vivo animal study showed that C021 infected NB cells in NB xenografted NSG mice secreted IL21 at day 1 and day 3 post infection. The combination of C021 and anti-ROR1 CAR exPBNK cells had better anti-tumor effect than single agent or C021+ NK or C134 + anti-ROR1 CAR exPBNK cells to reduce tumor burden in human NB xenografted NSG mice.

Conclusion: Our data demonstrated the anti-tumor efficacy of the combination of oHSVs C021 with anti-ROR1 CAR exPBNK cells targeting NB and GBM cells in vitro and in vivo. The genomic and immunologic mechanisms studies are ongoing. (This work is funded by U54 CA232561).

References

Chu/Cairo, JITC, 2021

Chu/Cairo, Cancer Immunol Res, 2015

Cassady, et al, Mol Ther Oncolytics, 2017

4) THEME: CELLULAR THERAPIES | MANUFACTURE, IMMUNOLOGICAL CHARACTERIZATION AND CLINICAL RESPONSE OF PEDIATRIC HSCT PATIENTS WITH GMP GRADE SARS-COV-2 CYTOTOXIC T LYMPHOCYTES (CTLS) UTILIZING THE CLINIMACS® CYTOKINE CAPTURE SYSTEM

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Background: Coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Treatment of COVID-19 has included dexamethasone, tocilizumab, remdesivir, Molnupiravir, nirmatrelvir/ritonavir and targeted antibodies. Currently there are no FDA approved targeted cellular therapies for the treatment of COVID-19. SARS-CoV-2 virus-specific cytotoxic T-cell lymphocytes (vCTLs) could provide a promising therapeutic option for COVID-19 patients.

Objective: To manufacture, validate and characterize SARS-CoV-2 vCTLs generated from convalescent COVID-19 donors using the CliniMACS® Cytokine Capture System on the Prodigy device and investigate the clinical response in patients with COVID-19.

Methods: Donor screening was done by stimulation of convalescent COVID-19 donor peripheral blood mononuclear cells (PBMCs) with SARS-CoV-2 peptides and identification of IFN-γ production by CD4 and CD8 T-cells using flow cytometry. Clinical grade SARS-CoV-2 vCTLs were manufactured using the CliniMACS® Cytokine Capture System. The enriched SARS-CoV-2 vCTLs were characterized by T-cell receptor (TCR) sequencing, mass cytometry analysis, and transcriptome analysis. Two patients were enrolled to a pilot Phase II trial of HLA matched or haploidentical related donor SARS-CoV-2 vCTLs in patients with mild or moderate COVID-19 disease (IND #27260) (NCT# 04896606) clinical trial.

Results: Ninety-three % of convalescent donor blood samples met the screening criteria for clinical manufacturing. Three validation runs resulted in enriched T-cells that were 79% $\pm$ 21% (mean $\pm$ SEM) IFN-γ^+ T-cells. TCR sequencing showed that SARS-CoV-2 vCTLs displayed a highly diverse TCR repertoire. Immunophenotyping analysis demonstrated enhancement of both memory CD8 and CD4 T-cells in the enriched SARS-CoV-2 vCTLs, especially in CD8 $T_{EM,}$ CD4 T_{CM} and CD4 T_{EMRA} cell subsets. SARS-CoV-2 vCTLs contained more CD4 T-cells than CD8 T-cells. Transcriptome analysis showed that SARS-CoV-2 vCTLs were polyfunctional with increased gene expression in T-cell function, interleukin, and tumor necrosis factor superfamily pathways. The two pediatric HSCT patients treated to date had moderate COVID-19 with pneumonia on CT scan and were recipients of T-cell depleted stem cell allografts with profound T-cell deficiency. Both patients

obtained a complete response (CR) following two doses of haploidentical donor-derived SARS-CoV-2 vCTLs and there was no evidence of any GVHD or CRS. Chest CT scans of the two patients at diagnosis revealed nodular opacities but had completely resolved on imaging after two SARS-CoV-2 CTLs infusion.

Conclusion: Our study demonstrates that highly functional SARS-CoV-2 vCTLs can be rapidly generated by direct cytokine enrichment from convalescent related donor PBMCs and are preliminary safe and effective in patients with moderate COVID-19.

5) THEME: CELLULAR THERAPIES | LINEAGE SWITCH POST IMMUNOTHERAPY: CURRENT STATUS AND FUTURE DIRECTIONS

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Background: Lineage switch (LS) is defined as the loss of B-lymphoid features and acquisition of myeloid or T-cell markers, and vice versa. LS from B-cell acute lymphoblastic leukemia (B-ALL) to acute myeloid leukemia (AML) has become increasingly prevalent with the use of targeted immunotherapies—but optimal diagnosis and treatment approaches are unknown. While select patient subsets (e.g., those with cytogenetic abnormalities such as KMT2A-rearrangement) may be predisposed to LS, cases without any predilection to LS are also being identified. Given both challenges in diagnosis and particularly dismal outcomes of LS, further study of this rare event is urgently needed. Objective: To describe a clinical case of LS and subsequent plan for a registry study.

Design/Methods: We report on a recent case of LS which prompted the development of an IRB-exempt multicenter, international registry study on LS—the latter of which is currently enrolling. Results: Case: A 20-year-old male with IgH-CRLF2 rearranged leukemia (CRLF2r) presented with relapsed/refractory B-ALL with extramedullary disease (EMD) that was refractory to standard chemotherapy, blinatumomab and inotuzumab. He enrolled on an investigational trial of CD19/22 CAR T cells with <5% marrow involvement. Although his B-ALL was undetectable by flow-cytometry on his post-therapy restaging bone marrow, and initial sites of EMD had resolved, a PET-CT demonstrated a new pancreatic mass not amenable to biopsy. Next generation sequencing detected leukemia specific transcripts consistent with the original clone in the blood and bone marrow at levels conventionally detectable by flowcytometry, which prompted concern for LS. Evaluation of myeloid markers confirmed AML, making this one of the first cases of LS occurring in a patient with a CRLF2r. Despite AML directed therapy, he died from rapid disease progression. Based on this case and a critical need to improve outcomes for patients experiencing LS, we have developed a registry study to capture cases of LS following immunotherapy. With the primary objectives to: 1) understand how LS is diagnosed and 2) delineate the various treatment approaches in treating LS, we established: "Project EVOLVE: Evaluation of Lineage Switch: An International Initiative". https://ccr.cancer.gov/pediatric-oncology-branch/carnation-consortium/project-evolve

Conclusion: With the rapidly evolving utilization of immunotherapy, alongside the increasing incidence of LS, Project EVOLVE serves as a collaborative global approach to profiling these cases and fills an unmet need to optimize outcomes. Collecting this data will support future physicians and patients facing LS diagnoses and unify the field in systematically identifying and treating such a devastating outcome following immunotherapy.

6) THEME: CELLULAR THERAPIES | IDENTIFICATION OF IL-1RA AS A POSSIBLE MARKER OF OPTIMAL NATURAL KILLER CELL FUNCTION IN KILLING PEDIATRIC CANCERS

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Background: NK cell therapies are rapidly evolving as cancer immunotherapies given their innate ability to target pediatric cancers with low mutational burden, lack of restriction across HLA barriers, low incidence of adverse reactions, and ability to combat viruses. There is wide variability in function and number across individuals related to variable inheritance of KIR and HLA, and donor exposure histories. Identifying an optimal universal donor of NK cells to be expanded, cryopreserved, and used as adjunctive off-the-shelf therapy for patients with high-risk pediatric cancers may improve efficacy, increase availability by eliminating manufacture delays, and decrease cost. Prior studies have defined optimal donor NK cell characteristics in the transplant setting, leading to suggested markers of improved NK cell functionality, but it is unclear whether these predict function of adoptively transferred NK cells.

Objective: Our goal was to define a potential universal donor by determining which characteristics of NK cell donors correlate with highest cytotoxicity against pediatric cancer cell lines.

Design/Method: Mononuclear cells from 26 donors were obtained from the local blood bank or through Be The Match BioTherapies®. Allogeneic NK cells were expanded from these donors using feeder cells expressing 4-1BBL and IL21. KIR genes were determined for each donor by PCR, and HLA typing was performed by Creative Biolabs®, both of which were used to determine licensing status of each donor. The expanded NK cells were tested for lytic potential against 21 pediatric cancer cell lines of acute myelogenous leukemia (AML), Ewing Sarcoma/ Primitive Neuroectodermal Tumor (EWS/PNET), Osteosarcoma (OS), Alveolar Rhabdomyosarcoma (ARMS), High Grade Gliomas (HGG), and Neuroblastoma (NB). Mass cytometry defined expression

of NK cell-specific receptors, and NK cells were activated with PHA to determine cytokine release ability. We then calculated Spearman correlation coefficients for each of these NK cell characteristics with average specific lysis among each tumor cell group. Results: Secretion of interleukin-1ra (IL-1ra) showed the strongest positive correlation with average specific lysis across donors, with a linear correlation most strongly demonstrated among the EWS/PNET group and a positive correlation seen in all tumor cell lines. The other characteristics were variably correlated with lytic ability.

Conclusion: These findings suggest that ability to secrete IL-1ra may be a marker of NK cell cytotoxic ability. Further experiments in our lab are underway to evaluate whether IL-1ra secretion is directly involved in, or is an indirect biomarker of, NK cell function.

