5th Symposium on Infectious Diseases in the Immunocompromised Host Abstracts

Adenovirus & BK Virus

Abstract #1: Incidence and Severity of Virus-associated Hemorrhagic Cystitis in Adult Allogeneic Hematopoietic Cell Transplant Recipients with Post -Transplant Cyclophosphamide - based GVHD Prophylaxis **Maria Gianniki, MD, MS** | *Memorial Sloan Kettering Cancer Center*

Background: We report the incidence & severity of hemorrhagic cystitis (HC) due to Adenovirus (ADV) and BK polyomavirus (BKV) and the associated mortality by day 180 post-HCT (D180) in a large single-institution cohort of adult patients (pts) who received Cyclophosphamide (PTCy).

Methods: This retrospective review includes pts who received HCT from January 2016 to February 2024 with PTCy-based GvHD prophylaxis at Memorial Sloan Kettering Cancer Center. The GvHD-prophylaxis regimen consisted of cyclophosphamide (50 mg/kg/day on Days +3 and +4) with mesna and hydration. Patients were routinely monitored for ADV by quantitative plasma PCR. ADV and BKV in urine were ordered at the physicians' discretion. Virus-associated HC was defined as ADV OR BKV viruria AND cystitis grade 2 or higher by Bedi criteria occurring after day 21 or platelet engraftment, whichever was longer, and no other identified causes of hematuria.

Results: Of 412 pts, 254 (62%) were male, 158 (38%) had haploidentical/related mismatched donors, 118 (29%) received myeloablative conditioning, and 78 (19%) received bone marrow allograft. By D180, 34 (8.3%) pts developed virus-associated HC, including 6 (1.5%) ADV and 28 (6.8%) BKV-associated HC, respectively. Of the 34 pts, the severity of HC was grade 2 in 26 (76.5%) pts and grade 3-4 in 8 (23.5%) pts. The median time to onset was 28 days (IQR, 14-50) post-HCT. The mean duration of symptoms was 28.25 days (IQR, 11-35). 8 patients received antivirals (7 cidofovir, one brincidofovir), including 1 pt with disseminated ADV infection. By D180, 57 (13.8%) pts of the entire cohort died. No death was attributed to virus-associated HC.

Conclusions: In our retrospective study, the proportion of virus-associated HC was 8.3%, and among these pts, 23.5% had grade 3-4. ADV and BKV hemorrhagic cystitis are essential complications of HCT, primarily related to PTCy. Novel antiviral prevention and treatment strategies are needed.

Abstract #2: Improving Tools Towards Individualized Risk Prediction and Management of BK Virus Infection in Renal Transplant Recipients **Bin Ni, MD** | *Duke University*

Background: BK virus reactivation after renal transplant can lead to complications such as ureteral stenosis and BK virus-associated nephropathy (BKVAN). Reported frequencies of these complications vary widely due to differences in BK management and immunosuppressive regimens, with sparse, outdated data on ureteral stenosis. Newer immunosuppressants, such as belatacept, are linked to more frequent and severe BK infections, though findings are mixed. This study aims to update the epidemiology of BK reactivation and complications in renal transplant recipients to develop risk prediction models from a large Duke University Hospital (DUH) cohort.

Methods: This retrospective study included all renal transplant recipients (single or multi-organ) at DUH between 1/1/2016 and 12/31/2020. Clinical and demographic data, including BK reactivation and outcomes, were abstracted from records, and donor data were collected from the UNOS STAR database.

Results: 840 renal transplants episodes were evaluated, with 754 (89.8%) having complete 2-year follow-up. Of those without full follow-up, 37 (4%) had died, 14 (2%) were lost to follow-up, and 35 (4%) lost their graft. Among patients with complete follow-up, 45 (6%) developed BKVAN (15 probable, 20 presumptive, 10 biopsy-proven), with a median diagnosis time of 161 days (IQR: 103, 284). BK DNAemia occured in 291 patients (39%), with a median time to DNAemia of 119 days (IQR: 66, 303). 136 (18%) patients had high-level DNAemia (≥10,000 copies/mL). Ureteral stenosis or obstruction occurred in 33 patients (4%), 17 of whom (52%) also had BK DNAemia, but none had histologically confirmed

BK-related ureteral complications.

Conclusions: We observed ureteral stenosis/obstruction in 4%, BKVAN in 6%, and BK DNAemia in 39% of transplant recipients. This study updates the incidence of BK reactivation and its complications in renal transplant recipients under modern immunosuppressive regimens, providing data to develop risk prediction models to improve patient outcomes.

Abstract #3: BKV-associated Hemorrhagic Cystitis after Allogeneic HCT: Preliminary Data from a Retrospective Cohort Study **Leonardo M. Parra** | *Hospital Dr Amaral Carvalho, Brazil*

Background: Hemorrhagic cystitis (HC) is a frequent complication after hematopoietic cell transplantation (HCT). HC may occur until 72 hours after HCT secondary to conditioning toxicity, or later, often due to BK virus reactivation (BKV-HC). In the absence of effective and safe antivirals to control BKV-HC, supportive therapy (hydration, bladder irrigation and uroprotective drugs) has been mainly used. We retrospectively evaluated the clinical findings, outcomes and variables associated with BKV–HC.

Methods: Electronic medical records of allogeneic HCT recipients were reviewed from 2020 to 2024. Patients (pts) who performed more than one HCT were excluded. During this period, BKV DNAemia was monitored weekly by quantitative PCR (Mobius Life Science, Pinhais, Brazil). BKV-HC was defined according to ECIL 2018. The cumulative incidence (CI) of BKV-HC, the variables associated with its occurrence, overall survival (OS) and non-relapse mortality (NRM) were determined by the software R.

Results: 310 pts were included: 96 matched related donor (MRD, 31%), 145 haploidentical (46.8%) 57 matched unrelated donor (MUD, 18.4%) and 12 mismatched unrelated donor (mMUD, 3.4%). BKV (in blood and/or urine) was detected in 169 pts (54.5%). BKV-HC was confirmed in 27 pts (CI=8.7%). Eleven pts (40.7%) had hematuria grade II, 15 grade III (55.6%) and one grade IV (3.7%). BKV-CH CI was 25% in mMUD, 7% in MRD and 8% in haploidentical and MUD (p=0.23). No patient received antiviral therapy. OS and NRM at 2 years were 66.8% and 20.6%, respectively. By multivariate analysis, variables affecting OS were non-myeloablative/reduced intensity conditioning (RIC), haploidentical and mMUD HCT, and performance status ≤80%. BKV-CH grade III-IV (HR 2.67, p=0.005) and RIC (HR 2.99, p<0.001) increased NRM.

Conclusions: We observed a low incidence of BKV-HC (8.7%) with no impact on OS. However, severe BKV-CH was frequent and associated with increased NRM in this series.

CMV

Best Abstract Oral: Probable CMV Pneumonia in Non-transplant Population with Hematologic Malignancies **Karolina Bełdzińska-Gądek, MD** | *Medical University of Gdańsk, Poland*

Background: Cytomegalovirus (CMV) pneumonia is associated with increased mortality in immunocompromised patients. Little is known about the incidence and clinical outcomes in non-transplant population.

Methods: This study aims to evaluate the burden of CMV DNAemia in bronchoalveolar lavage (BAL) fluid collected from patients with hematologic diseases with lower respiratory tract infections. BAL samples were tested for CMV DNA (ELITe InGenius). No viral cultures or lung tissue biopsies were available. Cultures, PCR and serological assays were done to detect other co-pathogens. Clinical outcomes were collected from medical records.

Results: In this study we included 108 BAL samples obtained between 2022 and 2024 from non-transplant patients. Chronic lymphoid malignancies (LM) were the most common diagnosis (55%) followed by myeloid leukemias (38%). 86% were actively treated with immune-/chemotherapy within 90 days before sample collection and 45% received various B-cell targeted therapies.
CMV DNA was detected in 14 BALs (13%) with the median viral load of 4151 IU/ml (256-810 000 IU/ml; all except 1 >500 IU/ml); in 4 (28%) of them CMV viremia was observed (642 IU/ml, range 331- 149 000). All were diagnosed with LM, no correlation with lymphopenia was observed. Co-detected pathogens included bacteria, fungal antigens, respiratory or herpes viruses in 28%, 36%, 36% and 21%, respectively. In 57% ground glass opacities were present in computed

tomography.
Preemptive therapy for CMV pneumonia was started in all patients. Three (21%) required oxygen support and 2 (14%) died due to the infection. In those cases, CMV was the main pathogen detected, in both cases there was lymphopenia and in 1 CMV viremia.

Conclusions: CMV DNA can be frequently detected in BAL samples, especially in patients with lymphoid malignancies; yet in most cases, with the presence of other co-pathogens. Based on these preliminary observations, survival seems more favorable than transplant recipients.

Abstract #4: Cytomegalovirus Modulation of CD8 T Cell Phenotype and Function in People Living with HIV-1 **Brandi Clark, PhD** | *St Jude Children's Research Hospital*

Background: Both human immunodeficiency virus 1 (HIV-1) and cytomegalovirus (CMV) cause lifelong infections that cannot be cured by antiviral chemotherapy due to persistent viral reservoirs. There is mounting evidence that chronic CMV alters immune responses to various subsequent infections, and that large clonal expansions of CMV-specific CD8 T cells in elderly persons denote immune senescence. We propose that CMV co-infection may contribute to dysregulated HIV-1 control.

Methods: Longitudinal peripheral blood samples and clinical data were prospectively collected over 18 months from 87 PLWH and 47 individuals without HIV-1 infection. All subjects were males (ages 18-28) receiving anti-retroviral therapy (ART) as treatment or pre-exposure prophylaxis (PrEP). HIV-1 viral titers, HIV-1 antigen/antibody screens, and CMV IgM and IgG ELISAs were monitored throughout the study. Flow cytometry and single-cell RNA sequencing were used to assess total and virus-specific CD8 T cells from 65 and 17 individuals, respectively.

Results: Subjects were categorized as "normal" or "high" CMV responders based on their frequency of CMV-specific CD8 T cells. Normal responses were observed in 112/126 samples (0-3.5% per pentamer used), and 14/126 had high responses (4.2-18%). All high responders were PLWH, and had increased HIV-1 viral loads and decreased CD4/CD8 ratios compared to normal responders. Responder status was associated with changes to both pan-CD8 and HIV-1-specific CD8 T cells. HIV-specific CD8 T cells from CMV high responders exhibited heightened cytotoxicity transcriptional profiles when compared to normal responder.

Conclusions: In our cohort, a subset of individuals displayed a pronounced expansion of CMV-specific CD8 T cells associated with markers of poor HIV-1 control, as well as changes in activation and transcription within CD8 T cells. This suggests an inappropriately elderly immune tone phenotype during HIV-1-CMV co-infection. Further work is needed to assess impacts to the HIV-1 reservoir, viral control, and non-AIDS-associated morbidity in PLWH on ART.

Abstract #5: CMV Infection after Autologous Hematopoietic Stem Cell Transplantation for Non-Malignant Autoimmune Conditions **Brennan Collis, MD** | *Duke University*

Background: Autologous hematopoietic stem cell transplantations (ASCT) is increasingly used to treat refractory autoimmune conditions such as systemic sclerosis (SSc) and multiple sclerosis (MS). Data on cytomegalovirus (CMV) infection post-ASCT in this population is limited. This study aimed to assess risk factors, rates, and outcomes of post-transplant CMV infection (CMVi) in ASCT recipients for autoimmune conditions.

Methods: We performed a single-center retrospective study of all ASCT recipients for autoimmune conditions complicated by CMVi. CMVi, defined as a quantifiable CMV viral load (VL) in blood, was monitored using a pre-emptive approach with regular PCR testing. CMV treatment was physician directed and generally initiated when VLs >450 IU/ml. The primary outcome was the rate of CMVi or CMV-disease post-ASCT. Secondary outcomes were the management, outcomes, and risk factors for CMVi.

Results: Forty-seven patients received ASCT for autoimmune conditions (median age: 45 years [IQR 34-54]; sex: 31 [66%] female; indication: 42 [89%] SSc, 5 [11%] MS). Twenty-one patients (45%) were CMV-seropositive pre-transplant. CMVi occurred in 12/47 (25.5%) patients post-ASCT, corresponding to 10/21 (48%) and 2/26 (8%) of CMV-seropositive and

CMV-seronegative ASCT recipients respectively. Median onset of infection was 28 days (IQR: 21-34 days) post-transplant with a median peak VL of 894 IU/mL (IQR: 383-1427). There were no cases of end-organ disease. CMV positive serostatus was a significant predictor of post-ASCT CMVi with a relative risk of 6.19 (95%CI: 1.51-25.2; p<0.002). Treatment was initiated in 8 (67%) patients; 5 patients received intravenous ganciclovir upfront, 3 patients commenced on oral valganciclovir, and 4 patients had resolution without treatment. Median duration of CMV-targeted therapy was 34 days (IQR: 28-39). One patient experienced gastrointestinal intolerance necessitating antiviral discontinuation. No patient died or required hospitalization due to CMVi.

Conclusions: CMVi post-transplant was almost exclusively in CMV-seropositive recipients. Though common, infection occurred early post-transplant and associated with minimal morbidity.

Abstract #6: Outcomes of Clinically Significant Breakthrough CMV Infections while on Letermovir Prophylaxis Compared to Pre-emptive Strategy in Allogeneic Hematopoietic Cell Transplant Recipients **Marilyne Daher** | *The University of Texas MD Anderson Cancer Center*

Background: Rates of clinically significant CMV infection (CS-CMVi) following HCT decreased with letermovir (LTV) prophylaxis compared to preemptive therapy (PET). It is unclear the impact of breakthrough CS-CMVi while on LTV prophylaxis, compared to CS-CMVi while on PET strategy, on the incidence of CMV disease, refractory/resistant CMV, and mortality.

Methods: We reviewed allo-HCT recipients with CS-CMVi up to 48 weeks from transplant between March 2016 and February 2023. Univariate analysis using Fischer's exact test and Wilcoxon rank sum for categorical and continuous variables were used to compare patients with CS-CMVi while on letermovir or PET strategy.

Results: CS-CMVi occurred in 438 patients; 163 (37.2%) on LTV and 275 (62.8%) during PET. Median age at time of HCT was 53 (range: 2-77), and majority had AML. Median LTV duration was 105 days (range: 8-416). Patients with breakthrough CS-CMVi while on LTV had longer median time to CS-CMVi compared to those on PET (77 vs 26 days, p<0.001), were less likely to have CMV disease (14.7% vs 29.1%, p=0.001), and refractory CMVi (4.9% vs 11.6%, p=0.02). UL56 mutations were identified in 4 out of 23 (23.5%) tested patients with breakthrough CS-CMVi while on LTV and UL54 mutations was identified in 3 out 91 (4.5%) tested patients with CS-CMVI while on PET strategy. All-cause mortality was lower in the LTV group at 24 weeks (12.3% vs 25.1%, p=0.001) and 48 weeks (23.9% vs 35.6%, p=0.01). Non-relapse mortality was significantly lower in the LTV group at 24 weeks (11.0% vs 19.6%, p=0.02), with trend towards significance at 48 weeks (19.0% vs 26.2%, p=0.09).