7) THEME: CELLULAR THERAPIES | ISOLATED NON-OCULAR EXTRAMEDULLARY RELAPSE AFTER TREATMENT WITH ANTICD19 CAR-T CELL THERAPY IN A PATIENT WITH HIGH-RISK B-ALL

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Background: The utilization of CD19-targeted chimeric antigen receptor T-cell (CAR-T) therapy has emerged as an efficacious treatment option for patients with relapsed/refractory B-cell acute lymphoblastic leukemia (ALL). Despite its promising results, a subset of patients may experience relapse, which is typically localized to the bone marrow. Objective: This case report aims to describe an infrequent pattern of relapse in B-ALL following CAR Tcell therapy.

Design/Method: Case report. Results: The patient presented at 18 years old with diagnosis of B-cell acute lymphoblastic leukemia, CNS1, and was hyperdiploid with gains of chromosomes 6, 8, 21 and 22. Next generation sequencing (NGS) showed mutations in KDM6A and NRAS. The evaluation of minimal residual disease (MRD) at the end of induction bone marrow (BM) by flow cytometry revealed 2.4% blasts. Following augmented Berlin-Frankfurt-Münster (BFM) consolidation, his MRD was 0.15%. He was salvaged with blinatumomab for 4 weeks, resulting in negative MRD. Following a second cycle of blinatumomab, the patient underwent allogeneic hematopoietic cell transplantation (HCT) from a matched sibling donor with myeloablative conditioning using cyclophosphamide and total body irradiation. Less than 90 days postHCT patient had BM relapse. The relapse was treated with 3-drug re-induction, Capizzi-style methotrexate escalation and inotuzumab, and subsequently anti-CD19 CAR-T therapy following lymphodepletion with fludarabine and cyclophosphamide. Post CAR T-cell therapy patient had low level NGS MRD (~6/million) from day +60 despite persistent B cell aplasia. At 7 months post CAR-T patient had multifocal, extramedullary, non-CNS B-ALL relapse with the largest lesion in the right lower abdomen (~ 8 cm) with negative MRD by flow in BM. The patient received focal radiotherapy, and reinduction using UK ALLR3 regimen leading to a partial response. Currently, he continues to have PETavid disease after additional blinatumomab despite undetectable bone marrow disease.

Conclusion: The mechanism of action of anti-CD19 cell therapies may contribute to the emergence of a distinct pattern of extramedullary recurrence in comparison to traditional chemotherapy. Reports have indicated a relatively high frequency of extramedullary relapse following treatment with blinatumomab. While there have been case reports describing isolated intraocular relapse after CAR-T- therapy, other extramedullary relapse localizations have not been reported. This case study presents an isolated extramedullary non-ocular relapse following CAR T-cell therapy and serves as a reminder for clinicians to remain vigilant for the potential occurrence of extramedullary relapse in patients who have undergone CAR-T therapy, even in the absence of BM involvement.

1) THEME: DISEASE-SPECIFIC, TRANSPLANT-RELATED | TCR AB+/CD19+–DEPLETED HEMATOPOIETIC CELL TRANSPLANT IN FANCONI ANEMIA: A PEDIATRIC CASE SERIES

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Background: Allogeneic hematopoietic cell transplantation (allo-HCT) is the only curative or preventive therapy for the hematologic aberrations (cytopenia, leukemia, or myelodysplastic syndrome (MDS)) of Fanconi anemia (FA). However, allo-HCT is especially challenging due to relatively higher risk of alkylating agents and radiation as well as graft-versus-host disease (GVHD) induced organ injury secondary to intrinsic DNA repair defect. Post-transplant immunosuppression (IS) with calcineurin inhibitor causes additional toxicities and increases risk of infections. Traditionally, HCT with an HLA-matched sibling donor (MSD) has shown best outcomes but many patients lack MSD. Recently, T-cell receptor (TCR) $\alpha\beta$+/CD19+ cell depleted HCT, with no need for posttransplant IS, has shown promising results in FA patients even after alternative donor HCT but current experience is limited to one large international study and small case series.

Objective: Describe outcomes after partially and fully matched related donor $\alpha\beta$+/CD19+ cell depleted HCT in pediatric patients with FA.

Design/Method: Retrospective case series.

Results: Three patients with FA with a median age of 8 years (range, 5-17) underwent matched (one) and partially HLA matched (two) $\alpha\beta$+/CD19+ depleted HCT for marrow failure at Children's National Hospital, Washington, DC. One patient had progressed to MDS with a

5q deletion at the time of transplant. Two patients had FANC-G mutations and one had FANC-E mutation. All patients received conditioning with fludarabine, rabbit anti-thymocyte globulin, methylprednisolone, and cyclophosphamide. Rituximab was given on day −1 for post-transplant lymphoproliferative disorder prophylaxis. Two patients with partially matched related donors also received total body irradiation of 3 Gray. No grade ³3 toxicities were observed. All patients successfully engrafted with a median time for neutrophil and platelet recovery of 9 days (range, 8-9) and 10 days (range, 9-10), respectively. All patients achieved full donor myeloid chimerism and no patient developed graft failure or clinically significant infectious complications at a median follow up of 340 days (range, 102-457). One patient required initiation of IS with sirolimus on Day +98 for recurrent Grade 1 Stage 2 acute GVHD of the skin; the other two patients developed Grade 1 Stage 1 skin acute GVHD, which resolved with topical steroids and did not require IS. Overall survival and disease-free survival were 100% and no patient developed any post-HCT malignancy at the median follow up. Conclusion In conclusion, TCR $\alpha\beta$+/CD19+ cell depletion is a safe and effective method for HCT with outcomes comparable or better than those for non-T cell depleted MSD HCT in patients with FA.

2) THEME: DISEASE-SPECIFIC, TRANSPLANT-RELATED | EXCELLENT PROGRESS IN OVERALL TRANSPLANT OUTCOMES FOR PATIENTS WITH FANCONI ANEMIA INCLUDING ADULT FA PATIENTS AND THOSE WITH MYELODYSPLASTIC SYNDROME USING RISK ADJUSTED CYTOREDUCTION WITHOUT RADIATION

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Objectives: Our goal was to minimize risks for younger patients with marrow failure, while improving outcomes in patients with MDS and adult patients with FA. We report results of 50 patients from our prospective multi-institutional study.

Methods: Patients with FA undergoing allogeneic HCT received a preparative regimen containing: BU x 4 doses on (D-7 to −6) (dosing per Fig 1), followed by cyclophosphamide 10 mg/Kg/day, fludarabine 35 mg/m2/day and rabbit ATG 2.5 mg/Kg/day x 4 days (D-5 to D-2). Compared to our previous experience, BU dose was decreased for all adult patients and increased for children with MDS/AML. Children with MDS/AML received PK adjusted dose to keep the steady state concentration of BU to <350 ng/ml. Donor PBSCs were T-cell-depleted by CD34+ selection. T-cell depletion was the sole GVHD prophylaxis (without calcineurin inhiibitor).

Results: Patient and donor characteristics are described in Table 1. All patients engrafted. Median time to neutrophil and platelet engraftment was 9 (range: 7-11) and 16 days (range: 11- 60) respectively. Two patients experienced secondary graft failure on day +19 and 58 respectively; and underwent 2nd transplant. Toxicities observed included mucositis (23), SOS (2), Hyperbilirubinemia (2) pulmonary hemorrhage (2), and infections (bacterial 17, viral reactivations 48, fungal 0). One patient developed acute GVHD (had also received viral specific T cells) and two developed limited chronic GVHD (all resolved with treatment).

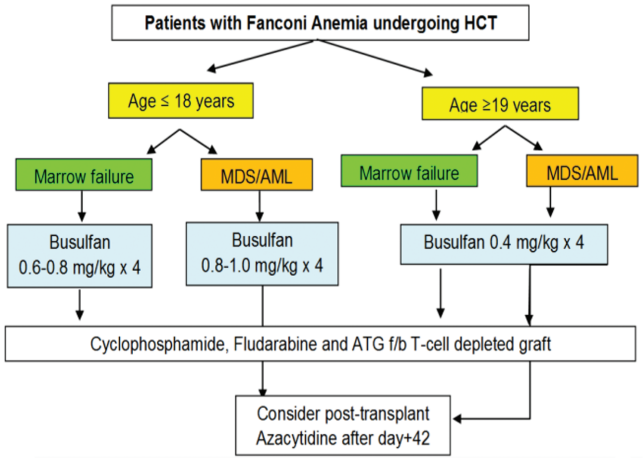

FIGURE 1 BU dose stratification based on age and disease status

Two patients with secondary graft failure underwent second HCT (one is alive). 45 of 48 patients are alive and disease-free at a median follow up of 56.2 months (0.7- 101 mo.) with an overall survival of 93%. All patients (N = 7, 100%) transplanted for MDS are alive and well. Five of six (83%) adult patients are alive and well, one with AML died of EBV PTLD on day +202 (AML was in remission). Two patients (<10 yrs) died from sepsis associated with pulmonary hemorrhage (day +33) and septic shock with multi-organ failure (days +92).

Current approach has improved overall survival for the entire group (93%; previously 80%), for patients with MDS (100%; previously 58%) and adult patients with FA (83%; previously 20%) (Blood 2017).

Conclusions: These results demonstrate excellent progress in outcomes utilizing our 'Risk adjusted' BU dosing-based chemotherapy-only conditioning for patients with FA undergoing allogeneic HCT. Compared to our previous results current approach has improved overall survival for the entire group but more importantly also for patients with MDS and adult patients with FA.

3) THEME: DISEASE-SPECIFIC, TRANSPLANT-RELATED | PATIENT REPORTED OUTCOMES OF NONMYELOABLATIVE HEMATOPOIETIC STEM CELL TRANSPLANTATION IN YOUTH3WITH SICKLE CELL

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TABLE 1 Patient and donor characteristics

Characteristics	Number (%)/Median (range)
Total number of patients	50
Males	30
Females	20
Median age in years	8 (2-29)
Transplant Indication	
Marrow failure	41
- single cell	12
- cytopenia	29
- pancytopenia	7
MDS	2
AML	
Donors	
URD	50
HLA matching	
10/10 match	29
9/10 match	14
8/10 match	6
7/10 match	1

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 long-term psychosocial health issues such as, quality of life (QOL), anxiety, depression, and sleep.

Objective: This exploratory study evaluated psychosocial health outcomes (e.g., QOL, anxiety, depression, and sleep) in youth who underwent HSCT for SCD.

Design/Methods: A cross-sectional study of youth who have undergone nonmyeloablative HSCT at the Alberta Children's Hospital in Calgary, Alberta, Canada for SCD was conducted using online surveys. Caregivers or parents also had the option to participate. Eligibility criteria included: a minimum of one-year post-HSCT for SCD; age between 8-25 years; able to read and speak English; and absence of any acute medical injury at the time of survey completion, or a diagnosed developmental disability. QOL was assessed using the Pediatric Quality of Life (PedsQL) Generic Core scale, self- and parent-proxy reports. The Patient Reported Outcomes Measurement Information System (PROMIS) assessed symptoms of anxiety, depression, and sleep difficulties.

Results: Survivors of HSCT (n = 10, 6 female, 17.93 years old) and parents (n = 8) participated. Mean QOL scores were 84.96 (SD = 13.10) as reported by parent-proxy and 88.70 (SD = 11.60) by self-report. Parent-proxy reports of youth who had undergone HSCT for SCD reported similar QOL to previously published norms of parent-proxy reports of healthy youth (82.29)1 , t(7) = 0.56, p = .582, Cohen's d = 0.20, but significantly better QOL than parents of children currently living with SCD (71.27)2 , t(7) = 2.96, p = .021, Cohen's d = 1.05. Similarly, youth who had undergone HSCT reported similar QOL to published self-reports of healthy peers (83.91)1 , t(9) = 1.31, p = .224, Cohen's d = 0.41, and significantly better QOL than previously published self-report of youth diagnosed with SCD (72.28)2 , t(9) = 4.48, p = .002, Cohen's d = 1.42. Average PROMIS psychosocial scores were 41.81 for anxiety, 39.41 for depression, and 47.85 for sleep disturbances, which are all considered to be within the normal range. Data collection remains ongoing.

Conclusion: Preliminary results from the current study reveal optimistic outcomes suggesting psychosocial health (QOL, anxiety, depression, and sleep) improves following transplant, and is comparable to healthy populations following HSCT of youth diagnosed with SCD. This study is an important first step in understanding patient-reported outcomes and QOL in individuals who have undergone HSCT for SCD. Ongoing surveillance for physical and psychosocial late-effects and potential long-term benefits should be prioritized for this population.

1) THEME: SUPPORTIVE CARE | REDUCED SPHINGOSINE-1-PHOSPHATE LEADS TO HYPOXEMIA AND TRANSPLANT-ASSOCIATED THROMBOTIC MICROANGIOPATHY AFTER HEMATOPOIETIC STEM CELL TRANSPLANT

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Background: The vascular endothelium is a selectively permeable membrane which is injured during hematopoietic stem cell transplant (HSCT), leading to the acquisition of a proinflammatory phenotype. Endothelial damage after HSCT puts patients at risk for complications including lung injury and transplant-associated thrombotic microangiopathy (TA-TMA), especially in patients with high body mass index (BMI). Sphingosine −1-phosphate (S1P) signaling pathways are potent modulators of endothelial function and injury responses. S1P pathway modulators represent potential therapeutic targets in mitigating endothelial injury during HSCT.

Objective: To determine if S1P levels are different in pediatric and young adult allogeneic-HSCT recipients who developed endothelial injury after HSCT.

Methods: We performed a study including 106 consecutive pediatric and young adult allogeneic-HSCT patients. Plasma S1P levels at day +14 from stem cell infusion were measured using mass spectrometry. Differences in plasma concentrations (μM) were analyzed in patients who developed TA-TMA.

Results: Median day 14 S1P concentrations in patients with TA-TMA were significantly lower (0.38 μM, (0.17 to 0.83 μM) than in patients

without TA-TMA (0.43 μM, (0.22 to 0.94 μM), p = 0.005). A significant proportion of circulating plasma S1P is reported to originate from platelets and red blood cells. In agreement with this, we found a strong correlation between day 14 plasma S1P concentration and day 14 platelet count (R^2 = 0.27, p <0.0001). Plasma S1P levels showed a weaker, but significant correlation between plasma S1P levels and day 14 hemoglobin concentration (R^2 = 0.05, p = 0.01). We extended our hypothesis and further hypothesized that patients with high BMI enter transplant with endothelium primed for subsequent injury and those who have low S1P will incur worse endothelial injury, leading to clinical manifestations of TA-TMA such as renal injury. In support of this, glomerular filtration rate (GFR) measured using cystatin C, was positively associated with S1P level at day 14 (R^2 = 0.03, p = 0.04) and serum creatinine was negatively associated with S1P levels (R^2 = −0.06, p = 0.01). Median day 14 S1P concentration was lower in those needing oxygen compared with those who did not (0.39 μM (0.17 to 0.77 μM) versus 0.42μM (0.25-0.94 μM), p = 0.04).

Conclusions: Concentration of S1P on day +14 from HSCT were significantly lower in patients who were diagnosed with TA-TMA and developed hypoxemia within 21 days of allo-HSCT. Further experiments are required with assessment in S1PR levels in tissues to determine the significance of the S1P signaling pathway as potential therapeutic targets of endothelial injury during HSCT.

2) THEME: SUPPORTIVE CARE | PERSISTENCE OF COVID-19 INFECTION IN TWO PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANT: A SINGLE CENTER EXPERIENCE

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Background: Despite over two years of experience with COVID-19 infections in hematopoietic stem cell transplant (HSCT) patients, there is a paucity of literature describing the natural course in pediatric HSCT patients. Here we describe our experience with two pediatric HSCT patients diagnosed with COVID-19.

Cases: Patient 1 is a 23-month-old girl with infantile B-ALL (KMT2A rearrangement) initially diagnosed with COVID-19 after CAR-T therapy and prior to her transplant admission, which was delayed ~2 months due to COVID-19. Signs of B cell recovery pre-transplant indicating possible impending disease relapse prompted moving forward with HSCT in the setting of a negative COVID-19 PCR. On day four of fludarabine she developed respiratory distress and was diagnosed with aspiration pneumonia secondary to previously unidentified silent aspiration. A gastrostomy tube was placed and conditioning was held until pneumonia resolved. She remained in the hospital for five weeks until her transplant course was reinitiated. During this period, the risk of re-acquisition of a new COVID-19 infection was low due to several factors including a smaller program size with fewer patients, strict PPE requirements, and visitor limitations. On Day +2 of her matched sibling HSCT she again began having respiratory distress and was found to be SARS-CoV-2 PCR positive after multiple negative PCRs. Her course was also complicated by *Stenotrophomonas maltophilia* bacteremia and she ultimately died from severe respiratory failure presumed to be secondary to bacteremia and COVID-19 induced acute respiratory distress syndrome.

Patient 2 is an 11-year-old girl with severe aplastic anemia who underwent haploidentical HSCT. She was admitted with dehydration secondary to COVID-19, diagnosed on Day +48, after exposure to infected family members. She initially received three days of remdesivir, but ultimately remained SARS-CoV-2 positive for over 12 months. In addition to significant adenoviremia, COVID-19 likely contributed to transplant-associated thrombotic microangiopathy (TA-TMA), prolonged bone marrow suppression and has led to recurrent episodes of graft versus host disease (GVHD).

Discussion: There are few reports of resurgent COVID-19 infection post-HSCT in the literature, none of which have been reported in pediatric patients. We highlight two patient cases with probable prolonged viral persistence in the setting of HSCT-mediated immunosuppression. Although cases of prolonged COVID-19 positivity lasting a few months have been reported, we highlight one with a prolonged period of PCR negativity prior to transplant and one with a significantly prolonged course of COVID-19 infection, likely contributing to complications including TA-TMA, chronic GVHD, and prolonged bone marrow suppression.

3) THEME: SUPPORTIVE CARE | A SECOND LOOK: RETROSPECTIVE IDENTIFICATION OF THROMBOTIC MICROANGIOPATHY IN PEDIATRIC STEM CELL TRANSPLANT PATIENTS WITH VENO-OCCLUSIVE DISEASE

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Background: Stem Cell Transplant (SCT) offers potential curative therapy for many diseases, complications including veno-occlusive disease (VOD) and thrombotic microangiopathy (TMA) remain a diagnostic and therapeutic challenge. There is possible association between these two diseases, as both share underlying etiology involving microvascular endothelial damage. Underrecognition of TMA in the context of VOD leaves SCT recipients vulnerable to additional endothelial damage, leading to increased risk of end-organ failure and even death.