Conclusions: Patients with breakthrough CS-CMVi on LTV had lower rates of CMV end-organ disease, refractory CMVi, all-cause and nonrelapse mortality compared to those on PET. Risk factors for breakthrough CS-CMVI and resistance need to be determined in future studies.

Abstract #7: Preferences and Practices in CMV Management, Including CMV Cell-mediated Immunity Testing in a Large Academic Transplant Center **Kyle T. Enriquez, MSc** | *Vanderbilt University Medical Center*

Background: Current strategies for stratification of CMV infection risk are based on seromatch at time of transplant, which provide incomplete understanding of patient risk at the end of standard primary prophylaxis (with vanganciclovir (VGC)) and in patients with persistent detectable, but asymptomatic viremia. The CMV cell-mediated immunity (CMV-CMI) inSIGHT ® Test has been utilized as a surrogate for CMV infection risk, but optimal implementation is under-investigated. CMV-CMI inSIGHT has the potential to apply to various areas of post-transplant CMV management, however, none of these have clear supporting evidence. To advance our institution's initiative to standardize practices, including CMV-CMI monitoring, we conducted a survey to define algorithm cutoffs and branching points.

Methods: We constructed and administered a clinical case-based RedCap survey to transplant infectious diseases adult and pediatric providers. Across four cases and fifty-one questions, provider opinions were solicited to address issues of primary/secondary prophylaxis and primary/relapsing viremia.

Results: Surveying of transplant infectious diseases faculty from a single center yielded critical data regarding the

diversity of CMV management in transplant patients. For primary CMV prophylaxis with development of cytopenias, providers were more likely to initially monitor with G-CSF support (83% prefer) rather than switching to letermovir or stopping prophylaxis early. After an acute cellular rejection episode, providers were more likely to restart valganciclovir prophylaxis for 3 months than for 1 month (100% prefer). Further, there are a wide variety of practices for managing low-grade persistent viremia after treatment, with 60% of respondents preferring secondary prophylaxis if there was history of end-organ involvement.

Conclusion: Taken together, these data suggest strong support for implementation of the CMV-CMI inSIGHT test in patients with persistent low-grade and relapsing/rebounding viremia. In addition, this study noted areas of agreement amongst providers that support a unified approach to post-transplant CMV management, including consideration of maribavir for patients with viremia over 10,000 IU/mL.

Abstract #8: Antigen-agnostic Screening to Develop Broadly Protective Antibodies for Immunotherapy against Human Cytomegalovirus **Hannah Lewis, PhD** | *Fred Hutch Cancer Center*

Background: One of the most challenging and devastating viruses in the transplant setting is human cytomegalovirus (HCMV), a herpesvirus that permanently infects between 40-90% of the global population. Although typically asymptomatic in immunocompetent people, HCMV frequently reactivates during periods of immunosuppression with mortality rates as high as 50%.
There remains an enormous unmet need for safe, effective, and durable therapies against HCMV reactivation. Although antivirals that block HCMV replication are approved for clinical use, they are limited by toxicity, interactions with other drugs, and viral resistance. Recent studies have shown that strain-specific antibody therapy can prevent CMV reactivation in a murine model of hematopoietic stem cell transplantation, suggesting that monoclonal antibodies (mAbs) may present a viable alternative to current therapies, especially ones that broadly neutralize multiple strains of HCMV.

Methods: We have developed a high-throughput, functional screen to identify potent neutralizing antibodies against HCMV in an antigen-agnostic manner. This is important because HCMV expresses as many as 25 glycoproteins on its surface that allow for different mechanisms of entry into many cell and tissue types. Instead of recombinant bait proteins to enrich for HCMV-binding B cells, we use a sequential sorting method to screen hundreds of thousands of memory B cells for virus neutralization without prior knowledge of antigenic targets.

Results: Using this antigen-agnostic screen, we have identified two neutralizing mAbs targeting different HCMV entry complexes that we named FA1 and 15-E5. FA1 can neutralize infection in epithelial cells at low concentrations (sub-nanogram/mL), but it cannot neutralize infection in fibroblasts. 15-E5, in contrast, can neutralize infection in both fibroblast and epithelial cells, with a 50% neutralization titer in the milligram/mL range.

Conclusions: The outcome of this work will result in production of several candidates for HCMV immunotherapy and an increased understanding of the HCMV antigenic landscape.

Abstract #9: Cytomegalovirus Chorioretinitis Associated with Teclistimab in a Relapsed/Refractory Multiple Myeloma Patient **Christopher Marino, MD** | *University of Pittsburgh Medical Center*

Background: Teclistimab is a bispecific T-cell engager monoclonal antibody increasingly used in the treatment of relapsed/refractory multiple myeloma and is known to impair humoral immunity. Cytomegalovirus (CMV) reactivation associated with teclistimab has been reported, though guidance on CMV surveillance while on therapy has not been well defined. We report a case of CMV chorioretinitis associated with teclistimab therapy.

Case Presentation: An 82 year-old male with relapsed/refractory IgG kappa multiple myeloma with a two-month history of teclistimab therapy and baseline left eye blindness due to a chronic retinal detachment nine years prior presented with left ocular pain and conjunctival chemosis and hyperemia. He was found to have a corneal ulcer with pseudomonal growth on culture and was managed with systemic antibiotics and antibiotic eye drops. The corneal ulcer was complicated by corneal perforation and underwent enucleation. Pathology of the enucleated eye showed atypical cells

of the retina and choroid with enlarged nuclei and cytoplasmic inclusions positive for CMV on immunohistochemical staining consistent with CMV chorioretinitis as well as acute necrotizing keratitis and panophthalmitis. Blood testing showed CMV viremia with 56,834 copies IU/ml (4.75 log IU/ml). The right eye had no evidence of CMV chorioretinitis and CMV testing of right eye anterior chamber fluid was negative. Serum IgG levels were 450 mg/dL. He was treated with valganciclovir and achieved undetectable serum CMV PCR levels at one month. Three months later valganciclovir was switched to acyclovir and he was resumed on teclistimab. The patient subsequently had reactivation of CMV viremia with suspected CMV syndrome and was transitioned to hospice in the setting of severe chronic illness.

Conclusion: Teclistimab can result in CMV reactivation and end-organ disease. Certain patients may benefit from baseline CMV serology and/or serum DNA viral load testing and surveillance by viral load testing to mitigate CMV-related complications.

Abstract #10: Evaluation of Risk of CMV Reactivation in Dasatinib-treated Patients **Lubna Osman, MD** | *Jackson Memorial Hospital; University of Miami*

Dasatinib is a tyrosine kinase inhibitor used in the treatment of certain types of leukemia by blocking the activity of proteins that signal cancer cells to proliferate. Multiple case series have reported associations between dasatinib use and colitis or hepatitis. Additionally, dasatinib has been identified as an independent risk factor for cytomegalovirus (CMV) reactivation following hematopoietic cell transplantation (HCT). However, data on CMV reactivation in non-HCT patients receiving dasatinib remain limited. We report a single-center retrospective study of 42 consecutive adult patients who received dasatinib therapy between 2016 and 2024. The primary outcomes assessed included CMV reactivation (any viremia), clinically significant CMV (cs-CMV), and tissue-invasive CMV disease. CMV viral load was monitored at the discretion of the treating physician.50% of patients were non-transplant recipients.62% were CMV IgG positive.38% of the CMV IgG sero-postive patients experienced CMV reactivation, all of whom developed clinically significant CMV. Among those with CMV reactivation, 60% had invasive disease, compared to 25% in the HCT group. Median follow-up duration: 842 days (interquartile range [IQR]: 414–1,509).Initial viral load in both HCT and non-HCT groups: 137 IU/mL (IQR: 137–137).Median time from dasatinib initiation to CMV reactivation: 201 days (IQR: 154–304).Median time from HCT to CMV reactivation: 36 days (IQR: 19–55).Median time to CMV clearance: 16 days (IQR: 9–28).
Our findings suggest that dasatinib is a significant risk factor for CMV reactivation and disease, warranting close monitoring for CMV viremia in patients receiving dasatinib therapy.

Abstract #11: Risk Factors for Cytomegalovirus (CMV) Transmission from CMV Seropositive Donors to Seronegative Allogeneic Hematopoietic Cell Transplant (HCT) Recipients: Significance of Cell Product Composition and Post-transplant Immunosuppression **Clarissa Santiano** | *Fred Hutch Cancer Center*

Background: CMV transmission occurs in ~20% patients following CMV D+/R- HCT, however, the risk factors for CMV transmission after CMV D+/R- HCT with modern HCT techniques and graft-versus-host disease [GVHD] prophylaxis regimens is unknown.

Methods: Adults and children who underwent allogeneic CMV D+/R- HCT between 1/1/2007 and 6/30/2024 were included in the analysis. Plasma CMV DNA PCR surveillance was performed at least weekly after HCT, and preemptive therapy was initiated according to institutional thresholds. Donor and recipient characteristics, stem cell product composition (total nucleated cell [TNC] and CD34 count per kg), antiviral therapy, and CMV end-organ disease data up to 1-year post-HCT were extracted from the medical record. CMV infection risk was analyzed by time-to-event curves and Cox proportional hazard models.

Results: Four-hundred ninety-six CMV D+/R- HCTs were analyzed. The cumulative incidence of any CMV detection in the first 100 days was 21.8% (95% confidence interval [CI] 18.3-25.5%). A high (i.e., ≥ median) weight-based TNC and mycophenolate mofetil (MMF) plus calcineurin inhibitor (CNI) GVHD prophylaxis were associated with an increased risk of any CMV detection (adjusted hazard ratio [aHR] 1.55, 95% CI 1.04-2.31, p=0.03 and aHR 1.71, 95% CI 1.10-2.67, p=0.02, respectively), whereas Caucasian race and sirolimus-based GVHD prophylaxis were associated with a decreased risk of any CMV detection (aHR 0.54, 95% CI 0.35-0.83, p=0.005 and aHR 0.31, 95% CI 0.13-0.71, p=0.005, respectively). Combinations of these risk factors defined subgroups of highest (72.7%, 95% CI 32.4-91.4%) and lowest (0%) risk of CMV

transmission.

Conclusions: The risk of CMV transmission in the D+/R- setting is determined by the stem cell graft cell count, recipient race, and GVHD prophylaxis regimens. These risk factors can be used to define algorithms that predict high transmission risk as well as protection from transmission, which can inform optimized CMV prevention strategies.

Respiratory Viruses

Abstract #12: Home Infusion Short Course Remdesivir for Solid Organ Transplant Patients with COVID-19 **Grace DeMarco, MD** | *MedStar Georgetown University Hospital*

Background: Solid organ transplant (SOT) recipients are high risk for severe COVID-19 infections due to immunosuppression and variable response to immunization (1-3). The recommended oral antiviral, nirmatrelvir/ritonavir has significant drug-drug interactions, including with tacrolimus. As an alternative, three-day intravenous (IV) remdesivir is efficacious in the outpatient setting (1,2). MedStar Georgetown Infectious Disease (ID) Division and Transplant Institute collaborated with an infusion company to administer remdesivir at home for SOT recipients to reduce hospital utilization and the risk of severe COVID infection, while avoiding both drug interactions and exposure of vulnerable patients in infusion centers.

Methods: We conducted a single center retrospective chart review study at MedStar Georgetown University Hospital of SOT recipients diagnosed with COVID-19 and referred to receive home IV remdesivir December 1, 2022 to May 6, 2024. As part of the referral process, patients were evaluated by ID physicians via telehealth, then started on a three-day course of remdesivir as an outpatient. Adverse events were noted by the infusion company and communicated to the ID physicians for management.

Results: The study included 80 SOT patients: 49% liver, 44% kidney, 4.5% combined kidney-pancreas, and 2.5% small bowel. The average age was 55 years old, with an average duration of COVID symptoms of 2.1 days prior to presentation. Two (2.50%) patients were hospitalized within 30 days of evaluation, and one (1.25%) patient died. The average cost of administration for three days was $4279, comparable to one day of hospitalization in DC ($4068), saving $634000 across the program (4).

Conclusion: Patients receiving home infusion remdesivir had low hospitalization and mortality rates, suggesting reduced risk of disease progression. Additionally, this program has netted a cost savings of $634000 by avoiding hospitalization for administration of remdesivir. Home infusion of remdesivir is an innovative delivery method and may reduce overall cost of healthcare.

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Best Abstract Oral: Shifting Trends in Respiratory Viral Infection Outcomes Among Patients with Hematology Malignancies During 2023-2024 Respiratory Viral Season **Tali Shafat Fainguelernt, PhD** | *The University of Texas MD Anderson Cancer Center*

Background: Respiratory viral infections (RVI) represent a critical challenge to the health and survival of patients with hematology malignancies (HM). The U.S. Centers for Disease Control and Prevention reported that SARS-CoV-2 was the predominant pathogen driving hospitalizations throughout the 2023-2024 respiratory viral season (RVS). However, our comprehensive cancer center observed fewer hospitalizations attributed to SARS-CoV-2 than prior years during the pandemic. Here, we aimed to compare RVI severity and outcomes of respiratory syncytial virus (RSV), influenza, and SARS-CoV-2 in HM patients during the 2023-2024 season.

Methods: We retrospectively analyzed adult HM patients diagnosed with RSV, influenza, or SARS CoV-2 RVIs from October 2023 to April 2024. Primary outcomes were lower respiratory tract infection (LRI), hospitalization, and all-cause 30-day mortality.

Results: We analyzed 503 patients with 536 viral episodes: 140 RSV cases (26.1%), 116 influenza cases (21.6%), and 271 SARS-CoV-2 cases (50.6%), including nine co-infections. Among RSV-infected individuals, 50.7% developed LRI, compared to 40.5% and 39.5% for influenza and SARS-CoV-2, respectively (p=0.080). The overall 30-day mortality rates were 5.9%, 9.3% for RSV, 7.8% for influenza, and 3.3% for SARS-CoV-2 (p=0.032). Multivariable analysis showed that RSV infection increased LRI risk compared to SARS-CoV-2 (aOR 1.72, 95% CI 1.11-2.63, p=0.016), as older age, refractory cancer status, and nosocomial infections, while previous autologous HCT was protective. Increased 30-day mortality was associated with older age, nosocomial infections, and LRI, while additional doses of anti-SARS-CoV-2 vaccination reduced mortality risk.

Conclusions: Among HM patients infected with RSV, influenza, or SARS-CoV-2 during the 2023-2024 RVS, RSV was associated with highest LRI risk and 30-day mortality, while SARS-CoV-2 presented the lowest risk. Hospitalization rates for all RVIs were similar. These findings emphasize the urgent need for increased vigilance and preventive measures for all RVIs in the post-pandemic era, as poor outcomes related to non-SARS-CoV-2 RVIs remain a significant concern.

Abstract #13: Virological Analysis of Severely Immunocompromised Patients Infected with Human Parainfluenza Virus **Trevor Gale, PhD** | *Asun BioPharma*

Background: By cleaving sialic acids (SAs), DAS181 inhibits entry of viruses which utilize SAs as attachment/binding factors or authenticated receptors to initiate the replicative cycle. In preclinical testing DAS181 has shown potent activity against influenza and parainfluenza viruses (PIV). A previously performed post hoc analysis of a phase 2 study of immunocompromised patients requiring supplemental oxygen resultant from lower respiratory tract PIV infection showed treatment with DAS181 gave statistically significant and clinically objective benefit compared to patients receiving placebo. During the course of the study virological specimens were sampled from nasopharyngeal swab, pharyngeal wash, tracheal aspirate, or bronchoalveolar lavage.

Methods: Virologic analysis of samples from patients were analyzed by quantitative reverse transcriptase polymerase chain reaction (qPCR).

Results: Of 110 subjects enrolled, there were 10 (9.1%), 4 (3.6%), 87 (79.1%), and 9 (8.2%) PIV 1, 2, 3, and 4 infections, respectively. There were 755 (60%), 350 (28%), 136 (11%) and 11 (1%) NPS, PW, TA, and BAL samples collected, respectively. Twenty-two patients had more than one sample type taken at the same time. Comparison of viral loads from different specimens reveals a high correlation between NPS and PW while TA have higher values compared with NPS. In the overall study population, there was a day 1 to day 15 delta of 1.660 and 1.011 Log10 viral load in DAS181 and placebo arms, respectively. Patients receiving DAS181 had 0.649 Log10 less virus than placebo on Day 15. In the subgroup with the highest observed clinical benefit there was a day 1 to day 15 delta of 1.475 and 0.341 Log10 viral load in DAS181 and placebo arms, respectively. Subgroup patients receiving DAS181 had 1.134 Log10 less virus than placebo on Day 15.

Conclusion: Virological analyses support the continued development of DAS181 for the treatment of PIV infection in the immunocompromised host.

Abstract #14: COVID-19 Vaccine Responses in Potentially Immunosuppressed Pregnant Individuals **Connor Hague** | *University of Washington*

Background: COVID-19 vaccination is important to protect against morbidity/mortality from SARS-CoV-2 infection among vulnerable groups such as pregnant and immunocompromised individuals. While studies demonstrate safety of the vaccine in both groups, questions remain about vaccine efficacy in individuals who are both pregnant and immunosuppressed. We aimed to evaluate COVID-19 vaccine maternal antibody responses among potentially immunosuppressed pregnant individuals.

Methods: We conducted a prospective cohort study between 2021-2023 among pregnant individuals with 1+ COVID-19 vaccine doses and tested maternal delivery blood samples for anti-Spike (S) antibody concentrations. We defined "immunosuppressed" as those with potentially immunosuppressing medical conditions including immunodeficiencies, autoimmune and inflammatory disorders and those taking immunosuppressive medications. Associations between potentially immunosuppressed status (medical condition or medication use) or immunosuppressive medication use and antibody concentrations were evaluated using linear regression analyses. We included as covariates time from last vaccine dose to delivery, dose number and vaccine type.

Results: We included 35 and 406 potentially immunosuppressed and non-immunosuppressed pregnant people, respectively. Of the 35 potentially immunosuppressed participants, 24 participants were taking immunosuppressing medications. In our linear regression analyses, when adjusting for time between vaccination and delivery and vaccine type, associations between potentially immunosuppressed status and maternal anti-S antibody concentrations were statistically insignificant. However, after also adjusting for number of COVID-19 vaccine doses, potentially immunosuppressed pregnant people had statistically significant lower maternal anti-S concentrations compared to non-immunosuppressed counterparts (beta:-0.92; 95% Confidence Interval [CI]:-1.62,-0.23; p=0.009). When controlling for the same covariates, immunosuppressive medication use was also significantly associated with lower maternal anti-S concentrations compared to non-immunosuppressive medication use (beta:-1.09; 95% CI:-1.92,-0.27; p=0.01).

Conclusions: Maternal COVID-19 anti-Spike concentrations were lower in potentially immunosuppressed compared to non-immunosuppressed pregnant individuals. Higher number of vaccine doses before delivery may have mitigated differences. More research into this highly vulnerable population is needed to optimize vaccine responses during pregnancy.

Abstract #15: Measuring Vaccine Responses following Immunoablative Cancer Therapy using Sequencing Based Neutralization Assays for Influenza **Catherine Jacob-Dolan, PhD** | *Fred Hutch Cancer Center*

Background: Hematopoietic stem cell transplant (HSCT) and Chimeric Antigen Receptor (CAR)-T therapy recipient populations are among the most vulnerable to severe disease caused by respiratory viruses such as influenza. Vaccines remain the most effective form of prevention and protection against influenza infection and disease. It is still poorly understood how well these patient populations respond to influenza vaccines. Furthermore, in healthy individuals, due to the constant evolution of Influenza A Viruses (IAV), immune memory to influenza spans a large range of strains dating back to the first influenza exposures of the individual. It is not known how different immune targeting cellular cancer therapies impact this immune memory and how that shapes responses to subsequent influenza vaccinations.

Methods: To measure responses to influenza strains ranging the span of HSCT or CAR-T therapy recipients' lifetimes we are leveraging cutting-edge sequencing-based neutralization assays to measure neutralization against a whole library of historical influenza strain HAs at once.

Results: Using data from NCBI and GISAID we have generated evolutionary trees of H1 and H3 hemagglutinins. We designed a library of historical HAs which encompass all North American vaccine strains, both the egg adapted and cell-

based versions, as well as representative circulating strains such that at least one strain, is represented every two years for each subtype. The circulating strain sequences have been selected from direct sample sequencing or sequencing from cell-based cultures to avoid egg adapted mutations which would not have been circulating.

Conclusions: This historical flu library is now being constructed, we anticipate the library will be ready for use by the beginning of February at which point we will test samples from healthy control, CAR-T recipient, and HSCT recipient cohorts to ascertain the effect of such therapies on influenza immune memory and vaccine responses.

Abstract #16: Hematopoietic Cell Transplant Recipients Produce More Respiratory Syncytial Virus Antibodies against the Attachment Protein (G) than Fusion Protein (F) Antibodies **Sara Ruth Kim, MD** | *Seattle Children's Hospital*

Background: Hematopoietic cell transplant (HCT) recipients are at high risk for severe complications from respiratory syncytial virus (RSV), including lower respiratory tract infection (LRTI) and death. Novel preventative therapeutics targeting the RSV pre-fusion F protein for infants and elderly adults have not been systematically evaluated for immunogenicity or efficacy in HCT recipients. Additionally, recent literature has identified G protein as a role in immune evasion and therefore, a potential target for future therapies. We sought to compare RSV-specific antibodies against F and G epitopes in HCT recipients with RSV infection using a novel immunosurvey, VirScan.

Methods: We evaluated 39 adult and pediatric allogeneic HCT recipients who acquired RSV from 12/2011 to 12/2019. Serum was collected at least 1 week before (pre-RSV) and 4-6 weeks after (convalescent) the RSV infection. Patients were categorized into 3 groups: URTI only, those who progressed from URTI to LRTI (progressors) and LRTI at diagnosis. We used VirScan, a phage immunoprecipitation sequencing technology, to identify antibodies binding to viral proteins in 56 amino acid segments (epitopes). Each epitope is scored as numeric 'hits' when antibody is detected and with an epitope binding signal (EBS) based on the frequency of detection, which serves as a surrogate for antibody titer. We generated heatmaps of the F and G protein sequences using the EBS for each epitope. F and G epitopes were compared in paired plots using Wilcoxon signed rank tests.

Results: Prior to RSV, we identified minimal antibodies to F epitopes (Fig 1A). During the convalescent phase, we identified an increase in antibodies against F, including regions targeted by currently available vaccines and monoclonals (Fig 1B, epitope range: 197-280). Within G, we identified antibodies targeting the central conserved domain (epitope range: 139-224) in both the transmembrane (Fig 1C-D) and soluble G (Fig 1E-F) epitopes at both timepoints. From the heatmaps, we identified one F and one G epitope with the highest number of hits across all patients. In paired plots, the soluble G epitope had significantly higher EBS than the F epitope (Fig 2).

Conclusions: Antibodies to G epitopes, representing the central conserved domain and the CX3C chemokine motif, were detected at higher levels in HCT recipients prior to and after RSV infection compared to antibodies against F epitopes. Further studies are needed to assess the significance of anti-G antibodies in HCT recipients, especially as vaccine strategies are considered in this population.

Abstract #17: Re-defining Vulnerability to COVID-19 in Cancer Patients: An Analysis of Mortality from the ISARIC WHO Clinical Characterisation Protocol Cancer UK Prospective Cohort Study **Rebecca Lenihan, BMBCh** | *University of Liverpool, United Kingdom*

Background: Meta-analyses show poor COVID-19 outcomes in haematological and lung cancer patients, and those receiving chemotherapy. However, most studies were retrospective with small sample sizes. Older patients face high absolute COVID-19 mortality, but cancer patients under 50 had higher excess mortality compared to contemporaneously matched non-cancer peers. We compared outcomes in hospitalised COVID-19 patients with and without cancer, focusing on cancer type, stage and treatment.

Methods: The International Severe Acute Respiratory and emerging Infections Consortium (ISARIC) Clinical Characterisation Protocol UK (CCP-UK) and Cancer CCP-UK were prospective observational cohort studies. Data were collected between 17.01.2020 and 28.02.2022. The primary outcome was in-hospital mortality within 30 days of a positive SARS-CoV-2 test. Patients with and without cancer were matched by age, sex, co-morbidity, frailty, deprivation

score and country. The study is on the ISRCTN Registry (ISRCTN66726260) and approved by the South Central-Oxford C Research Ethics Committee in England (Ref:13/SC/0149) and the Scotland A Research Ethics Committee (Ref:20/SS/0028).

Results: Of 286,525 inpatients recruited, 27,897 died. Of 4,819 cancer patients, 1,108 solid and 194 haematological cancer patients died. Compared with age-matched non-cancer patients, there was greater excess mortality in patients under 50 (OR 4.71, 95% CI 1.97–9.94) than over 80 (OR 1.20, 95% CI 1.02–1.40). Of 14 patients under 50 who died, 5 did not meet UK clinical vulnerability criteria. Metastatic solid malignancy (p=0.002), systemic therapy (Multivariable OR 1.88 (95% CI 1.28–2.78), p=0.001) and radiotherapy (Multivariable OR 1.81 (95% CI 1.22–2.69, p=0.003) were associated with increased risk of death.

Conclusion: Cancer patients under 50 are clinically more vulnerable to COVID-19 compared to age-matched peers than older patients. Whilst patients receiving chemotherapy met UK clinical vulnerability criteria, we identified patient groups at increased risk of mortality not eligible for early vaccination due to their age, primary malignancy or treatment status.

Abstract #18: Strategizing Inpatient Delivery of Pemivibart: Lessons from a Single-Center Tixagevimab/Cilgavimab Quality Improvement Initiative **Christopher Marino, MD** | *University of Pittsburgh Medical Center*

Background: Monoclonal antibody (mAb) prophylaxis remains a strategy to protect immunocompromised patients from COVID-19 infection. While tixagevimab/cilgavimab (Tix-Cil) was used during the COVID-19 pandemic, its Emergency Use Authorization (EUA) was withdrawn in January 2023. Pemivibart has since been developed as a mAb prophylaxis against contemporary COVID-19 strains, however healthcare systems face operational challenges to optimally and equitably administer it in the outpatient setting. A protocol to administer mAb prophylaxis to new solid organ transplant (SOT), hematopoietic stem cell transplant (HSCT), and chimeric antigen receptor T-cell (CAR-T) recipients during their index hospitalization may enhance delivery of mAb prophylaxis to highest-risk patients.

Methods: We describe a single-center quality improvement initiative to administer Tix-Cil to patients prior to discharge from their index transplant or CAR-T admission. A retrospective analysis was conducted of SOT, HSCT, and CAR-T recipients from January 1, 2022, to January 26, 2023, when the Tix-Cil EUA was in effect. Patients who received Tix-Cil during their index hospitalization underwent chart review and data collection of demographic information, comorbidities, immunosuppressive therapies, COVID-19 vaccination history, and COVID-19 infection outcomes.

Results: Among SOT (n=341), HSCT (n=139), and CAR-T (n=70) recipients, Tix-Cil was administered to 270 of 550 (50.4%) patients during their index hospitalization. Most SOT recipients (263/341, 77.1%) successfully received Tix-Cil during hospitalization, whereas in-hospital Tix-Cil administration rates were lower in HSCT (12/139, 8.6%) and CAR-T (2/70, 2.8%) recipients who often received Tix-Cil prior to hospitalization (HSCT 30/139, 21.6%; CAR-T 23/70, 32.8%). Among in-hospital Tix-Cil recipients (n=277), 258 (93.1%) were vaccinated against COVID-19 and 23 (8.3%) acquired COVID-19 infection within 6 months, of whom seven were hospitalized and three died, though no deaths were attributed to COVID-19.

Conclusion: Our experience suggests that the inpatient administration of pemivibart in SOT, HSCT, and CAR-T recipients may bypass logistical barriers and facilitate access to COVID-19 mAb prophylaxis.

Abstract #19: A Retrospective Descriptive Analysis of Respiratory Syncytial Virus Infection after Allogenic Hematopoietic Stem Cell Transplantation **Anna Nordlander, MD, PhD** | *Karolinska University Hospital, Sweden*

Background: In patients that have undergone allogenic hematopoietic stem cell transplantation (allo-HSCT), respiratory syncytial virus (RSV) may potentially cause severe respiratory tract disease associated with high morbidity and mortality. This study aimed to investigate whether the outcome of RSV infection post allo-HSCT had improved in the last period and if there was an effect of treatment with ribavirin.

Methods: A retrospective cohort of 102 allo-HSCT patients with RSV infection was studied. The patients were identified through a search of positive RSV PCR results at Karolinska University Laboratory from January 2010 to April 2024.

Results: The median time to infection after transplantation was 310 days. In total, 82 patients (78.5% of the total cohort) had upper respiratory tract infections (URTI) at diagnosis of RSV. 8 infections evolved into LRTI (7.8%) while 20 patients (19.6%) were diagnosed at the LRTI stage. 43 patients (42.2%) were treated with ribavirin. 5 out of 31 patients that received ribavirin due to URTI developed LRTI (16.1%), two of these patients required intensive care unit (ICU) admission due to RSV but survived. Untreated patients with URTI, only 2 out of 52 (3,8%) developed LRTI, no death. Patients diagnosed with LRTI, 12 out of 20 patients were treated with ribavirin (60%), of whom one required ICU and died. 19 patients had early infection (60 days post HSCT), 17 out of 19 had URTI of which 4 evolved into LRTI, one required ICU but survived. In total, only 2/102 (2.0%) patients had RSV-attributable mortality; none of these had been treated with ribavirin.