Objective: We retrospectively analyzed a cohort of patients with clinically diagnosed VOD to determine incidence, presence of comorbidities, and overall survival of those with presumed undiagnosed

TMA. Design/Method: A cohort of 44 pediatric SCT recipients from 2010 – 2019, were retrospectively evaluated for the development of TMA within 1 week before and 2 months after VOD diagnosis. Patients who died within 1 week of VOD diagnosis were excluded (n = 2). Patients were classified into three categories: sole diagnosis of VOD, clinical diagnosis of TMA during the VOD course (VOD+TMA), and patients with VOD who on retrospective review satisfied criteria for diagnosis of TMA (VOD+rTMA), defined as ≥ 4 TMA diagnostic criteria: thrombocytopenia, anemia, elevated LDH, low haptoglobin, elevated SC5b9, schistocytes, proteinuria. Overall Survival was compared using Kaplan-Meier methods and the log-rank test.

Results: Out of 42 patients diagnosed with VOD, 21 patients had a sole diagnosis of VOD, 5 (12%) patients were diagnosed with TMA (VOD+TMA) and treated with eculizumab during their VOD course, and 16 (38%) were retrospectively diagnosed with TMA. 18/21 (86%) of the sole diagnosis of VOD patients received defibrotide and 13/16 (81%) received defibrotide in the VOD+rTMA group. One-year survival was 66.7% for VOD only patients, compared with 60% of VOD+TMA, versus 62.5% of VOD+rTMA patients (p = 0.9582). Further, mean length of stay in the intensive care unit (ICU) was 20.7 days for VOD only patients, 31.6 days for VOD+TMA, and 17.6 days for VOD+rTMA (p = 0.3114).

Conclusion: The majority of our retrospective analysis is from a time when TMA screening was not routine. In our patient cohort, 50% of patients had TMA diagnosed clinically or retrospectively, demonstrating a possible correlation between VOD and TMA. VOD treatment with defibrotide may have offered therapeutic benefit for TMA due to the shared endothelial pathology. Screening for TMA is critical, as 38% of this cohort had a missed diagnosis of TMA. Better understanding of the association between these two endotheliopathies is essential to improve treatment and outcomes in transplant recipients.

4) THEME: SUPPORTIVE CARE | STEROID-ASSOCIATED ADVERSE EVENTS ARE DOSE-DEPENDENT FOLLOWING HEMATOPOIETIC CELL TRANSPLANTATION

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Background: Hematopoietic cell transplantation (HCT) is a successful treatment of relapsed acute lymphoblastic leukemia (ALL) but can be associated with high systemic steroid exposure due to primary treatment of ALL and graft-versus-host disease (GVHD). Steroid use is associated with many late complications including poor bone heath and cataracts. We hypothesized that systemic steroid exposure would increase late bone and eye toxicities in a dose-dependent manner after pediatric HCT for ALL.

Objectives: To enumerate avascular necrosis (AVN), fractures and cataracts following pediatric HCT for ALL and examine the association of post-HCT steroid exposure with the incidence of these toxicities.

Design/Method: In this IRB approved retrospective study, consecutive pediatric recipients of first HCT for ALL at a single institution between 2011 to 2017 and survived at least 100 days post-HCT were captured. Exclusions from subset analysis included: pre-existing AVN, fractures, and cataracts. Patients were censored at time of relapse, graft failure, and death.

Results: Forty-seven patients were identified with a median age of 12 years old (range 3.2 – 21) at HCT. Thirty-five (74%) patients were exposed to post-HCT systemic steroids, 29 (83%) had acute and 23 (66%) had chronic GVHD. Median follow up post-HCT was 1.7 years (IQR 0.8 – 5.3) in those without and 5.1 (IQR 3.2 – 8.5) with post-HCT systemic steroid exposure. Median systemic steroid exposure was 46 mg/kg prednisone equivalents (PE) (IQR 2.2 – 178). Nine (24%) patients experienced bone events, including AVN (n = 3), axial (n = 1) and appendicular (n = 5) fractures. The median time to event was 1.3 years (range 0.4 – 5.3) post-HCT. In those that received ≥100 mg/kg PE versus less, the cumulative incidence of bone events was 8 (53%) versus 1 (4%) (p = 0.002). Thirteen (30%) patients developed cataracts a median of 5.1 years (range 1.7 – 6.8) post-HCT. Cumulative incidence of cataracts was 8 (57%) if exposed to ≥100 mg/kg PE versus 5 (17%) if <100 mg/kg PE (p = 0.025). Adjusting for age at transplant and complete remission status, cumulative steroid exposure remained significantly associated with bone events and cataracts.

Conclusion: Our data suggest that adverse bone events and cataracts are common in pediatric patients with ALL following HCT and are increased in patients who received higher cumulative steroid dose following HCT. These data reinforce that patients should be closely followed for late complications of steroid exposure and highlights the need for steroid-sparing approaches to GVHD treatment to avert these long-term HCT toxicities.

5) THEME: SUPPORTIVE CARE | LIPOSOMAL AMPHOTERICIN B FOLLOWED BY MICAFUNGIN PROPHYLAXIS OF INVASIVE FUNGAL INFECTIONS IN CHILDREN ADOLESCENT AND YOUNG ADULTS ALLOGENEIC STEM CELL TRANSPLANTATION RECIPIENTS WITH HEMATOLOGICAL MALIGNANCIES

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Key words: invasive fungal infections, prophylaxis, Liposomal amphotericin B, Micafungin, Allogeneic stem cell transplant, Hematological malignancies.

Conflict of interest: The authors declare no conflict of interest.

Background: Children adolescent and young adults (CAYA), who are recipients of an allogeneic stem cell transplant (AlloSCT) due to a hematologic malignancy (HM), are among the highest risk for invasive fungal infection (IFI). Historically, the incidence of IFI in this population has ranged from 5%−35%. With the emergence of Molds as the most common causes of IFIs after AlloSCT, an optimal approach to the prevention of IFI with a mold active agent is yet to be determined. Micafungin has comparable efficacy to Liposomal Amphotericin B (L-AmB) against invasive candidiasis and a diminished side effect profile compared to L-AmB.

Objective: To determine the feasibility, tolerability and efficacy of prophylactic L-AmB followed by micafungin in preventing Invasive mold infection (IMI)/IFI in the first 100 days post-AlloSCT in CAYA with HM.

Methods: Between August 2011 and April 2021, we evaluated 60 CAYA AlloSCT recipients due to HM who received L-AmB (1.5 mg/kg/day) (day 0-44) followed by micafungin (1.5 mg/kg/day, age adjusted dose, max 50 mg) (day +45-100) prophylaxis. The primary endpoint was the incidence of probable and proven IFI as defined by the European organization for research and treatment in cancer mycosis study group. Secondary endpoints included overall survival at day +365 post-transplant.

Results: Median age was 14.2 years (0.7-24), 68% had haploidentical or unrelated donor, 70% received myeloablative conditioning. Eight patients (13.3%) had a grade III/IV acute kidney injury (AKI) probably related to L-AmB. The incidence of IFI during the first 100 days post AlloSCT was 15.3% (n = 9), with 8 patients having a proven infection. Only 2 patients had a mold infection with Aspergillus and day 100 probability of 4.0% (CI_{95}: 1.0-15.0). IFI was a risk factor for mortality with a 1-year overall survival of 45.4% in IFI group (CI_{95}: 16.7-70.7) compared to 77.5% in patients without IFI (CI_{95}: 63.1-86.9) ($p < 0.05$). The probability of grade III/IV acute GVHD was 23.3% (CI_{95}: 8.5-42.3). CMV infection had a relative risk of 4.81 for IFI (CI_{95}: 1.68 to 13.67) ($p < 0.01$).

Conclusions: L-AmB followed by micafungin appears to be feasible, safe and effective in preventing IFI/IMI in the first 100 days post AlloSCT in historical CAYA recipients with HM. While aspergillosis infection post AlloSCT has become the leading cause of IFI related death, in our cohort, only 4.0% had an IMI. A large randomized multicenter clinical trial will need to be conducted to further investigate the benefit of such approach.

6) THEME: SUPPORTIVE CARE | HHV-6A ENCEPHALITIS WITH CHROMOSOMAL INTEGRATION IN PEDIATRIC LEUKEMIA POST CHIMERIC ANTIGEN RECEPTOR T-CELL (CAR-T) THERAPY

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Background: HHV-6 reactivation and progression to encephalitis is a concern for the immunocompromised and can be difficult to distinguish from CAR-T associated neurotoxicity. Furthermore, diagnosis of HHV-6 encephalitis may be complicated by chromosomal integration of HHV-6. Objective: We present the first pediatric patient with chromosomally integrated HHV-6A who developed HHV-6 encephalitis in the setting of Grade 4 ICANS post CD19/22 dual CAR T-cell therapy.