Conclusions: Our results show that RSV infection today has low attributable mortality after allo-HSCT. Data suggests that the morbidity and mortality of RSV-LRTI have decreased compared to earlier studies. Our results suggest that ribavirin has limited effect in preventing development of LRTI in patients treated for RSV-URTI.

Abstract #20: Exanthematous Eruption in a Patient with Known Chronic Graft-vs-Host Disease and Recent Measles Vaccination **Bianca Patel** | *Morehouse School of Medicine*

Background: Measles is a contagious, respiratory viral disease, preventable through a 2-dose measles, mumps, and rubella (MMR) vaccine series. Serious vaccine adverse effects are uncommon, typically seen in immunocompromised patients. We present a rare case of vaccine-associated measles that highlights the considerations of vaccine administration in immunocompromised hosts.

Case Presentation: A 46-year-old man presented to the dermatology clinic with a diffuse rash, revealing an erythematous exanthematous eruption with generalized distribution across the trunk, extremities, and face, alongside erythematous erosions in the buccal mucosa. One week before the rash onset, he received the MMR vaccination, reporting fever, chills, malaise, myalgias, loose stools, and dyspnea the next day. The rash was asymptomatic. The patient has a history of a matched, sibling allogeneic stem cell transplantation for diffuse large B-cell lymphoma 7 years prior. He relapsed disease 1 year later and was treated with donor lymphocyte infusion. Graft-vs-host disease (GVHD) complication was treated with systemic steroids and tapered off. The most recent GVHD flare occurred 1 year prior to the rash presentation with no immunosuppression treatment for the past 6 months. Histopathological skin biopsy results depicted overlapping features of cutaneous GVHD and cutaneous manifestations of measles. Nasopharyngeal and urine PCR was positive for measles. Measles IgM EIA results were positive and IgG results were equivocal. Symptoms resolved with supportive care alone and no contacts developed symptoms.

Conclusion: Vaccine-associated measles is very rare. Notably, there are no reports of viral transmission. In immunosuppressed patients, clinicians must carefully evaluate vaccine administration based on current recommendations and the immunosuppressed state of the patient. Guidelines look towards continuing nonlive vaccinations given the risk of serious infections. However, this may be postponed based on the individual patient. Live-attenuated vaccines should be avoided in patients with GVHD until control has been maintained without immunosuppression for a significant duration.

Abstract #21: T-cell responses to Influenza and RSV vaccination in Allogeneic Haematopoietic Stem Cell Transplant Recipients **Ellen Walsh, MBBCh, MSc** | *St. James Hospital Dublin, Ireland*

Background: Respiratory viruses are a significant cause of morbidity and mortality among allogeneic haematopoietic stem cell transplant recipients (HSCT). Vaccination is one of the most important and cost-effective public health interventions available. There is a lack of information on vaccine immunogenicity in immunocompromised patients due to exclusion from clinical trials assessing vaccine effectiveness. Particularly, there is a lack of research on cellular immune responses to vaccination in this patient cohort. Two vaccines were licensed against respiratory syncytial virus (RSV) in 2023.

Methods: A prospective observational study is being conducted through the 2024/2025 winter season. Allogeneic HSCT

recipients and healthy volunteers were vaccinated with QIV and AS01E–adjuvanted RSVPreF3 vaccine. Peripheral blood was drawn at baseline and post-vaccination at median of 4 weeks. A whole blood multiplex cytokine release assay was performed following overnight stimulation with inactivated influenza A/H1N, A/H3N2 reference antigens, RSV, and positive controls at 37oC.

Results: Preliminary data are described from 6 HSCT recipients and 5 healthy donors are reported. Median time from HSCT was 9 months(range 4-12 months). 3 (50%) remained on low-dose immunosuppression. 83% (5) had a CD4+ T-cell count of<400. All were vaccine-naïve post-transplant.
Interferon-γ and IL-2 production in HSCT recipients were lower than healthy donor samples, however this difference was not significant due to small numbers. HSCT patients were more likely to have a fold increase in production of IFNγ and IL-2 of >1 to A/H1N1 and A/H3N2 despite lower absolute cytokine levels.
Interferon-γ and IL-2 responses to the RSV vaccine increased significantly post-vaccination in both HSCT patients and healthy donors. Production of IFNγ in response to RSV was significantly increased in the HSCT group post-vaccination and IL-2 significantly increased in both groups post-vaccination

Conclusions: This preliminary data supports immunogenicity of RSV vaccination in controls and HSCT recipients in the early post-transplant period.

Diagnostics

Abstract #22: Diagnosis of Invasive Fungal Diseases by Microbial Cell-Free DNA in the Immunocompromised Patient: A Descriptive Review Update **Melissa Kerkelis, MD** | *Mayo Clinic*

Background: Invasive fungal disease (IFD) is a significant cause of morbidity and mortality in immunocompromised patients. Early detection is critical for effective treatment but remains challenging with traditional diagnostic methods. The Karius test (KT), a microbial cell-free DNA next-generation sequencing (mcfDNA-NGS) test allows for detection of circulating fungal DNA and may improve diagnosis of IFD.

Methods: We performed a retrospective review of immunocompromised patients with suspected IFD for which a fungal pathogen was identified on KT at Mayo Clinic. The patient population included those with hematologic malignancies, solid organ transplants, and hematopoietic stem cell transplants. Clinical data, including demographics, comorbidities, laboratory and radiologic investigations and treatment regimens, were collected to assess the diagnostic utility of mcfDNA-NGS in these cases.

Results: A total of 20 patients had positive fungal testing on mcfDNA-NGS. Among them, 12 had hematologic malignancies, with four also having undergone hematopoietic cell transplantation (HCT). Seven patients had solid organs transplants, and one had primary immunodeficiency. The spectrum of fungal pathogens identified included Aspergillus species in four cases, non-Aspergillus molds in seven cases, Candida species in five cases, Pneumocystis in three cases, and endemic mycoses in two cases. Of the invasive mold infections, three had positive histopathology suggestive of invasive fungal disease and one had a positive fungal culture from bronchoalveolar lavage (BAL). In seven patients, the results of KT prompted changes in antifungal therapy. McfDNA-NGS may have helped avoid invasive diagnostic methods in three cases.

Conclusions: These findings highlight the diverse range of fungal pathogens encountered in immunocompromised populations and underscore the need for targeted diagnostic tools. KT may be a useful diagnostic tool for detection of invasive fungal disease in immunocompromised patients, though interpretation of this test should be approached with caution given frequent polymicrobial detection by mcfDNA-NGS (often endogenous flora or viral reactivation).

Abstract #23: Disseminated *M. haemophilum* Infection Involving the CNS in a Patient with History of Renal Transplant **Xaviera Ortiz Soto, MD** | *University of Texas Health Science Center San Antonio*

Background: Mycobacterium haemophilum is a rare pathogen that most commonly causes skin infections and bone and joint infections in immunocompromised people including those with advanced HIV and people with history of organ transplant. Disseminated infection with CNS involvement is rare and highly morbid. Diagnosis of M. haemophilum is challenging given that the organism needs cooler incubation for growth and an iron-enriched culture media.

Case Presentation: We present the case of a 69-year-old woman with history of living donor kidney transplant in 2020 for diabetic nephropathy, with chronic bilateral leg ulcers, who was admitted for ESBL E. coli bacteremia. An MRI brain done due to a pre-admission fall from standing revealed a 10 x 10 x 22 mm FLAIR/T2 hyperintense mass-occupying lesion within the right posterolateral medulla. Given the inability to biopsy the area, plasma microbial cell-free DNA sequencing (Karius test) was obtained and resulted positive for Mycobacterium haemophilum. Subsequent biopsy of the leg ulcers was smear positive for AFB and blood cultures were positive for mycobacterium at 4 weeks of incubation. The patient was started on azithromycin, levofloxacin and rifabutin for disseminated M. haemophilum involving the CNS. A review of the literature identified 7 other cases of intra-cerebral M. haemophilum infection—6 in patients with advanced HIV and 1 in a renal transplant recipient.

Discussion: M. haemophilum disseminated infection involving the CNS is rare and the diagnosis of it can be challenging due to the poor growth of M. haemophilum on standard mycobacterial culture, as well as the inability to safely biopsy lesions within the CNS. This case highlights the utility of the use of metagenomics in making the diagnosis of a rare infection with an atypical presentation.

Abstract #24: Detecting Primary Effusion Lymphoma Using HHV8 Cell-free DNA Methylation Markers **Sabina Pathan, MD, MHS** | *National Institutes of Health*

BACKGROUND: Diagnosing AIDS-related malignancies, including those associated with human herpes virus 8 (HHV8), remains a significant challenge, with current methods relying on risky, invasive procedures. Developing alternative diagnostic methods is crucial. One promising approach involves the detection of methylation differences in cell-free DNA extracted from plasma samples, a method that has proven successful in differentiating healthy conditions from malignant ones for various cancer types.
A novel extension of this technique involves directly examining HHV8-specific methylation rather than host genomic methylation. Within infected cells, HHV8 episomes attach to the host genome, and undergo DNA methylation, whereas virions released from these cells lack methylation. These differences in methylation patterns in viral DNA between those with malignancy and those without could serve as a diagnostic marker. We seek to determine if viral methylation differences exist between patients with untreated and treated PEL (primary effusion lymphoma).

Method: Following from our work in cell free DNA in cancer diagnostics, we have developed a pipeline to evaluate HHV8-specific DNA methylation in patients with PEL. Plasma samples were obtained from four HIV-positive PEL patients, before and after treatment, alongside four pleural and ascitic fluid samples from untreated PEL patients. The pipeline involves cell-free DNA extraction, enzymatic methylation and hybridized to targeted HHV8-specific probes. Samples will then be sequenced with methylation levels at CpG sites on the HHV8 genome calculated as average methylation beta values.

Results: Data analysis is ongoing, with results expected to reveal differential methylation patterns in HHV8-specific CpG sites between untreated and treated PEL samples, and between plasma, pleural, and ascitic fluids.

Conclusions: This study aims to establish HHV8-specific methylation patterns as a non-invasive biomarker for diagnosing and monitoring primary effusion lymphoma. If successful, this approach could reduce reliance on invasive procedures, improving diagnostic options for AIDS-related malignancies.

Abstract #25: Single-Center Organ Procurement Organization Assessment of *Trypanosoma cruzi* Screening in Potential Organ Donors **Stella Radosta, MD, MS** | *University of Texas Southwestern Medical Center*

Background: To minimize the burden of donor-derived T. cruzi infection, in June 2023, the Organ Procurement and Transplantation (OPTN) Board approved a policy to screen all potential deceased donors born in a T. cruzi endemic country. Herein, we describe the post-implementation performance of the policy in a single organ procurement organization in the OPTN Region 4.

Methods: We conducted a retrospective single-organ procurement organization cohort study of all potential deceased

organ donors from 11/12/2023 to 11/11/2024. Donors with risk factors for T. cruzi infection were screened with the Chagas Detect Plus Rapid Test (InBios). A risk factor for T. cruzi infection was defined as being born in an endemic country, being born in a non-endemic area with prior residency in an endemic area, traveling to an endemic area, or being unable to assess. Donors with a positive screening result had confirmatory testing performed by the Parasitic Branch Laboratory of the Centers for Disease Control and Prevention using both T. cruzi enzyme immunoassay (EIA) and immunoblot Trypomastigote excretory secretory antigen (TESA).

Results: A total of 550 potential organ donors were assessed for T. cruzi risk factors. Of these, 75 (13.6%) met the screening criteria and underwent serological testing. Birth in an endemic area was the most frequent risk factor (58,77.3%), with Mexico being the most common country of birth. The median age of screened donors was 50, and 61 (87.1%) were male. Two (2.7%) donors had a positive screening test but tested negative by confirmatory testing. Both donors were born in a non-endemic area but had prior residency in an endemic area.

Conclusion: In this retrospective single-organ procurement organization cohort study, a targeted screening approach for T. cruzi over one year did not identify an infected donor. Larger studies are needed to determine the impact of the OPTN policy.

Pulmonary Complications

Abstract #26: Evaluation of Respiratory Risk Scores for Predicting Outcomes in Lower Respiratory Tract Infections Among Non-Transplant Hematologic Patients **Karolina Bełdzińska-Gądek, MD** | *Medical University of Gdańsk, Poland*

Background: Lower respiratory tract infections (LRTI) are common infectious complications in patients with hematologic malignancies (HM), but clinical outcomes vary depending on etiologic factors and patient features.

Methods: We retrospectively analyzed 115 bronchoalveolar lavage fluid samples (BAL) collected between 2022-2024 from non-transplant patients with symptomatic LRTI and HM. Data on microbiological findings (cultures, PCRs, galactomannan) and clinical outcomes were collected from medical records. A univariate model was used to determine risk factors (RF) for death due to infection by day 90 after BAL. A respiratory risk score (RRS), including RF with an increased hazard ratio (HR) for death, was used to divide the population into three categories – low (0-1), intermediate (2-3), and high (≥4) risk.

Results: Half (56%) of the study population suffered from lymphoid malignancies, and most of the patients were actively treated with immuno-/chemotherapy within 90 days prior BAL. In 24%, prolonged agranulocytosis (> 7 days) and in 42%, lymphopenia (<500 cels/ul) were observed before BAL. Bacterial, viral, or fungal infection was observed in 33%, 28%, 24% respectively and in 33% BAL result was negative. In 11% CMV and in 20% EBV DNA was detected.
Increased risk of death was observed in patients requiring oxygen support HR 4.82 (95% CI 1.73-13.3), with agranulocytosis HR 2.52 (1.01-6.27), probable fungal infection HR 2.61 (1.04-6.5) and EBV DNA in BAL, HR 2.7 (1.04-6.98). Other factors with HR>1.5 (age>65, bacterial pneumonia and lymphopenia) were included in RRS. Day 90 overall survival was 94%, 90% and 50% in low, intermediate and high-risk groups, respectively categorized by RSS, with HR 12.98 (2.90-58.19) when ≥4 of 7 RF were found.

Conclusions: Overall survival of patients with HM depends on multiple risk factors. According to our study EBV detection can be a novel risk factor associated with survival of patients with HM and LRTI.

Abstract #27: Clinical Outcomes in Lung Transplantation in People Living with HIV: A Competing Risk Analysis **German A. Contreras, MD, MSc** | *University of Texas Medical School Galveston*

Background: Little is known about post-transplant outcomes in people living with HIV (PLWH). Traditional survival analysis typically assumes the presence of a single outcome, but in real-world scenarios, multiple competing events can influence survival and other key metrics. This study aims to assess clinical outcomes in PLWH post-LTx using a competing risk analysis to better understand the true incidence of complications and death.