Design/Method: Single subject case report

Results: We present a 9-yearold Hispanic male with trisomy 21 with relapsed B-cell acute lymphoblastic leukemia (ALL) with no central nervous system involvement. He received bispecific CD19/22 CAR T-Cell therapy and subsequently developed cytokine release syndrome (CRS) on day 5 post CAR T-Cell infusion and immune effector cell-associated neurotoxicity syndrome (ICANS) on day 6. By day 7 post infusion he had multiple seizures, was aphasic, intubated and not responding to stimulus. CT scan revealed findings concerning for non-occlusive sinus venous thrombosis (SVT) in the left lateral transverse sinus which was confirmed with a CT venogram. Lumbar puncture was performed and revealed 1,100 copies/mL of HHV-6 and serum was positive at 2500 copies/mL. MRI findings revealed multiple areas of cortical diffusion restriction along bilateral hippocampi and limbic encephalitis consistent with HHV-6 encephalitis. He was subsequently started on foscarnet. Despite this therapy, serum HHV-6 viral copies continued to rise (35,000 copies/mL) and ganciclovir was added one week later. His ICANS was treated with dexamethasone, high dose methylprednisolone, anakinra and dasatinib, and his CRS was treated with tocilizumab. His neurologic status slowly improved over the course of 3 weeks. Due to his prolonged ICANS course and persistent HHV-6 viremia, a chromosomal integration test was sent and returned positive for the integration of HHV-6 type A virus to cell ratio 1.09. He received foscarnet treatment dosing for 4 weeks and maintenance dosing for 7 weeks, as well as ganciclovir for 2 weeks. He has made a full neurologic recovery.

Conclusion: This is the first reported case of HHV-6 encephalitis in the setting of HHV-6 chromosomal integration, severe ICANS, and SVT. This case demonstrates the importance of identifying and diagnosing HHV-6 encephalitis, especially in the presence of other concurrent neurologic conditions since they require different therapeutic approaches. It is imperative for providers to have a low threshold to consider diagnostic evaluation for HHV-6 encephalitis in children with neurological symptoms receiving high dose immunosuppressive therapy after CAR-T therapy.

7) THEME: SUPPORTIVE CARE | DARATUMUMAB FOR THE TREATMENT OF REFRACTORY AUTOIMMUNE HEMOLYTIC ANEMIA IN PEDIATRIC PATIENTS POST-HEMATOPOIETIC CELL TRANSPLANT

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Background: Allogenic hematopoietic cell transplant (HCT) can be complicated by immune-related cytopenias after engraftment. Autoimmune hemolytic anemia (AIHA) can occur post-HSCT and can be refractory to standard therapies leading to protracted hospitalizations. There are scant data for the efficacy and tolerability of newer plasma cell-directed therapies to treat AIHA after pediatric HCT. Daratumumab is a monoclonal antibody targeting CD38 expressed on plasma cells with data in other populations supporting its use in refractory AIHA.

Objective: We hypothesized that daratumumab therapy safely treated AIHA after pediatric HCT.

Methods: On an IRB-approved protocol, a retrospective chart review captured all allogeneic HCT recipients who received daratumumab for refractory AIHA at a single institution between 2015-2022.

Results: We identified six patients, 83% male, aged 2-20 years (median 11 years), 50% Caucasian, 33% Hispanic, and 17% African American, with transplant indications of hematologic malignancies (50%) and primary immunodeficiencies (50%). Donors were matched unrelated (n = 2), matched related (n = 1), 4/6 cord blood (n = 1), 7/8 match unrelated donor (n = 1), haplo (n = 1). AIHA was diagnosed at a median 223 days post-transplant (range 37-441), at which time, all patients had 100% CD33 donor chimerism, and 83.3% had>50% donor CD3 chimerism; one patient had 29% donor CD3 and rising. At the time of AIHA diagnosis, 4/6 had a history of GVHD, with one active acute GVHD and one recent late acute flare. 4/6 were tapering immunosuppressant (IS) or discontinued IS within 2 months of AIHA presentation. 50% had active detectable viral infection at diagnosis (CMV reactivation, BK viuria, rhinovirus/enterovirus). The median number of treatments given before daratumumab was 4 (range 2-4) including steroids (6/6), rituximab (5/6), sirolimus (3/6), IVIG (5/6). After diagnosis of refractory AIHA, daratumumab was given at 16 mg/kg/dose with median of 4.5 doses (range 4-8). 83.3% of the patients achieved transfusion independence, all alive, with a median of 48 days (range 0-110) from the first dose of daratumumab to the last blood transfusion. There has been no recurrence of AIHA in the 375 median days (range 145-1237) of follow up to date. One patient remained transfusion dependent and died of unrelated causes (mycobacterial pneumonia).

Conclusion: AIHA post allogeneic HCT is often refractory to standard therapies. In our small cohort, daratumumab appeared to be safe and effective in refractory AIHA. Post-HSCT AIHA was temporally related to viral infections and immunosuppressant taper. Our data supports the need for additional studies of daratumumab in pediatric refractory AIHA after HCT.

8) THEME: SUPPORTIVE CARE | ANTI-CD38 MOAB DARATUMUMAB IS EFFECTIVE IN THE TREATMENT OF POST-TRANSPLANT PURE RED CELL APLASIA AND REFRACTORY AUTOIMMUNE HEMOLYTIC ANEMIA IN AN INFANT WITH HURLER SYNDROME

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Background: Pure red call aplasia (PRCA) is a rare but serious complication following hematopoietic cell transplant (HCT) and is without any standard treatment options. Autoimmune hemolytic anemia (AIHA), a more common complication following HCT, has been treated with corticosteroids, Rituximab and IVIG, but a number of patients either do not respond or become refractory to these therapies. Both AIHA and PRCA are considered to be mediated by donor/host derived antibodies and B cell dysregulation.

Objective: To determine the effectiveness of Daratumumab in the treatment of post-transplant pure red cell aplasia and refractory autoimmune hemolytic anemia in an infant with Hurler syndrome

Design/Method: Subject with Hurler syndrome who had received a myeloablative (Bu/Cy/ATG) unrelated cord blood transplant at 3.5 months of age presented at day + 180 with a 2 g hemoglobin drop, reticulocytosis (6.25%, 232.3), 4+ Coombs and undetectable haptoglobin. Diagnosed with autoimmune hemolytic anemia (AIHA), she was treated with methylprednisolone 2 mg/kg/day, IVIG 1gm/kg x 2 and weekly Rituximab x 4. Peak reticulocyte count was 16.3%. Following the 3rd dose of Rituxan, she presented with 1 g HgB drop and steadily decreasing reticulocyte count reaching a nadir of <0.5% for 5 weeks requiring three PRBC transfusions. Bone marrow studies revealed 80% cellularity with total absence of erythroid precursors consistent with pure red cell aplasia (PRCA). There were no discrete B cells or phenotypically abnormal cells. Due to lack of B cells, potential of immune mediated PRCA, and institutional experience with successful use in 5 other children with AIHA, Daratumumab (16 mg/kg/dose weekly x 8) with standard premedication was added to her steroid therapy.

Results: Daratumumab led to resolution of PRCA with reticulocyte steadily rising from 0.78 % to 7.8 % after the 5th dose. Hemoglobin stabilized and reticulocyte slowly returned to normal for 4 months with weaning of Daratumumab and steroids. She had a recent flare up of AIHA and equired 4 PRBC transfusions but has had no further evidence of PRCA. The patient tolerated all Daratumumab infusions without any reactions or toxicity.

Conclusion: Daratumumab is well tolerated in pediatric patients and can be used safely to treat PRCA as well as AIHA in post-HCT patients.

9) THEME: SUPPORTIVE CARE | GRANULOCYTES ARE HELPFUL IN TREATING INFECTIONS IN CHILDREN UNDERGOING HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Background: Neutropenia, often encountered in patients undergoing hematopoietic stem cell transplantation (HSCT), increases the risk of bacterial and/or fungal infections. Granulocyte transfusions (GT) are indicated for patients with severe infections with neutropenia along with antimicrobial therapy. There is paucity of pediatric studies regarding GT, leading to reluctance in using GT even when severe documented infections are present.

Objectives: To study indications, dosage, safety, and tolerability of GT in HSCT patients.

Design/Method: Retrospective chart review of all patients who received at least a single GT at our institution until January 2022.

Results: Thirteen patients who underwent 15 transplants (hematological malignancies = 11, immune dysregulation = 1, severe aplastic anemia = 1) were included in the study. All patients had prolonged neutropenia and received a median of 5 (range 1-69) GT for fungal (n = 5), bacterial (n = 10), or fungal and bacterial infection (n = 1). The doses of GT ranged from 145-470 mL per infusion, once a day. The number of GT per patient varied from 1 (n = 3), 5 (n = 5), 8 (n = 1), 11 (n = 1), 13 (n = 2) and 69 (n = 1). One patient received 69 GT over 4 separate infections (3 bacterial and 1 fungal) and got 8, 22, 11, and 28 GT from the first through fourth infection. Nine patients received premedication with acetaminophen, diphenhydramine, and/or hydrocortisone. No patient had any adverse transfusion reactions or hemodynamic instability during or after the GT.

Complete resolution of infection was seen in 5/5 (100%) cases with localized infection (bacterial or fungal), 5/6 (83%) cases with bacteremia and no response was seen in 4 cases with fungemia and 1 case with fungemia and bacteremia. Overall, the primary indication for GT, resolved in 10/16 (62.5%) cases with no response in the remaining 6 cases.

Three/13 patients were alive and the cause of death of the remaining 10 patients was relapse (n = 1), primary or secondary graft failure (n = 2), veno-occlusive disease (n = 1), steroid refractory acute graft versus host disease (GvHD) (n = 1), and disseminated fungal disease (n = 5). Of 3 patients still living, all are in remission with 2 having chronic GvHD.

Conclusion: GT were well tolerated and able to be given on the transplant floors. Patients given GT for localized infections or bacteremia in the setting of neutropenia had better outcomes compared to those with disseminated fungal diseases. GT can be a promising therapeutic modality (along with antimicrobials) in patients with localized or systemic infections, during the neutropenic period in children undergoing HSCT.