Methods: We conducted a retrospective cohort study of PLWH and non-PLWH, aged 18 and older, who underwent LTx

between 2022 and 2024. Data were collected from 64 healthcare organizations within the TriNetX U.S. Network. We applied the Aalen-Johansen method to estimate the cumulative incidence function (CIF) for three post-transplant outcomes: non-infection complications (e.g., surgical complications), infection complications (CMV, bacterial pneumonia, bacteremia, mycosis, CDI, RSV), and death. The analysis spanned one year after transplantation, stratifying by HIV status.

Results: A total of 63 PLWH and 3,874 non-PLWH were included in the study. The median age at the time of transplantation was 56 years for both groups, with a higher proportion of males (66.1% vs. 59%) and non-Hispanics (71% vs. 67.1%) in each respective cohort. Non-infection complications were the most common outcome in both groups, with similar CIFs (35.3% vs. 32.5%). PLWH had a higher CIF for infection-related complications (25.3% vs. 18.7%) yet a lower mortality CIF (3.8% vs. 6.9%) than non-PLWH. CMV infection was the most frequent infection complication in both groups, with PLWH experiencing a higher incidence within the first year (18.1% vs. 13.6%). Notably, the risk of mycosis was higher in PLWH (5.5% vs. 2.6%), while RSV cumulative incidence was significantly higher in the non-PLWH group $p<0.05$.

Conclusions: PLWH undergoing LTx experience a distinct post-transplant complication profile, particularly regarding infection risks. Despite a higher incidence of infection complications, PLWH had lower mortality within the first year post-LTx, suggesting that further investigation into tailored infection prevention strategies and post-transplant management is warranted. These findings underscore the importance of using competing risk analysis to capture the full spectrum of outcomes in this unique patient population.

Abstract #28: Endobronchial Mass as a Presentation of Mycobacterium Kansasii Infection in Myelofibrosis on Ruxolitinib - A Case Report **Ren Dongdong, MBBS** | *Tan Tock Seng Hospital, Singapore*

Background: Ruxolitinib is a potent Januse Kinase(JAK) inhibitor, improving survival in patients with myelofibrosis[1]. However, it is also associated with significant risk of opportunistic infections including cryptococcus, viruses and mycobacteria[2]. Here we report a case of Mycobacterium kansasii infection presenting as an endobronchial mass in a myelofibrosis patient on ruxolitinib.

Case presentation: A 76-year-old Chinese female with CALR exon 9 mutation myelofibrosis, diagnosed in 2016 and on ruxolitinib since April 2023, presented with intermittent cough for several months. During an admission for fever and cough in October 2023, chest X-ray showed right lower-to-mid zone opacities, which worsened by December 2023. CT thorax in January 2024 revealed a 6.3 × 7.8 × 5.1 cm right lower lobe lesion with soft tissue extension into the bronchus intermedius, causing complete occlusion and consolidation of the right middle and lower lobes, along with multiple right hilar and mediastinal lymphadenopathy suggesting malignancy. Ruxolitinib was discontinued. Multiple bronchoscopies revealed an endobronchial mass in the bronchus intermedius with enlarged lymph-nodes. Histology of the mass showed ulcer with acute on chronic inflammation, while lymph node revealed non-necrotizing granulomas. CT-guided lung biopsy demonstrated granulomatous inflammation but acid-fast bacilli and fungal stains were negative. Tissue cultures subsequently all grew Mycobacterium kansasii. Treatment with rifampicin, ethambutol, and azithromycin was initiated in February 2024. A follow-up PET-CT in May 2024 showed marked improvement, with right infra-hilar mass reduce to 3.3 cm, partial resolution of consolidation, and re-expansion of the right middle lobe. At her last follow-up in September 2024, after seven months of treatment, imaging revealed mild scarring and atelectasis, reflecting significant recovery.

Conclusion: This is the first reported case of non-tuberculous mycobacterium infection presenting as endobronchial mass mimicking malignancy in a patient on JAK inhibitor. Clinician should consider opportunistic infection and atypical presentations in patients receiving ruxolitinib.

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Abstract #29: Single Center Experience with Peri- and Post-operative Mycoplasma/Ureaplasma (Mollicute) Molecular Testing in Lung Transplant Recipients as Part of a Hyperammonemia Syndrome Prevention Protocol **Luke Fenlon, MD** | *University of Utah*

Background: Post-lung transplant hyperammonemia syndrome is linked with Mollicute infection. Peri-operative screening with pre-emptive antibiotics has been proposed as a preventive strategy, however the rate of positive donor/recipient detection, concordance between right and left sided sampling, and likelihood of new recipient colonization after transplant have not been clearly defined.

Methods: We reviewed results of peri-operative donor and recipient testing from August 2023-2024 after the initiation of a testing protocol. Swabs of both the left and right bronchus of donors and recipients were tested using a four target Mollicute PCR (Ureaplasma parvum, Ureaplasma urealyticum, Mycoplasma hominis, Mycoplasma genitalium). We identified positivity rate of donors vs recipients, determined right and left concordance, and examined whether post-transplant BALs identified colonization not detected at the time of transplant.

Results: Of 39 bilateral lung transplants from August 2023-2024, 35 (90%) underwent both donor and recipient PCR. There were no positive PCR results from recipient samples, and 8/38 (21%) of donors were positive for at least 1 PCR target. Combining donor and recipient testing performed bilaterally, 95% (70/74) of lungs had concordant left and right sided testing. The remaining 4 had samples either inhibited or inconclusive (levels of nucleic acid bordering analytical sensitivity or factors influencing sample integrity) for at least 1 target. Of 14 patients that had follow up BAL testing post-transplant, 12/12 with negative initial testing remained negative. One patient that was positive converted to negative, and one patient that was inconclusive in both right and left donor samples for 1 target resulted positive. The median test turnaround time was 67 hours 23 minutes for all tests.

Conclusion: Our results demonstrate and inform feasibility of a PCR based screening protocol. Positive results were exclusively identified from donors, while right and left sided sampling was largely concordant. Results were available within 72 hours.

Best Abstract Oral: Early Host Blood Transcriptional Signatures Predictive of Lower Respiratory Tract (LRT) Disease Progression during Parainfluenza Infection in Hematopoietic Cell Transplant (HCT) Recipients **Fang Yun Lim, PhD** | *Fred Hutch Cancer Center*

Background. Parainfluenza virus (PIV) LRT infection (LRTI) following HCT is associated with increased mortality and post-transplant complications. Clinical risk scores for progression from upper respiratory tract infection (URTI) to LRTI have limited predictive value and early host blood transcriptional signatures may enable early stratification of patients at risk of progression, reducing overall mortality rate and disease burden in HCT recipients.

Methods. Blood samples were collected in HCT recipients at the time of PIV URTI. Subjects were followed for progression to LRTI and classified as: URTI (non-progressors), possible LRTI progressors (upper tract PIV detection with radiographic changes), or proven LRTI progressors (lower tract PIV detection with radiographic changes). Libraries were prepared using TruSeq mRNA Stranded Library Kit and sequenced on the NovaSeq 6000. Linear models of gene expression and comparisons for “possible LRTI vs URTI” and “proven LRTI vs URTI“ were fit using kimma. An adjusted p-value < 0.1 (Benjamini-Hochberg) defined significant genes. Gene ontology enrichment analyses of overexpressed and underexpressed genes were performed using clusterProfiler.

Results. 46 subjects with PIV infection following HCT (2010 - 2019) were included (URTI = 32; possible LRTI = 7; proven LRTI = 7). Robust differences in gene expression (881 genes, Fig. 1A) were observed in URTI samples from proven progressors relative to non-progressors, while possible LRTI progressors showed higher similarity to non-progressors (102 genes, Fig. 1B). Notably, processes involved in rRNA metabolism, ribosome biogenesis, and T cell differentiation were underexpressed in proven LRTI progressors, whereas immunoinflammatory pathways were overexpressed (Fig. 2A and 2B).

Conclusions. We demonstrated that early PIV URTI blood samples can identify predictive signatures of progression to

LRTI in HCT recipients presenting with URTI. Underexpression of T cell immunity and ribosome/rRNA metabolic pathways in proven progressors suggest a protective role in reducing risk of progression to PIV LRTI in HCT recipients.

Abstract #30: Pneumocystis Pneumonia after Chimeric Antigen Receptor T-cell (CAR-T) Therapy: A Systematic Review and Meta-analysis **Bibi Maryam, MD** | *University of Oklahoma Health Sciences*

Background: Chimeric antigen receptor T-cell (CAR-T) therapy represents a new therapeutic option for patients with hematological malignancies. Despite the therapeutic benefits of this intervention, it is associated with multiple side effects, including a higher risk of infection. Patients receiving CAR-T have impairment in their cellular and humoral immune response to infection, which can increase the risk of Pneumocystis pneumonia (PJP). Despite this, data regarding the incidence of PJP in this population remains limited.

Aims: We sought to describe the incidence and outcomes of Pneumocystis pneumonia in patients who received CAR-T therapy for management of hematological malignancies.

Methods: We performed a systematic search in Pubmed, Embase and Medline, and included observational studies that reported the incidence of Pneumocystis pneumonia (PCP) in cohorts of patients who CAR-T therapy for management of hematological malignancies. Case series and case reports were excluded, as well as studies with a follow up period of less than 30 days. Data extracted from studies meeting inclusion criteria was pooled in a single-arm, proportion meta-analysis for the outcomes of interest (incidence of PCP, incidence of PCP between 30-180 days after infusion date, incidence of PCP more than 180 days after infusion date and mortality in patients with PCP). A random effects model was used considering the high heterogeneity of observational studies.

Results: We screened 6209 studies, and 17 studies were included in the final analysis, with a total cohort of 1942 patients. 13 out of 17 studies specified the CAR-T product used, which was a CD19 CAR-T therapy. PJP prophylaxis was described by 9 out of 17 studies, and Trimetroprim-Sulfametoxazole (TMP-SMX) was the most common agent prescribed. The pooled incidence of Pneumocystis pneumonia was 9.7 cases per 1,000 patients included (0.97%, CI-95% 5-18.7). A sensitivity analysis was performed with exclusion of study from Melica et al (2024), and pooled incidence of PCP was 12.4 cases per 1,000 patients included (1.24%, CI-95% 8-19.2), with unsignificant heterogeneity after sensitivity analysis. Analysis of other outcomes, performed with exclusion of the study from Melica et al (2024), reported: a pooled incidence of PCP between 30 to 180 days after CAR-T infusion of 2.7 cases per 1,000 patients (0.27%, CI-95% 0.3-2.09); a pooled incidence of PCP more than 180 days after CAR-T infusion of 8.1 (0.81%, CI-95% 4.1-16.2); pooled mortality among patients with PCP was 22% (CI-95% 5.6-57.9).

Conclusions: Patients treated with CAR-T therapy are at risk for multiple infections. Pneumocystis pneumonia occurs in this population, after 30 days of infusion, and with predominance after 180 days of infusion. Despite its low incidence, mortality in patients with PCP remains significantly high.

Cellular Therapy & HHV-6

Abstract #31: Incidence of Sexually Transmitted Diseases in Patients Undergoing Hematopoietic Stem Cell Transplantation and Chimeric Antigen Receptor T-Cell Therapy: A Large Database Analysis of the United States Data **Chia-Yu Chiu, MD** | *University of Colorado*

Background: As hematopoietic stem cell transplantation (HSCT) and chimeric antigen receptor T-cell (CAR-T) therapy survivorship increases, it is essential to investigate sexually transmitted diseases (STDs) in this population. We aimed to study the incidence and predictor of STDs in these populations.

Methods: We queried the TriNetX research database in December 2024 to evaluate the incidence of syphilis, gonorrhea, chlamydia, and trichomonas among HSCT and CAR-T recipients. The diagnosis was made using the ICD-10 code, and the laboratory LOINC code was used to confirm the STD diagnosis. Age categories were defined as young (18–40 years), middle-aged (41–64 years), and older adults (≥65 years). Geographic regions were classified into Northeast, Midwest, South, and West. Multivariate analysis was used to identify predictors of positive STD testing.

Results: Only 5% (3,692/79,158) of HSCT and 6% (180/3,152) of CAR-T recipients underwent at least a single STD test. In the HSCT group, the incidence rates of syphilis, gonorrhea, chlamydia, and trichomonas were 3% (75/2,438), 0.5% (8/1,463), 1% (15/1,553), and 6% (39/684), respectively. In the CAR-T group, the incidence rates were 3% (4/129), 2% (1/58), 14% (8/58), and 6% (4/68), respectively. Multivariate analysis identified the following independent predictors of STDs in the HSCT group: young adult age (odds ratio [OR] 2.1), Asian (OR 2.9), residence in the Northeast (OR 3.1) or West (OR 5.6), history of STDs before transplantation (OR 4.5), and urogenital symptoms at the time of testing (OR 5.7). In the CAR-T group, Black/African American (OR 7.5) and residents in the West (OR 11.7) were identified as independent predictors of STDs.

Conclusions: STD testing was infrequently performed in HSCT and CAR-T populations. However, when performed, the predictors of positive results were generally similar to, though not entirely consistent with, those seen in the general population.

Abstract #32: Preventing Donor-derived HHV-8: Is Screening with Serology Enough? **Julie England, MD, MPAS** | *University of Texas Southwestern Medical Center*

Several donor-derived human herpesvirus-8 (HHV-8) related diseases have been reported, including Kaposi sarcoma and Kaposi Sarcoma-associated herpesvirus inflammatory cytokine syndrome. Herein, we describe a proven episode of donor-derived HHV-8 from a donor who retrospectively tested negative for HHV-8 by serology.
The patient is a 64-year-old female with a past medical history of FSGS-induced end-stage renal disease status post deceased donor kidney transplant 2.5 years ago, complicated by antibody-mediated rejection at four and twenty-four months, treated with methylprednisolone. After the second episode, she developed ascites. Ultimately, exploratory laparotomy revealed violaceous lesions on bilateral ovaries. Pathology and diagnostic markers (CD31, D2-40, HHV-8 positive) were consistent with Kaposi sarcoma. The recipient had no risk factors for HHV-8 infection and retrospectively tested negative for HHV-8 by serology in an archived pre-transplant sample. The donor also tested negative for HHV-8 by serology. The donor was a male who had sex with males, and his partner had well-controlled HIV. Given high suspicion for donor-derived HHV-8, nested PCR was performed on donor peripheral blood mononuclear cells targeting the viral LANA and ORF26 genes. The results were positive, confirming the donor-derived event. There were no other recipients from this donor. The patient's immunosuppression was changed from mycophenolate, tacrolimus, and prednisone to everolimus and prednisone, with improvement in ascites and PET imaging.
To our knowledge, this is the first case of confirmed donor-derived HHV-8-related disease from a donor who initially tested negative for HHV-8 by serology. This raises important questions regarding the optimal strategy to screen donors for HHV-8 infection. Prospective studies assessing the yield of multiple testing modalities are needed to minimize the burden of donor-derived HHV-8.