10) THEME: SUPPORTIVE CARE | DNASES MODIFY EARLY ENDOTHELIAL DAMAGE IN PEDIATRIC PATIENTS UNDERGOING ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANT

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Background: Lysis of the hematopoietic system during conditioning leads to rapid and large-scale release of toxic intracellular molecules into the circulation, including cell free DNA and proteins like actin. Neutrophil extracellular traps (NETs) are released at time of neutrophil engraftment releasing more cell free DNA. Free DNA is toxic, and is associated with tissue injury. Cell free DNA and NETs are cleared from the circulation by DNaseI and DNase1L3.

Objective: To analyze longitudinal changes in DNaseI and DNase1L3 levels and their effect on outcomes of HSCT.

Methods: We measured circulating DNaseI (MBS2515385), DNase1L3 (MBS925159), and double stranded DNA (dsDNA) (Quant-iT PicoGreen) levels in 108 consecutive patients receiving allogeneic HSCT. Plasma samples were collected prior to transplant and on days 0, 7, 14, 30, and 100. We reviewed supplemental oxygen use during the peri-engraftment period as a marker of early pulmonary injury.

Results: DNaseI levels decreased significantly at day 7 (155.9 ng/ml), recovered to a level above baseline at day 14, and continued to increase further at day 100 (301.9 ng/ml vs 438.5 ng/ml; $p = <0.0001$). Day 7 DNaseI level was positively correlated with dsDNA ($r = 0.29$, $p = 0.003$). DNase1L3 levels declined, reaching its lowest level at day 7 (19.6 ng/ml), returning to baseline levels by day 30, and continuing to rise to a level significantly higher than baseline at day 100 (31.9 ng/ml vs 42.7 ng/ml; $p = 0.001$). DNase1L3 levels were positively correlated with dsDNA at day 7 ($r = 0.21$, $p = 0.04$) and day 14 ($r = 0.27$, $p = 0.006$). Patients with a peri-engraftment oxygen requirement had higher median levels of DNaseI at baseline (389 ng/ml vs 270.3 ng/ml) and days 0 (325.9 ng/ml vs 251.5 ng/ml), 14 (588 ng/ml vs 316.8 ng/ml) and 30(559.9 ng/ml vs 360.8 ng/ml). DNaseI was also higher in patients with TMA at baseline (380 ng/ml vs 270.3 ng/ml), and days 0 (311.5 ng/ml vs 270.3 ng/ml), 7 (189 ng/ml vs 154.4 ng/ml), 14 (465.9 ng/ml vs 334.9 ng/ml), and 100 (586.3 ng/ml vs 423.3 ng/ml). DNase1L3 was not associated with any HSCT complications.

Conclusion: DNases are depleted early after HSCT. Yet, it is high levels of DNases that correlate with clinical endothelial injury. DNase I is known to bind free actin and is rendered inactive upon binding. We have previously reported high levels of free actin in the circulation early after HSCT (1). Extensive binding of actin and subsequent inactivation of DNase may be leading to an induction of expression in response to this reduced DNase activity. Further mechanistic studies are ongoing.
References: 1. Luebbering, Hematologica, 2021

11) THEME: SUPPORTIVE CARE | IMPACT OF TRANSPLANT ASSOCIATED THROMBOTIC MICROANGIOPATHY AND ACUTE GRAFT VERSUS HOST DISEASE ON SURVIVAL IN CHILDREN AFTER ALLOGENEIC HEMATOPOIETIC CELLULAR TRANSPLANTATION

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Background: Transplant associated thrombotic microangiopathy (TA-TMA) and acute graft versus host disease (aGVHD) are severe complications of allogeneic hematopoietic cellular therapy (HCT) which often occur together and share a common feature of endothelial damage. The objective of this study was to understand the incidence and outcomes of TA-TMA in children with aGVHD.
Methods: In this IRB approved prospective single institution study, consecutive allogeneic HCT recipients from 8/2019 to 8/2022 who developed aGVHD were included. All patients were screened for TA-TMA. Cumulative incidence (CI) curves and sub-distribution hazard ratios (HR) were generated with relapse as competing risk.
Results: 64 children developed aGVHD a median of 61.5 days post HCT (range 13-319); 41 (65%) had maximum grade I-II aGVHD and 25 (39%) had grade III-IV. Mean age was 10.4 years, 39 (61%) had underlying hematologic malignancy, 43 (67%) had an unrelated donor, and 19 (30%) had a $\leq$7/8 HLA match. 1-year CI of TA-TMA was 36.4 $\pm$ 0.06%, developing at median of 61.5 days post HCT (range 18- 712). Twenty out of 24 patients with TA-TMA (83%) had intermediate/high risk disease and 19 received eculizumab. Eleven (55%) had no response to eculizumab; neither GVHD severity nor timing of TA-TMA were associated with response.
Patients with aGVHD who also developed TA-TMA were more likely to have grade III-IV aGVHD (50% vs 20%, p = 0.02) and steroid refractory aGVHD (54% vs 12.5%, p = 0.0005) than those without TA-TMA. Their survival was significantly lower (1-year 68% vs 95%, p = 0.005) and non-relapse mortality significantly higher (1-year 4.2 % vs 31.2%, p = 0.0002). The HR of NRM in patients with TA-TMA and GVHD, adjusted for maximum aGVHD severity, was (HR 14.95, 05% CI 1.512-147.8, p = 0.02).
Of those with GVHD and TA-TMA, 16 (67%) developed TA-TMA after aGVHD (median 34 days, range 0-540). Eight (33%) developed TA-TMA before GVHD (median 37.5 days, range 4-436). Despite differences in onset dates, 92% of patients had concurrent active TA-TMA and aGVHD. Of the 53 treated with systemic steroids, day 28 response was significantly lower in the aGVHD & TA-TMA group vs GVHD alone (4/24 non-responders vs 0/29, p = 0.03). There were no significant differences in NRM in those who developed GVHD or TA-TMA first.
Discussion: Children who developed both TA-TMA and acute GVHD had significantly worse outcomes than those with aGVHD only, with lower-than-expected response to eculizumab. Additional studies to understand the intersection of these diseases and novel therapies are needed.

12) THEME: SUPPORTIVE CARE | OUTCOMES OF VENO-OCCLUSIVE DISEASE (VOD) IN INFANTS AND TODDLERS POST-HEMATOPOIETIC STEM CELL TRANSPLANT (HCT)

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Background: Dyskeratosis congenita (DKC)is a rare genetic bone marrow failure syndrome. Patients with DKC present with opportunistic infections as a result of leukopenia. The only curative therapy is allogeneic hematopoietic stem cell transplantation (HSCT). Cytomegalovirus (CMV) infection is a common cause of viral infection post-transplant. There is a wide spectrum of infection, from asymptomatic viremia to fatal organ infiltration. CMV can also cause viral suppression of the bone marrow, resulting in graft failure and increased risk for other bacterial or fungal infections. An agent recently approved for the treatment of refractory CMV post-transplant is maribavir. Maribavir is a benzimidazole riboside antiviral that works through competitive inhibition of protein kinase activity of human CMV enzyme pUL97. Approved dosing for patients 12 years of age and older is 400 mg twice daily. Maribavir comes in 200-mg tablets which may be crushed for administration. To date, there is no published data for use in patients less than 12 years of age.
Objective: To describe the use of maribavir for refractory CMV in a pediatric patient administered via feeding tube.
Design/Method: Case report
Results: The patient was a 3-year-old male with DKC and CMV viremia referred for HSCT. The patient was taken to his first HSCT with low level CMV viremia and had graft failure with an increase in his CMV quantitative PCR to 217,244 IU/mL and development of CMV pneumonitis and colitis. After treatment failure of ganciclovir, foscarnet, cidofovir, and letermovir as well as CMV-specific cytotoxic lymphocytes, the decision was made to try maribavir. Based on available tablet size, patient's weight of 13 kg, and guidance from the upcoming pediatric trial by the manufacturer[1], he was started on maribavir 200 mg BID, administered through his gastric feeding tube, given in combination with foscarnet. On this combination regimen, his CMV

quantitative PCR declined to 4902 IU/mL, though we were never able to achieve complete clearance of viremia. Patient subsequently received two more transplants that both resulted in graft failure and ultimately succumbed to a combination of infections. No dose toxicities were noted.

Conclusion: Maribavir was well-tolerated and able to successfully decrease level of viremia in a pediatric patient with refractory CMV and a feeding tube at a dose of 200 mg BID. This is the first reported use of maribavir in a pediatric patient. The manufacturer trial will provide additional data for its use.

Reference: [1]ClinicalTrials.gov Identifier: NCT05319353

13) THEME: SUPPORTIVE CARE | OUTCOMES OF VENO-OCCLUSIVE DISEASE (VOD) IN INFANTS AND TODDLERS POST-HEMATOPOIETIC STEM CELL TRANSPLANT (HCT)

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Background: Younger age is a recognized VOD risk factor, yet no prior studies have focused on outcomes of VOD in the infant and toddler population.

Objective: This retrospective study compared the overall survival (OS) and acute care utilization of infants and toddlers diagnosed with and without VOD. We also compared OS for those diagnosed with VOD (Cohort A) versus those not diagnosed but retroactively met EBMT, modified Seattle (MS), or Baltimore criteria (BC) (Cohort B), versus those without VOD nor met criteria (Cohort C).

Design/Method: Patients who received their first HCT for any indication at age $\leq$ 3 years from January 1, 2016 - October 31, 2021 were included. The pediatric EBMT, MS, and BC criteria were used to retroactively determine if subjects met VOD criteria by Day +100, +21, and +20, respectively. Autologous and allogeneic HCT recipients were analyzed separately.

Results: Of 150 HCT recipients [89 allogeneic and 61 autologous], 18 were diagnosed with VOD [14 (15.7%) allogeneic, 4 (6.6%) autologous] at a median of 14d [2-23d] post-HCT. Defibrotide was administered to 14 (78%) patients. All patients survived to hospital discharge. In autologous recipients, median age at HCT was lower in patients with VOD than those without [1.1y vs 2.5y, $P = 0.02$]. All allogeneic recipients who developed VOD received busulfan-based conditioning.

In allogeneic recipients, OS at Day +365 [100% vs 98.7%, $P = 0.69$], cumulative incidence of acute GVHD at Day +100 [21.4% vs 17.6%, $P = 0.70$], and chronic GVHD at Day +365 [22.1% vs 22.0%, $P = 0.87$] were similar between those with and without VOD. Median length of stay was longer in those with VOD versus those without [60.5d vs 38d]. More patients with VOD were admitted to the intensive care unit [79% vs 15%]. Of the 14 patients with VOD, 11 (79%) required peritoneal fluid drainage, 2 (14%) required pleural effusion drainage, and 10 (71%) developed respiratory failure.

More patients retroactively met criteria for VOD than were clinically diagnosed, with EBMT criteria capturing the most patients [11/61 (18%) autologous, 45/89 (51%) allogeneic met EBMT criteria]. OS at 1-year post-HCT was not significantly different across Cohorts A, B, and C for any of the criteria.

Conclusion: While VOD in young children can be highly morbid, the majority have promising survival probabilities at 1-year post-HCT. Retroactive evaluation demonstrates that only a portion of patients who met various VOD criteria were captured. Further work is needed to understand the sensitivity and specificity of these definitions in this younger aged cohort.

14) THEME: SUPPORTIVE CARE | DIFFUSE ALVEOLAR HEMORRHAGE IN CHILDREN AFTER HEMATOPOIETIC CELLULAR THERAPY: RISK FACTORS FOR MORTALITY AND RESPONSE RATES TO INHALED AGENTS

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Background: Diffuse alveolar hemorrhage (DAH) is a rare, life-threatening complication of hematopoietic cellular therapy (HCT). High dose steroids were historically used but current data have prompted the use of inhaled tranexamic acid (INH TXA) and novo-seven (INH Novo-7). We hypothesized that steroid sparing approaches would be associated with improved survival.

Methods: In this IRB approved retrospective study, data from consecutive HCT patients clinically diagnosed with DAH from 3 institutions between January 2018- August 2022 were extracted. Bleeding cessation for $\geq$ 24 hours equated a complete response (CR). Subdistribution hazard models (HR) were used to generate hazard ratios (HR) for non-relapse mortality (NRM) with relapse as a competing risk.

Results: Forty children developed DAH with initial hemorrhage a median of 56.5 days post HCT (range 1-760), with a median of 1 pulmonary bleed (range 1 to 5). First DAH was diagnosed by bronchoscopy (n = 15), frank blood in the endotracheal tube (n = 21), or other (n = 4). The median age was 6.55 years, 23 (57.5%) were female, and 35 (87.5%) underwent allogeneic HCT (allo-HCT). Allo-HCT included 21 bone marrow,10 peripheral blood, and 4 umbilical cord sources with 21 from unrelated donors. All autologous HCT recipients developed DAH after second tandem HCT for neuroblastoma. Thirty (75%) children had transplant associated thrombotic microangiopathy, 19 (47.5%) sinusoidal obstructive syndrome (SOS), 23 (57.5%) had a systemic infection within 4 weeks of DAH and 20 (50%) had documented pulmonary infection at time of bleed. Treatment for the 60 separate pulmonary bleeds included steroids (n = 18, 61% CR), INH TXA (n = 43, 86% CR), and INH Novo-7 (n = 11, 91% CR). NRM was 37.5 $\pm$ 0.08 and 58.8 $\pm$ 0.08 at day 100 and 1-year post HCT respectively. TA-TMA and

grade III-IV GVHD were not associated with NRM. However, SOS (HR 2.44 95% CI 1.11-5.39, p = 0.03) and steroid treatment (HR 2.25 95% CI 1.07-4.71, p = 0.03) were associated with increased risk of NRM. Treatment with INH TXA (HR 0.43, 95% CI 0.19- 0.96, p = 0.04) and INH Novo-7 (HR 0.22, 95% CI 0.07-0.62, p = 0.005) were associated with decreased risk of NRM.

Conclusions: This study highlights that NRM in children with DAH remains high. In this contemporary multi-institutional study, 75% of children with DAH had TA-TMA. While all therapies resulted in similar rates of cessation of pulmonary bleeding, steroid use for DAH was associated with significantly higher NRM, while INH DAH and Novo-7 were associated with decreased NRM and warrant prospective investigation.

15) THEME: SUPPORTIVE CARE | CARING FOR INFANTS UNDERGOING PEDIATRIC HEMATOPOIETIC STEM CELL TRANSPLANTATION (HSCT): A SINGLE CASE REPORT OF A PATIENT <3 MONTHS OF AGE

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Background: Allogeneic HSCT provides curative therapy for a range of malignant and non-malignant diagnoses. As newborn screening programs expand, more patients are being identified for HSCT at an earlier age. Proceeding with HSCT in an infant present challenges for the HSCT team compared to standard pediatric patients. A paucity of data exists regarding recommendations in this population.

Objective: A 2-month-old male infant diagnosed with adenosine deaminase severe combined immunodeficiency (ADA-SCID) underwent cord blood HSCT (CBT). His weight on admission was <4 kg. We want to share the planning our program went through to get the patient safely through HSCT.

Method: We retrospectively reviewed a single infant who underwent CBT for ADA-SCID.

Preparative regimen included fludarabine 1 mg/kg daily x5, thiotepa 4 mg/kg every 12 hours x2, and melphalan 4.7 mg/kg once. He received UCB cell dose of 10x10e7 TNC/kg. He started G-CSF Day+1 and continued through engraftment Day+13. He received mycophenolate mofetil and cyclosporine for graft-versus-host-disease prophylaxis. Bone marrow analysis Day+30 showed 100% donor chimerism. He started ADA-enzyme repletion pre-HSCT and continued through Day+100. During his transplant stay, he required modifications in nursing care, labs and medications due to age and weight.

Results: This infant underwent successful HSCT for ADA-SCID, albeit required changes from standard pediatric HSCT practice. He had infant nursing care with a focus on nutrition, growth (weight, length, and head circumference) and development (OT/PT/ST). Central access was limited by size and function. Minimum volume lab draws spaced to avoid max volume (<2.5% TBV/day). Medications required weight-based dosing and were concentrated to avoid hypervolemia. He required adjustments in rate of mannitol and cyclosporine infusions. Cyclosporine created a distinct challenge as it cannot be dispensed via syringe due to PVC. Thus, new tubing was used each dose and primed with drug to avoid the 30 mL flush. Even with concentrating IV medications, he still required close fluid monitoring, titrating all infusions to remain at maintenance rate. In addition, he required KVO fluids until off IV medications to limit heparin flushes and risk of systemic anticoagulation.

Conclusions: A 2-month-old male with ADA-SCID underwent successful CBT.

Our program planned for this infant by:

Limiting max blood draw volume per day

Adjusting orders for daily labs to a modified QOD schedule

Readministering standard waste volume with blood draws

Concentrating medications

Setting a total daily fluid goal

With the number of neonatal diagnoses requiring curative HSCT, guidelines are needed to provide adjustments in care for these patients.

16) THEME: SUPPORTIVE CARE | "PATIENT AND CAREGIVER EXPERIENCES POST-HEMATOPOIETIC STEM CELL TRANSPLANT (HSCT) TO DRIVE APP DEVELOPMENT: A QUALITATIVE STUDY"

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Patients going through HSCT need a full-time caregiver during their hospital stay and for several months following HSCT as patients are at high risk for infection and other acute complications that can result in significant morbidity and mortality. Caregivers of HSCT patients have been found to experience post-traumatic stress disorder and experience less social support and spiritual well-being in addition to greater marital dissatisfaction and loneliness (1). In recent years, there has been increased attention placed on how best to support caregivers and promote caregiver well-being through education, counseling and skills training (2). Mobile health and technology have and can continue to serve as a platform to support HSCT patients and caregivers (3).

The BMT Roadmap 2.0 app is aimed to improve HSCT caregiver quality of life through promotion of caregiver resilience (4). Given that HSCT caregiver needs are unique to each individual and may change over the transplant course, we implemented qualitative interviews throughout the study to assess patient and caregiver needs further and to help guide design of future versions of the BMT Roadmap app. A total of ten dyads (patient and caregiver) were interviewed

at five timepoints post-HSCT with interview times ranging from 15 to 45 minutes per interview. Interim content analysis and thematic coding using the Framework Method resulted in four themes, each with multiple subthemes. The four themes highlighted by patients and caregivers throughout the interviews included important information (such as assessment of progress and warnings/reasons to call), missing information (such as scheduling errors/communication and medication specific information), coping strategies (with family, friends, and/or activity) and app/intervention design (such as care coordination, medication tracking, side effects tracking and symptom tracking). The findings from this qualitative study illustrate specific areas of education, or "important information," to provide patients and their families during HSCT and well as how best to shed light on information patients and families feel like is "missing information." Patients and caregivers commented on a variety of coping strategies throughout their HSCT process as well. Additional app/intervention design comments centered around making a more comprehensive app. Complete interview analysis is expected in the near future with goal to take qualitative findings forward in designing the next version of BMT Roadmap.