Abstract #33: Altered Expression of IgG and FcRn in Intestinal Tissue of Hematopoietic Stem Cell Transplant Recipients **Lea Kipnis** | *Fred Hutch Cancer Center*

Background: Previous data have shown that monoclonal antibody (mAb) exposure may be reduced in hematopoietic stem cell transplant (HCT) recipients, potentially due to increased gastrointestinal (GI) clearance in patients with GI graft-versus-host-disease (GVHD). Thus, we hypothesized that antibodies overall are cleared more rapidly in patients receiving an allogeneic HCT compared to autologous HCT recipients, as allogeneic HCT recipients are at a higher risk of GI protein loss due to GVHD. Here, we investigate if total immunoglobulin G (IgG) and neonatal Fc receptor (FcRn) distribution in the GI tract differ between autologous vs. allogeneic transplant patients with GVHD involving the GI tract.

Methods: Tissue biopsies of small and large intestines were obtained from autologous and allogeneic HCT recipients. Allogeneic HCT recipients were further grouped based on severity of GVHD (0=none, 1=mild, and 2=moderate/severe/life-threatening). Samples were stained for nuclei, endothelial cells (CD31), total IgG, and FcRn. Stained samples were analyzed using HALO image analysis software. The percentage of the analyzed area that stained positive and median intensity were graphed to compare the amount and distribution of IgG and FcRn present in tissue from autologous and allogeneic HCT recipients with different GI GVHD severity.

Results: Allogeneic HCT recipients with worse GI GVHD tended to have decreased levels of FcRn in the small intestine

but not the large intestine, as compared to recipients of autologous HCT. Additionally, allogeneic HCT recipients with more severe GI GVHD tended to have lower total levels of IgG in the small and large intestine, as compared to autologous HCT recipients or allogeneic HCT recipients with only mild GI GVHD.

Conclusions: This data shows that allogeneic HCT recipients may have lower levels of total IgG and FcRn expression in the small intestine and large intestine, as compared to autologous HCT recipients. More data from future studies is needed to determine statistical significance.

Abstract #34: Neutrophil Function against *Candida albicans* is Preserved following Reduced-Intensity Conditioning and Allogeneic Stem Cell Transplant **Maria Lampou** | *Massachusetts General Hospital*

Background: Neutrophils are essential immune effector cells against fungal pathogens, including Candida albicans. In the early period after allogeneic stem cell transplant (allo-SCT), clinicians monitor the absolute neutrophil count (ANC) to assess for myeloid engraftment as well as prognosticate the overall risk for systemic infections [1]. However, neutrophil function after allo-SCT is not well understood. A prior study from our lab demonstrated impaired neutrophil function in patients who underwent fully myeloablative and reduced-intensity conditioning (RIC) regimens [2]. In our current study, we focus on RIC allo-SCT patients. We hypothesized that neutrophil function remains impaired with RIC after transplant compared to healthy controls.

Methods: Peripheral blood samples were collected from patients at day +30 to +70 (median: day +47) after RIC allo-SCT and from healthy donors. Four neutrophil functions were assessed by flow cytometry: phagocytosis, degranulation, reactive oxygen species (ROS) formation, and ectodomain shedding. Red-fluorescent protein expressing C. albicans was diluted at a multiplicity of infection (MOI) 1,2,4,8. ROS production was measured with dihydrorhodamine-123, while anti-CD62L and anti-CD66 antibodies indicated neutrophil ectodomain shedding and degranulation, respectively. After incubation of neutrophils with C. albicans and antibody staining, a multiparametric flow cytometry-based assay was used to detect neutrophil functional outputs.

Results: Twenty-three (N=23) patients were included. The most common underlying malignancies were non-Hodgkin lymphoma and acute myeloid leukemia (6/23 patients, 26% each). Most patients underwent peripheral blood matched unrelated donor transplants (20/23, 87%). Most patients underwent conditioning with fludarabine/melphalan (22/23 patients, 96%), followed by post-transplant cyclophosphamide and tacrolimus for graft-versus-host disease prophylaxis. Median ANC was 4.93. Neutrophil functional assessment showed no significant differences between RIC patients and healthy controls, with both groups exhibiting increased functions with higher C. albicans challenges, but without statistical difference. These results suggest that patients undergoing a non-myeloablative regimen may retain functional neutrophils, contributing to bone marrow recovery.

Conclusion: Contrary to our hypothesis, neutrophil function early after RIC allo-SCT was not impaired compared to healthy controls at two months post-engraftment. Future studies with larger patient cohorts are needed to define neutrophil function at earlier time points and more traditional ablative regimens.

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Abstract #35: Decoding Low HIV Viral Reservoirs: Insights from 3 US Cohorts of People Virologically Suppressed on ART **Nancy Liu** | *Morehouse School of Medicine*

Background: People with HIV (PWH) receiving antiretroviral therapy (ART) can achieve durable suppression of viremia, but persistent HIV reservoirs pose a barrier to cure. Low Viral Reservoir Treated (LoViReT) persons can provide insight

into mechanisms involved in HIV reservoir control. We identified clinical factors associated with viral reservoir size across three cohorts of PWH virologically suppressed on ART.

Methods: We measured total HIV-1 DNA in peripheral blood mononuclear cells from 75 PWH virologically suppressed on ART from three cohorts: RID (Emory; n=40), DoD (Military; n=28), and CNICS (CFAR national; n=7). Backward model selection evaluated relationships among 30 clinical, immunologic, and virologic variables with reservoir measures. RID and DoD cohorts were analyzed separately; pooled analyses included all cohorts.

Results: Participants had a mean age of 48 years (±13); 71% were African American, and 20% were White. In the RID cohort, 90% were African American, half were women, 28% had history of tuberculosis, and 7.5% had history of pneumocystis pneumonia. In the DoD cohort, all were men, half were African American, and 11% had history of CMV. For RID, minimum CD4:CD8 ratio (β = -1.74 [95% CI, -2.7 to -0.7]) was inversely associated while time to virologic suppression (0.36 [95% CI, 0.08 to 0.6]) was directly associated with reservoir size. For DoD, %CD4 at suppression (-1.64 [95% CI, -2.9 to -0.4]) was inversely associated with reservoir size. In pooled analyses, minimum CD4:CD8 ratio (-1.77 [95% CI, -2.8 to -0.8]) showed an inverse association while time to virologic suppression (0.43 [95% CI, 0.2 to 0.7]) was directly associated with higher reservoir size.

Conclusions: Minimum CD4:CD8 ratio and time to virologic suppression were associated with HIV reservoir size, highlighting rapid virologic suppression as a predictor of LoViReT status. Association with minimum CD4:CD8 ratio emerged as a novel finding, expanding prior findings from European cohorts.

Abstract #36: A Retrospective Study on Infection-Related Mortality after Outpatient CAR-T Cell Therapy **Bibi Maryam, MD** | *University of Oklahoma Health Sciences*

Background: CAR T cell therapy is a major development in cancer therapeutics in the past decade; however, infections remain a significant complication and a leading cause of mortality in CAR T cell recipients. This study aims at describing the timing, risk factors and predictors of infection-related mortality after CAR T.

Methods: This is a single-center, retrospective analysis of all adult patients who received FDA-approved CAR T cell products in an outpatient setting between September 2019 and July 2024 at the OU Health Stephenson Cancer Center. Descriptive statistics were created for both continuous and categorical variables. Chi-Square analysis and independent samples t-tests were used to measure association with infections and response (CR vs Other). Logistic regression was used to explore these associations for all covariates with each outcome. SAS 9.4 was used to perform all analysis. An alpha of 0.05 was used to determine significance.

Results: Out of 108 patients who received CAR T cell therapy during the study period, 11 patients (8.8%) died due to an infection, at a median of 295 days after CAR T (IQR 119-515 days), of which 3 deaths occurred in the first 60 days. These included 5 bacterial infections (C difficile, E. coli, Klebsiella pneumoniae ESBL, MRSA, and MSSA), 3 viral infections (Adenovirus, SARS-CoV-2, and co-infection with PIV-3 and HSV), and 2 fungal infections (Candida krusei and Cryptococcus neoformans). For these 11 patients, average length of stay (LOS) in hospital was 21.91 days, and 10 were admitted to ICU, for which average LOS in ICU was 6.64 days. Mean duration of infection for these patients was 8 days. We observed that 7 out of 11 patients had relapsed malignancy at the time of infection. Before adjustment of number of prior lines, lymphocyte count and ICANS was associated with infections in the first 100 days of receiving therapy. After adjustment only neutrophil count and prior transplant was associated with infection.

Conclusion:
Relapse is associated with increased risk of infection and infection-related mortality after CAR-T therapy. Additionally, we found evidence that having a prior transplant and neutrophil count contributed to different odds of infection. Continued study of these findings is warranted.

Best Abstract Oral: Incidence of Breakthrough HSV in Adult Allogeneic Hematopoietic Cell Transplant Recipients on Standardized Antiviral Prophylaxis **Ria Mohan** | *Virginia Commonwealth University*

Background: Reactivations of herpes simplex viruses (HSV) can occur in the early post-allogeneic hematopoietic cell transplant (aHCT) period despite universal antiviral prophylaxis. Few studies have assessed HSV recurrence in the era of standardized antiviral prophylaxis, in which val/acyclovir is recommended for up to 1 year post aHCT. We evaluated the incidence and management of clinical HSV during the first 100 days post-aHCT over two decades.

Methods: All aHCT recipients at Fred Hutchinson Cancer Center between 2002-2022 were reviewed to determine the incidence of HSV within the first 100 days on prophylaxis (acyclovir 800 mg or valacyclovir 500 mg twice daily). HSV cases were identified via viral culture, polymerase chain reaction, and/or direct fluorescent antibody testing, and clinical records were reviewed for symptoms, clinical outcomes, use of prophylaxis, and treatment regimens. Resistance was categorized as clinical (presumptive) or virologically-proven.

Results: We reviewed data from 4,358 aHCT recipients aged ≥18 years, among whom 3,749 (86%) were HSV seropositive and 30 developed HSV recurrence (cumulative incidence = 0.8%). Most (n=21) reactivations were HSV-1 and 9 were HSV-2; 2 were unspecified. The median time from transplant to first positive test was 35 days (IQR: 19-74 days). HSV was detected at multiple anatomic sites; oral recurrences were most common. In total, 14/30 (46.7%) patients developed acyclovir-resistant HSV (8 virologically confirmed, 6 clinical). Treatment duration was significantly shorter for patients with susceptible (median 21 days [IQR: 14-25]) compared to resistant infections (38 days [IQR: 25-57.5], p = 0.02). Few patients (n = 4) had recurrences attributed to non-adherence/malabsorption.

Conclusions: HSV complications are rare in aHCT recipients receiving standardized antiviral prophylaxis. These findings highlight the importance and effectiveness of universal val/acyclovir coverage in the early post-transplant period. Although rare, resistant infections remain challenging.

Abstract #37: Immune Response to Routine Vaccination in Patients after CAR-T Cell Therapy for B Cell Malignancies
Stosh Ozog, MD PhD | *Fred Hutch Cancer Center*

Background: The immunogenicity of routine vaccines after B-cell chimeric antigen receptor T cell therapies (CARTx) is largely unknown beyond SARS-CoV-2 vaccines.

Methods: We prospectively enrolled patients who received CARTx for B-cell malignancies and were in remission. We obtained blood pre- and post-clinically administered vaccinations. We measured pathogen-specific IgG titers, as well as pre-vaccination immunoglobulins and B and T cell subsets. Samples obtained within eight weeks after IVIG infusion were excluded.

Results: Among 72 patients, 60 (83%) received CD19/20-CARTx and 12 (17%) received BCMA-CARTx with a median age of 59 years (range, 15-79). First vaccination occurred a median of 8.6 months (IQR, 7.1-13.6) after CARTx. Participants received a median of 5 unique vaccinations (IQR, 5-6) targeting 6 pathogens (IQR, 5-8), with a median of 2 doses (IQR, 1-3) per vaccine. Prior to vaccination, IgG, IgM, and CD4+ T cells were similar across participants; CD19+ B-cells were lower in CD19/20-CARTx recipients. Most pre-vaccine pathogen-specific IgG levels were quantitatively lower in BCMA-CARTx recipients, although the proportion of patients with seroprotective titers were similar. Among 58 participants seronegative pre-vaccine, 37 (64%) had a ≥2-fold increase in pathogen-specific IgG titers post-vaccination for at least one pathogen (BCMA 7/10, 70%, CD19/20 30/48, 63%). In multivariate Cox modelling of a subset of 5 pathogens, BCMA-CARTx recipients (adjusted HR, 2.53; 95% CI: 1.05-6.08; p=0.04) and those with higher CD19+ B-cell counts (adjusted HR per log10 increase, 2.16; 95% CI 1.44-3.23; p<0.001) were more likely to achieve a ≥2-fold increase in titers.

Conclusion: In this cohort of CARTx recipients initiating routine vaccines after treatment, BCMA-CARTx recipients were more likely to achieve a ≥2-fold increase in titers compared to CD19/20-CARTx recipients. CD19+ B cell count was the primary immunologic predictor of response to vaccination.

Bacterial Resistance-Microbiome

Abstract #38: "To Draw or Not to Draw": Does Obtaining Peripheral Blood Cultures Change Outcomes in Febrile Neutropenia in Children with Cancer?
Muayad Alali, MD | *Indiana University*

Background: The utility of peripheral blood cultures (PC) in managing febrile neutropenia (FN) in children with cancer remains unclear, with recent pediatric FN guidelines identifying this as a research gap. While systematic reviews show that PC detects 8–17% of true bacteremia cases when central venous catheter (CVC) cultures are negative, its clinical relevance is often questioned, leading to practice variability and reluctance among clinicians.

Methods: This single-center retrospective study at Riley Hospital for Children analyzed FN episodes in pediatric hematology-oncology and stem cell transplant patients (January 2017–December 2023). Episodes with paired PC and CVC cultures were included, excluding contaminant or culture-negative episodes. Outcomes assessed included PC bacteremia detection, changes to empiric therapy, missed bacteremia treatments due to lack of PC, influence on CVC removal, PICU admissions within one week, and contamination rates.

Results: Among 1,683 FN episodes with paired PC and CVC cultures, 223 episodes (13.3%) were microbiologically confirmed as bacteremia. Of these, 33 episodes (14.8%) had bacteremia detected exclusively by PC, 63 episodes (28.3%) by CVC alone, and 127 episodes (57.0%) by both. Episodes with PC positivity alone prompted empirical therapy modification in 12 cases (36.4% of the PC positive/CVC culture-negative group, 5.4% of the total FN episodes with bacteremia). PICU admission was required in five cases (2.2%) and CVC removal in 3 cases (1.3%) of FN episodes with PC positivity alone. Additionally, 17 episodes (7.6%) would have risked incomplete bacteremia treatment if PC was not obtained due to early ANC recovery in the FN episode which would have resulted in the cessation of empiric antibiotic therapy. Contamination rates were comparable between PC (4.0%) and CVC (3.5%).