(1) Liang J, Lee SJ, Storer BE, Shaw BE, Chow EJ, et al. (2019). Rates and risk factors for post-traumatic stress disorder symptomatology among adult hematopoietic cell transplant recipients and their informal caregivers. Biology of Blood and Marrow Transplantation. 25(1): 145-150.

(2) Gemmill R, Cooke L, Williams AC, Grant M. Informal caregivers of hematopoietic cell transplant patients: A review and recommendations for interventions and research. Cancer Nursing. 2011;34(6): E13-21.

(3) Shin JY, Kang TI, Noll RB, Choi SW. Supporting caregivers of cancer patients: A summary of technology-mediated interventions and future directions. American Society of Clinical Oncology Educational Book. 38:838-849.

(4) Rozwadowski M, Dittakavi M, Mazzoli A, et al. Promoting Health and Well-Being Through Mobile Health Technology (Roadmap 2.0) in Family Caregivers and Patients Undergoing Hematopoietic Stem Cell Transplantation: Protocol for the Development of a Mobile Randomized Controlled Trial. JMIR Res Protoc. 2020;9 (9):e19288.

1) THEME: TRANSPLANTATION BIOLOGY | SEVERE DARATUMUMAB REACTION IN A PEDIATRIC PATIENT WITH DONOR SPECIFIC ANTIBODIES PLANNING TO RECEIVE HAPLOIDENTICAL STEM CELL TRANSPLANT (SCT)

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Background: Success of haploidentical stem cell transplantation (SCT) has increased secondary to the development of innovative methods to control alloreactive donor lymphocytes. Donor specific anti-HLA antibodies (DSAs) are a major culprit of engraftment failure in patients receiving haploidentical SCT. The mechanism behind DSA-induced engraftment failure is complement fixation with DSA levels greater than 5,000 mean fluorescence intensity (MFI). To reduce the risk of DSA-induced graft failure, patients undergo desensitization with monitoring of complement and DSA levels.

Objective: Discussion of a rare adverse reaction to Daratumumab in a pediatric patient.

Design/Method: Case Report.

Results: A 17-year-old female post two multi-visceral transplants, initially due to necrotizing enterocolitis requiring bowel resection as a preterm infant, developed severe aplastic anemia (SAA) in the post-organ transplant period. Bone marrow evaluation demonstrated evidence of graft versus host disease with hypocellularity and marrow chimerism 100% of solid-organ-donor. She failed standard therapy for SAA. An attempt was made to reset hematopoiesis with a T-cell depleted stem cell product, but apheresis yield was low, resulting in failed engraftment. She remains transfusion dependent with secondary iron overload, so the family agreed to proceed with SCT.

Given her mixed ethnicity, her only donor option is haploidentical-SCT with her sister or father. However, she has MHC class I and class II DSAs (> 20,000 MFI) to both donors. A desensitization protocol was initiated using Bortezomib, intravenous immunoglobulin, Rituximab, and plasma exchange. DSA improved but continued to be elevated. She began therapy with daratumumab, an anti-CD38 monoclonal antibody. She was premedicated prior to the daratumumab infusion. After receiving 26 mL of the 500 mL infusion, she developed a severe headache with hypertension and tachycardia; the infusion was discontinued. Subsequently, the patient complained of blurry vision with sudden development of yellow discoloration of the sclera with conjunctival swelling consistent with chemosis. Laboratory evaluation after the infusion reaction revealed transaminitis 6 times above previous results. CT brain was negative for intracranial bleeding. Ophthalmologic evaluation was consistent with ciliary body effusion. No intervention was required, and her liver enzymes returned to normal. This reaction was reported to the Food and Drug Administration (FDA).

Conclusion: Daratumumab has been crucial in the treatment of DSA prior to solid organ and HLA-mismatched SCT to avoid graft failure in adult patients. The use of daratumumab in pediatrics is still limited. Infusion reactions to daratumumab are uncommon, and ocular side effects to daratumumab have not been reported in the pediatric literature.

2) THEME: TRANSPLANTATION BIOLOGY | ALL RASHES AFTER HEMATOPOIETIC STEM CELL TRANSPLANTATION ARE NOT GRAFT VERSUS HOST DISEASE

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Background: Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE), a skin reaction previously known as "Baboon Syndrome," is diagnosed if four or more of the following criteria are met: symmetry, involvement of at least one intertriginous zone, erythema of the gluteal, inguinal, or axillary region, systemic exposure to a drug, and lack of systemic toxicity. In this case, a 13-year-old male patient with severe aplastic anemia treated with an upfront matched unrelated donor (MUD) hematopoietic stem cell transplant (HSCT), is the presumed first ever identified pediatric case of SDRIFE. This case was complicated by the confounding diagnostic concern for presumed acute skin graft versus host disease (GvHD).

Objective: We aim to produce an improved awareness of a unique diagnosis, SDRIFE, in post-HSCT patients with ongoing skin eruptions despite treatment for refractory GvHD. Methods Chart review of clinical notes, laboratory results, and treatment history.

Results: The patient underwent upfront MUD HSCT after conditioning with fludarabine, cyclophosphamide, and alemtuzumab; tacrolimus was used for acute GvHD prophylaxis. He engrafted on day +18 and had full donor chimerism on day +30. He presented with a maculopapular erythematous rash on day +28 and was managed successfully with topical steroids and topical tacrolimus for presumed acute skin GvHD stage 1, grade 1. Subsequently, similar eruptions but more extensive skin rashes, diagnosed as stage 2, grade 2 skin GvHD, occurred on days +105, +271, +320, +391, +482, and +552, and were treated with topical steroids, topical tacrolimus, and oral steroids. Rabbit ATG, and later, rituximab were used for recurrence of rashes surrounding days +320 and +391, respectively. Initial skin biopsies performed throughout the course were non-specific to a diagnosis. The final skin biopsy obtained on day +552 showed definitive spongiotic dermatitis and the diagnosis of SDRIFE was established. Systemic and topical tacrolimus were weaned off with dramatic improvement of the overall skin condition of the patient.

Conclusion: In addition to acute GvHD, viral exanthems are common causes of skin rashes seen after HSCT. Transplant providers are not familiar with the diagnosis of SDRIFE, a drug induced skin rash, in this case due to tacrolimus. Our patient was treated as a case of acute GvHD with steroids and other medications for refractory acute GvHD for approximately 6-7 episodes (over 10-18 months) before a diagnosis of SDRIFE was made. SDRIFE should be considered in the differential diagnosis of refractory GvHD and is easily treatable by avoiding the offending medication.

3) THEME: TRANSPLANTATION BIOLOGY | Longitudinal Assessment of Oxidative Stress after HSCT and Associations with Outcomes

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Background: Lysis of the body's entire hematopoietic system during conditioning causes toxic molecules to be released into the circulation, which we hypothesize contributes to significant oxidative stress. The physiological consequences of this massive oxidative stress may contribute to endothelial injury and many of the complications of hematopoietic stem cell transplant (HSCT).

Key molecules involved in the cell's response to oxidative stress included glutathione reductase (GSR) enzyme and nuclear factor erythroid 2-related factor 2 (NRF2). GSR maintains supply of reduced glutathione, a reducing thiol which controls reactive oxygen species (ROS). NRF2 is a transcription factor which regulates expression of genes central to the cellular response to oxidative stress and has been shown to attenuate endothelial injury by ROS in other clinical settings.

Objective: The goal of this study was to identify the longitudinal time course of oxidative stress after HSCT and to describe the impact of oxidative stress on clinical outcomes of HSCT.

Design/Method: GSR levels in plasma were measured using ELISA in 122 consecutive allogeneic transplant recipients at CCHMC at 6 time points: pre-transplant (baseline) and days 0, 14, 21, 42 and 93 after HSCT. NRF2 gene expression on day 21 was measured using RT-PCR for 40 patients from this same cohort.

Results: GSR levels increase markedly between baseline and day 0 (87 ng/mL vs 459 ng/mL, $p < 0.0001$), continuing through day 14 after transplant (518 ng/mL), then falling back to baseline by day 21. A higher baseline GSR level prior to HSCT is associated with death at one year ($p = 0.01$). Higher GSR at day 21 is associated with increased risk of death at 1 year ($p < 0.001$), acute GVHD2-4 ($p = 0.001$) and TA-TMA ($p = 0.031$). NRF2 is activated by oxidative stress and our preliminary data show an association between higher GSR enzyme levels and higher NRF2 expression by RT-PCR ($p = 0.11$, $n = 40$ patients). We are currently examining the expression of genes downstream from NRF2.

Conclusions: Our longitudinal data show an early marked increase in GSR expression in response to HSCT, likely representing a brisk host response to remove ROS released by conditioning. Higher GSR expression very early after transplant is associated with later complications and death, suggesting outcomes are defined in the first two weeks after HSCT, or in some cases, prior to the start of HSCT. These data support the importance of events in the first 2 weeks after HSCT in the initiation of later adverse events and investigation of early anti-oxidant prophylactic therapies.