Conclusion: PC enhances bacteremia detection and guides key management decisions in pediatric FN, supporting their inclusion in diagnostic protocols. Prospective validation is needed.
Word count= 293

Abstract #39: An International Survey Establishing Current Infection Prevention and Surveillance Practice in the Care of the Australasian Cancer and Transplant Population (INTERACT Study) **Priya Garg, MBBS** | *Peter MacCallum Cancer Centre, Australia*

Background: Cancer and transplant patients are a globally expanding immunocompromised host (ICH) subgroup with significant vulnerability to opportunistic and healthcare-associated infection, leading to substantial morbidity, mortality and healthcare expenditure. With growing use of novel immunosuppressants and prolonged survivorship, infectious risks continue to amplify. Approaches to infection prevention and control (IPC)/ surveillance for the high-risk ICH are non-standardised across Australian healthcare facilities (HCFs), and guidelines limited internationally.

Methods: A cross-sectional survey was performed among infectious disease (ID), microbiology and IPC specialists caring for adult cancer (oncological/haematological) and transplant patients in Australasian HCFs. This aimed to determine knowledge and IPC/ surveillance practice.

Results: 140 healthcare workers (HCWs) from all Australian jurisdictions and New Zealand responded, predominantly physicians (60.7%) employed in public (95.7%), metropolitan (78.6%) non-specialist (77.8%) HCFs. Despite the majority having on-site IPC (95.7%), few had an ICH-ID service (40.7%) or followed ICH-specific IPC guidelines (35.0%). HAI surveillance was frequent (75.7%), however monitoring for infectious opportunists uncommon (22.9%). Although 51.4% of respondents reported a mask-wearing mandate for HCWs on the ICH ward, primarily surgical-masks (75%), there was minimal agreement on the appropriate clinical setting for routine use, visitor (34.3%) or patient (15.0%) masking. A smaller proportion (19.3%) employed universal gown and glove use, principally in neutropenia (70.4%). There was additionally no consensus on routine multi-drug-resistant organism screening strategy, including for pathogenic threats such as C. auris. HCF resources were also limited; although 77.9% had single rooms, fewer reported positive-pressure (40.7%) or HEPA-filter (37.9%) capacity, with variability in routine indication for use. Challenges to ICH-IPC including infrastructure and lack of definitive policy were also expressed.

Conclusion: This is the first survey of IPC/surveillance practice in the Australasian high-risk ICH population, demonstrating multiple key areas of heterogeneity and highlighting the need for standardisation. Evidence-based consensus policy will help optimise care of the ICH and reduce preventable infectious disease.

Abstract #40: Minding the Gap: Impact of Sulfonamide Allergy Label in Kidney Transplant Recipients **Jennifer Hu, MD** | *University of Washington*

Background: Sulfonamide allergy labels (SAL) affect 8% of the population; these labels impact prescribing. Recent studies demonstrate increased risk of opportunistic infections in patients with SAL following solid organ transplantation; alternate prophylaxis regimens are also associated with increased costs. In 2023, a widely used penicillin allergy tool (PEN-FAST) was adapted and validated as a trimethoprim-sulfamethoxazole (TMP-SMX) allergy decision rule (SULF-FAST), with scores <3 associated with low risk for hypersensitivity. This study aims to describe the impact of SAL on clinical outcomes in kidney transplant recipients at UW Medicine and identify missed opportunities for de-labeling.

Methods: This is a single center, retrospective, descriptive study. Adult kidney transplant recipients transplanted March 21, 2021 to December 31, 2024 (1) with sulfonamide allergy label, (2) receiving non-TMP-SMX prophylaxis, and (3) with >6 month follow up were included. Data regarding prophylaxis regimen, SAL, allergy consultation, complications from alternate therapy (Pneumocystis pneumonia, dapsone related anemia, methemoglobinemia, Toxoplasmosis), and TMP-SMX-preventable urinary tract infection within 6 months were collected. SULF-FAST score was calculated for each patient.

Results: Of 24 adult kidney transplant recipients with SAL, 23/24 received non-TMP-SMX prophylaxis: dapsone (19), atovaquone (2), pentamidine (2). While 13/24 patients had low-risk SAL by SULF-FAST score, only 3 received allergy evaluation, all occurring only after recommendation by Infectious Diseases. 6/23 (26%) patients developed adverse effects from alternate therapies, including dapsone induced methemoglobinemia (2/19), anemia/hemolytic anemia (3/19), and dyspnea requiring discontinuation of inhaled pentamidine (1/2). Within 6 months of transplant, use of alternate prophylaxis resulted in 14 potentially avoidable courses of antibiotics for urine organisms sensitive to TMP-SMX. None developed Pneumocystis pneumonia nor Toxoplasmosis.

Conclusions: SAL impacts antimicrobial prescribing and has downstream effects on clinical outcomes. Measures to evaluate and de-label SAL, including better documentation of allergies, can offer benefits for outcomes and antibiotic stewardship, and should be considered as part of routine pre-transplant evaluation.

Abstract #41: Trending Intestinal Microbiome and Metabolome Fluctuations in Patients Receiving Intense Chemotherapy for Aml: Results from A Pilot, Prospective Observational Study **Sabrina Imam, MD** | *University of Chicago*

Loss of a diverse intestinal microbiome, particularly through the depletion of anaerobic bacteria, is associated with poor outcomes in people undergoing treatment for leukemia. We present preliminary results from a pilot, prospective observational study characterizing longitudinal changes in the fecal microbiome and metabolome in patients undergoing intensive chemotherapy for newly diagnosed acute myeloid leukemia (AML) with the goal of identifying biomarkers associated with disrupted microbiomes.

Methods: We recruited 14 patients with newly diagnosed AML. The subjects underwent daily serum and stool collections during the admission for induction chemotherapy and periodic serum and stool collections during subsequent admissions. Metabolome profiling was conducted by targeted GC- and LC-mass spectrometry of serum and stool specimens, and fecal microbiome composition was determined by Shotgun metagenomic sequencing. Clinical characteristics, including responses to chemotherapy and development of infections, were monitored.

Results: Metagenomic sequencing demonstrated marked variations in microbiome compositions between patients in our cohort. However, microbiome compositions and diversities remained stable within patients who maintained a higher prevalence of obligate anaerobes belonging to the Lachnospiraceae and Bacteroidaceae families. In contrast, patients who lost obligate anaerobes in their intestinal microbiomes were more prone to colonization by pathobionts. Moreover, we detected large fluctuations in fecal metabolite concentrations, particularly among secondary bile acids and conjugated and unconjugated bile acids, over the course of induction chemotherapy. Correlations between metabolites, microbiome shifts, and clinical events are ongoing. Our results suggest that preservation of intestinal anaerobes enhances the stability of the microbiome over time.

Future directions: We will examine trends in how the microbiome is reconstituted after periods of disruption, particularly as patients transition in and out of the hospital. We also plan to use broad targeted and untargeted platforms to identify metabolites in stool or serum that can be used as biomarkers to correlate with microbiome compositions.

Abstract #42: CYP2C19 Pharmacogenomic Voriconazole Dosing: Impact on Clinical Management and Level Attainment
Julian Lindsay, BPharm, MClinPharm, PhD | *Fred Hutch Cancer Center*

Background: Pharmacogenomic testing of CYP2C19 is a potential tool to optimize dosing of voriconazole (VCZ), a drug with a narrow therapeutic index and interpatient variability. An onsite CYP2C19 assay was developed to improve the accessibility and turnaround time of results. In this pilot study, we evaluated the utility, clinical impact and level attainment of antimicrobial stewardship (AMS)-guided CYP2C19 testing.

Methods: Starting 5/1/2022, the AMS team provided recommendations regarding CYP2C19 testing and dosing for selected patients receiving VCZ at our comprehensive cancer center. We conducted a retrospective chart review of all adult cancer patients with a VCZ order between 5/1/2022 and 10/31/2023 and captured clinical characteristics, result turnaround time, VCZ dose adjustment and therapeutic levels.

Results: Among 239 patients prescribed VCZ that were eligible for CYP2C19 testing, 23 (10%) were tested for CYP2C19, 10 at time of VCZ initiation, 2 when restarting a VCZ course, and 11 with ongoing VCZ following sub/supratherapeutic levels. In 6/23 (26%) patients, VCZ management was impacted by guiding dose change or alternative antifungal based on CYP2C19 genotype. Of 11 patients with initial sub/supratherapeutic VCZ levels before testing, 5/11 were CYP2C19 ultra/rapid metabolizers; 10/11 either changed or confirmed management based on CYP2C19 genotype. Of these, 7/10 had a therapeutic level after first dose adjustment, while 3/10 changed antifungal. The median time from CYP2C19 order to results was 4.3 days. Therapeutic level attainment at between CYP2C19 patients and those without CYP2C19 testing are pending and will be reported.
Conclusion: AMS-guided onsite CYP2C19 testing impacted clinical management of VCZ dosing or selection of alternative antifungals. While our data suggest its utility in patients with sub/supratherapeutic levels, further research is needed to evaluate its role in guiding initial VCZ dosing in high-risk patients.

Abstract #43: Effectiveness of Non-Quinolone-Based Antibiotic Prophylaxis in Pediatric Acute Myeloid Leukemia with High-Dose Cytarabine-Containing Chemotherapy
Toshihiro Matsui, MD, PhD | *National Center for Child Health and Development, Japan*

Background: Children with acute myeloid leukemia (AML) receiving chemotherapy that includes high-dose cytarabine (HiDAC) are highly susceptible to bacterial infections. While quinolones are commonly used for antibiotic prophylaxis (AP), evidence on the efficacy of alternative strategies remains limited. This study aimed to evaluate the effectiveness of non-quinolone-based AP following HiDAC-containing chemotherapy in children with AML.

Methods: Children (0–18 years) newly diagnosed with AML between January 2009 and December 2020 at our center were included. Patients with acute promyelocytic leukemia or Down syndrome were excluded. The incidence of bacteremia and the frequency of febrile neutropenia (FN) within 30 days of each HiDAC-containing chemotherapy cycle were retrospectively compared between those receiving non-quinolone-based AP and those without AP.

Results: A total of 108 chemotherapy cycles (87 with AP and 21 without AP) involving 35 patients were analyzed. AP was administered in 51% (19/37) of cycles from 2009 to 2014 and 96% (68/71) from 2015 to 2020. Intravenous piperacillin was used in 84% of cycles before 2015, whereas intravenous ampicillin was preferred in 91% after 2015. In univariate analysis, the incidence of overall bacteremia (9% vs. 19%; p=0.24) and that of bacteremia caused by antimicrobial-resistant bacteria (2% vs. 5%; p=0.48) showed no significant difference between groups. However, α-streptococcal bacteremia occurred significantly less frequently in the AP group (0% vs. 10%; p=0.036). In addition, FN was less common in the AP group (84% vs. 100%; p=0.067), and the median duration of neutropenia was significantly shorter with AP (17 days vs. 24 days; p=0.001). Acute respiratory distress syndrome was not observed in any case.

Conclusion: Non-quinolone-based AP in children undergoing HiDAC-containing chemotherapy for AML demonstrated potential in reducing α-streptococcal bacteremia and FN. Given the growing threat of antimicrobial resistance, this strategy may offer a promising alternative to broad-spectrum AP for this patient population.

Abstract #43.5: Effectiveness of Non-Quinolone-Based Antibiotic Prophylaxis in Pediatric Acute Myeloid Leukemia with High-Dose Cytarabine-Containing Chemotherapy **Toshihiro Matsui, MD, PhD** | *National Center for Child Health and Development, Japan*

Background: *Aeromonas* species, pathogens commonly found in freshwater, pose a high risk of fatal infections, in patients with liver dysfunction or immunosuppression. Whether similar risks exist in liver transplant recipients (LTrs) remains unclear. This study aimed to describe the clinical features of *Aeromonas* bacteremia in liver transplant recipients.

Methods: A retrospective review was conducted at the National Center for Child Health and Development, the largest pediatric liver transplant center in Japan, covering cases from 2002 to 2023. Demographic, clinical, and microbiological data were extracted from electronic medical records.

Results: Among 743 pediatric LTrs, five cases of *Aeromonas* bacteremia (0.67%) were identified. The median age at onset was 7 years (range: 4–26 years), occurring a median of 6 years post-transplantation (range: 2 months–24 years). Biliary atresia was the most common underlying condition requiring liver transplantation. Four patients received grafts from living donors and one from a deceased donor, with all undergoing biliary reconstruction using choledochojejunostomy. All patients were on calcineurin inhibitor-based immunosuppression and none had significant liver dysfunction or severe neutropenia prior to the onset of bacteremia. Most infections were community-acquired, occurring during summer, and three patients reported freshwater exposure. Fever was a common symptom, with two patients experiencing abdominal symptoms. Three patients had no apparent source while the rest developed cholangitis and enteritis, as a suspected source respectively. *Aeromonas* isolates (*A. hydrophila, A. caviae, A. sobria*) were the only isolated pathogen identified and susceptible to fourth-generation cephalosporins. Either cefepime or cefotaxime initiated within a day of onset by itself or in combination with metronidazole, for 10–14 days. All patients recovered without septic shock or complications.

Conclusions: *Aeromonas* bacteremia among LTrs can occur as febrile illness long after liver transplantation even without prior liver dysfunction or severe neutropenia. Early and appropriate antibiotic therapy may result in favorable outcomes.

Abstract #44: Clinical Outcomes of Enteropathogenic *Escherichia coli* (EPEC) Detections by Multiplex Molecular Panel with Masked Results in Immunocompromised Hosts **Sabrina Newstead, MD** | *University of Utah*

Background: Enteropathogenic Escherichia coli (EPEC) is frequently detected on multiplex gastrointestinal molecular panels (MMP), however, the clinical relevance of this is unknown. Leveraging the masking of EPEC results in our health system, our goal is to determine the outcomes associated with EPEC detection in immunocompromised patients.

Methods: We electronically identified a retrospective cohort of immunocompromised patients seen within the Intermountain Health system who tested positive for EPEC by MMP from 1/1/2017-12/9/2024. We determined healthcare re-engagement (any subsequent visit at 14 and 30 days) in patients who did or did not receive antibiotics within 72 hours of testing positive. Additionally, we selected a subset of highly immunocompromised patients receiving allogeneic transplant (n=5), acute leukemia treatment (n=2), or both (n=1) to determine whether another etiology of diarrhea was apparent.

Results: 4,133 patients tested positive for EPEC; 692 (17%) were immunocompromised (22% received an antibiotic). Patients prescribed antibiotics within 72 hours of a GI PCR had higher healthcare re-engagement at 14 (47% vs. 24%, $p<0.0001$) and 30 days (70% vs.32%, $p<0.0001$). The majority of repeat visits occurred in the ambulatory setting (85%) and 4% were admitted to the hospital. Most antibiotics were prescribed inpatient (24%).

Of 8 highly immunocompromised patients, 6 had an alternative cause of diarrhea, one remained undiagnosed, and one

did not have diarrhea. Two patients received a fluoroquinolone for diarrhea (one who also tested positive for ETEC). Five patients were deemed mild in severity (no antibiotics) and one had severe diarrhea (graft vs. host disease).

Conclusion: Receiving an antibiotic within 72 hours of a detection of EPEC was associated with a higher rate of 14- and 30-day healthcare re-engagement in immunocompromised patients. This suggests that current use of molecular testing for EPEC has limited value and masking EPEC results had no adverse consequences.

Abstract #45: ID-led, Allergy-supported Beta-lactam Allergy De-labeling in Solid Organ Transplant Patients **Ellie Oken, ARNP, DNP** | *University of Washington*

Background: Over 10% of solid organ transplant (SOT) patients carry a beta-lactam allergy label (BLAL), yet fewer than 1% are truly allergic. The negative impacts of BLALs are well known, including an increase in antibiotic days, cost, and all-cause mortality. Most BLALs can be safely de-labeled through a detailed history or direct oral challenge (DOC) without formal Allergy consultation. This study evaluated the feasibility and effectiveness of an Infectious Disease (ID) clinician-led BLAL de-labeling program.

Methods: SOT patients admitted to UWMC or referred to SOT ID clinic with a BLAL were reviewed by an ID clinician. Based on chart review, BLALs were stratified into five categories: (1) eligible for de-labeling by chart review alone, (2) eligible for DOC, (3) requiring formal Allergy consultation, (4) requiring avoidance of beta-lactams, or (5) needing additional history. For patients needing additional history, the ID clinician gathered detailed history at bedside or during clinic visits and appropriately stratified.
Actions included (1) de-labeling the BLAL, (2) recommending or performing DOC, (3) referring to Allergy clinic, or (4) reaffirming the BLAL.

Results: From May 2024 to January 2025, 63 SOT patients were evaluated — 20 (32%) in clinic and 43 (68%) inpatient. Of these, 36 (57%) were pre-SOT and 27 (43%) were post-SOT. BLALs were de-labeled from history or chart review in 20 (32%) patients, and 36 (57%) underwent DOC. Only 3 (5%) required Allergy clinic referral or had their BLAL reaffirmed. One patient (2%) experienced a mild reaction (hives, itching) following DOC. Overall, 55 (87%) patients had their BLAL removed by an ID clinician.

Conclusion: BLALs are a significant burden for immunocompromised patients, who are high utilizers of antibiotics. An ID clinician-led de-labeling program is highly effective, offering substantial benefits for antibiotic stewardship and patient outcomes.

Abstract #46: Effectiveness and Safety of Strategies to Optimise Antimicrobial Use in Solid Organ Transplant Recipients. Systematic Review and Meta-analysis **María Paniagua García, MD, PhD** | *Hospital Universitario Virgen del Rocío, Spain*

Background: Solid organ transplant recipients (SOTr) are at high risk of infectious complications and effective antimicrobial stewardship (AMS) programmes need to be developed. We aimed to review the available evidence on the effectiveness and safety of different strategies to optimise antibiotic use in SOTr.

Methods: In this systematic review and meta-analysis, we searched MEDLINE (via PubMed), EMBASE and SCOPUS for original research articles published up to 15 December 2024. Studies with a control group evaluating different strategies to optimise the antimicrobial use in adult SOTr were included. The management of asymptomatic bacteriuria in kidney transplant recipients and the indication of antifungal prophylaxis were not included in the review. The outcomes assessed were mortality, transplant-related complications, infectious outcomes, development of antimicrobial resistance, antimicrobial consumption, hospital related variables, and antimicrobial toxicities. A risk-of-bias assessment was performed using the Cochrane EPOC group's criteria. Available data were pooled in a meta-analysis, and inconsistency between studies was evaluated using the I2 statistic. This study follows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. PROSPERO ID: CRD42024554606.

Findings: Of the 4050 articles identified, 30 studies met the inclusion criteria. 14 studies addressed perioperative antimicrobial prophylaxis (seven studies evaluated specifically duration of antimicrobial prophylaxis), two studies

reported information about decolonisation strategies, other two studies addressed duration of antimicrobial treatment as target therapy, one study evaluated antibiotic oral step-down strategy, and six studies reported the impact of AMS implementation approach on SOTr. The rest five studies evaluate specific targeted prophylaxis. No studies regarding false antibiotic allergy delabelling and antimicrobial optimisation of empirical treatment were found. Further evidence was found to support a shorter duration of perioperative antimicrobial prophylaxis, especially in liver and kidney transplant recipients, and the implementation of AMS approach in different transplant units. The meta-analysis of three studies on the effect of AMS programmes showed that this intervention may reduce the rate of surgical site infections, with an odds ratio of 0.57 in favour of AMS programmes (95% CI 0.35 to 0.94) and low heterogeneity between studies.

Interpretation: Strategies to optimise antimicrobial use are safe, with no negative impact on mortality or transplant-related complications, and appear to improve infectious outcomes in SOTr, particularly in the case of shorter perioperative antimicrobial prophylaxis and implementation of AMS programmes. According to the results of the meta-analysis, the implementation of AMS programmes may lead to a reduction in surgical site infection rates. However, further high-quality clinical trials are needed to better understand the effects of these strategies in SOTr and to design optimal AMS interventions in this population.

Funding: There was no funding source for this study.

Abstract #47: Risk factors for Infection Development in Hematological Patients with Colonization of MDR-Enterobacterales **Francesco Peracchi, MD** | *University of Milano-Biocca, Italy*

Introduction: Infections due to multidrug-resistant (MDR) pathogens remain a leading cause of mortality among onco-hematological patients. The aim of this study was to identify risk factors for developing infections in onco-hematological patients colonized with MDR-Enterobacterales at admission.

Methods: A single-center prospective observational study in onco-hematological patients treated with continuous infusion (CI) piperacillin/tazobactam, meropenem, cefatzidime/avibactam and cefidercol in the period Jan-Dec 2024 was conducted. Optimal pharmacodynamic target attainment was defined as steady-state plasma concentration over MIC (Css/MIC) ratio of 4-6-fold pathogen MIC or the clinical breakpoint. Colonization at admission, type of infection, microbiological isolates and plasma exposure were collected.

Results: Among the included patients (n=358), MDR-Enterobacterales colonization was observed in 21.5% (77/358) of the population at admission. Of them, 62.3% (48/77) were males, with median (IQR) age of 57 (52-66) years. Non-Hodgkin-lymphoma and acute myeloid leukemia (AML) accounted for 41.6% (32/77) and 20.6% (20/77) of the hematological malignancies, respectively. Previous antimicrobial exposure was observed in 42.9% (28/77) patients. Optimal target attainment was observed 89.7% (26/29) of patients treated with piperacillin/tazobactam, in 100% (34/34) of patients treated with meropenem, in 84.6% (11/13) of patients treated with ceftazidime/avibactam and in the single patient treated with cefiderocol. Infection by the same MDR-Enterobacterales isolated in the swab at admission occurred in 31% (27/77) of patients, after a median (IQR) time of 11 (2-32) days. Univariate analysis showed that risk factors for developing infections from the same colonizing microorganism were age ≥56years (p=0.003), body weight <66kg (p=0.013), AML (p=0.036), prior antimicrobial exposure (p=0.03), colonization by ESBL (p=0.025) and OXA-48 (p<0.001) pathogens. Multivariate analysis showed that colonization with OXA-48 (OR=7.67, p=0.019) and age ≥56years (OR=3.65, p=0.044) remain the only significant risk factors.

Conclusion: Among onco-hematologic patients admitted with colonization with MDR-Enterobacterales age ≥56 years and being colonized with OXA-48-Enterobacterales are significant risk factor for infections development.

Abstract #48: Impact of Cancer on the Incidence, Outcomes, and Trends of Catheter-Associated Bloodstream Infections: A Nationwide Analysis from Inpatient Hospitalizations (2016–2021) **Anil Matthew Philip, MD** | *Kuriakose Chavara Memorial Hospital*

Background: Central venous catheters are a source of local and bloodstream infections in cancer patients. This study compared the incidence of Catheter-Associated Bloodstream Infections (CLABSI) in patients with and without cancer.

Secondary objectives included evaluating the effects of CLABSI and multidrug-resistant organisms (MDRO) on length of stay (LOS), total hospitalization charges (THC), mortality, and trends from 2016–2021.

Methods: The National Inpatient Sample (2016–2021) was analyzed using ICD-10 codes to identify CLABSI and MDRO. Sociodemographic characteristics were described, and regression models assessed trends in MDRO, LOS, THC, and mortality.

Results: Among 228,109 CLABSI admissions, 24% involved cancer patients, who were older (mean 60.2 vs. 47.4 years) and predominantly had solid malignancies (59.4%). Cancer patients had 2.9 times higher odds of CLABSI but 28% lower odds of MDRO ($p < 0.001$). Factors like neutropenia and malnutrition increased odds of CLABSI by fivefold ($p < 0.001$), while odds of MDRO rose by 34% with malnutrition ($p < 0.01$).

Cancer patients with CLABSI had shorter LOS and lower THC than non-cancer patients, but 1.12 times higher mortality risk ($p < 0.001$). However, neutropenia, MDRO, and malnutrition increased LOS and THC significantly. Malnutrition also increases odds of mortality by 74% ($p < 0.001$).

Solid malignancies were linked to 32% lower mortality risk and shorter LOS compared to hematological malignancies ($p < 0.001$). Over the years, the odds of CLABSI rose by 2.5% annually ($p < 0.001$), and MDRO odds increased by 13.4% annually ($p = 0.02$). THC rose by $4,321 each year ($p < 0.001$).

Conclusion: Cancer patients are at higher risk for CLABSI but lower risk for MDRO. Factors like malnutrition significantly impact outcomes, highlighting the need for targeted interventions.

Abstract #49: Management of Brucellosis in a Cardiac Transplant Recipient: A Case Report and Review of Cases
Julieta L. Rodriguez, MD, MPH | *University of California, San Francisco*

Background: Brucellosis is a zoonotic infection caused by Brucella species, typically transmitted to humans who consume raw milk products or work closely with infected animals.
Globally, brucellosis remains a major public health problem with 500,000 cases annually, while the U.S. reports 80-140 cases yearly. Although known for its undulating fever course, brucella can cause several clinical manifestations mimicking systemic diseases. Despite appropriate treatment, relapse can occur in up to 5-15% of cases within the first six months of completing therapy. Little is known about brucellosis in patients undergoing solid organ transplant (SOT), including clinical outcomes, as well as optimal treatment and monitoring strategies. We describe a case of brucellosis in a patient with fulminant heart failure requiring heart transplantation, outlining the treatment approach, monitoring protocol, and outcome post-SOT. A review of relevant cases in the literature is also provided.

Case Presentation: A 62-year-old man with history of Brucella melitensis bacteremia and non-ischemic cardiomyopathy presented with worsening cardiogenic shock requiring heart transplantation and brucella infection complicated by spinal osteomyelitis. Post-transplant, he was treated with rifabutin 150mg BID and doxycycline 100mg BID for three months, with monitoring of brucella titers monthly for three months, and quarterly thereafter. The patient responded well to therapy with down-trending brucella titers and had no signs of relapse post-transplant. Review of the three cases of pre-transplant brucellosis diagnosis seen in the literature revealed a range in treatment practices from 4-6 weeks of therapy and one case of relapse leading to a six-month treatment course. These regimens often included a rifamycin, doxycycline and/or streptomycin/gentamicin.

Conclusion: Data regarding post-SOT management of patients recently infected with brucella are limited. Future studies are required to help identify the appropriate timing for transplant candidacy, treatment regimens, post-transplant monitoring, and to better define clinical outcomes.

Abstract #50: Characterization of Late Positive Blood Cultures and Late-Onset Bloodstream Infections in Persistent Febrile Neutropenia
Emily Rosen, MD | *Fred Hutch Cancer Center*

Background: The objective of this study is to describe the timing and microbiology of positive blood cultures and characterize new bloodstream infections (BSI) occurring after day 3 of persistent febrile neutropenia (FN). These findings

will be used to inform diagnostic stewardship of blood cultures in FN.

Methods: This is a retrospective cohort study of adult patients with hematology/oncology diagnoses who were admitted for an episode of persistent FN, defined as FN lasting >3 days. Blood cultures collected during each FN episode and patient clinical characteristics were extracted from the medical record.

Results: Of 459 patients who met inclusion criteria, 126 (27%) had ≥1 positive blood culture at anytime during their FN episode and 23 (5%) had ≥1 positive culture after FN day 3. Sixteen (3%) patients had ≥1 late positive blood culture after FN day 3 that grew a new organism not previously isolated from any cultures on FN days 1-3. Among 18 late positive blood cultures with a new organism, coagulase negative Staphylococci were isolated in 6 (33%) and all but one was a contaminant. Gram negative organisms and yeast were isolated in 7 (39%) and 2 (11%) late positive cultures that grew a new organism after FN day 3, respectively. After excluding late positive cultures that represented contaminants, there were 13 new-onset BSIs after day 3 of FN among 12 patients. Late-onset BSIs were not always associated with preceding signs of sepsis, including hypotension, tachycardia, or tachypnea.

Conclusions: New, clinically significant BSI after FN day 3 is infrequent and nearly one-third of positive blood cultures with a new organism after FN day 3 were found to contain skin contaminants. Additional studies are needed to determine the optimal frequency of repeat blood cultures in persistent FN and to identify risk factors for late-onset BSI.

Abstract #51: Nontyphoidal Salmonella in Immunocompromised Hosts: A Case Report and Discussion **Syeda Sahra, MBBS** | *Mayo Clinic*

Introduction: Salmonella is a gram-negative bacterium that causes gastrointestinal infections. It is spread by fecal-oral route, via contaminated foods such as undercooked meats, eggs, and dairy products, or between household contacts. Common serotypes include S. Typhimurium and S. Enteritidis. While healthy individuals typically experience mild symptoms, those with compromised immune systems are at a greater risk of severe infections that require intensive medical management.

Case Presentation: A 20-year-old female with a history of ulcerative colitis (UC) was admitted due to complaints of bloody diarrhea and left lower quadrant pain. She was receiving monthly infliximab infusions for UC. She had a history of primary sclerosing cholangitis, necessitating an orthotopic liver transplant five years ago, and was receiving immunosuppressive therapy with tacrolimus, mycophenolate, and prednisone. Notably, she had experienced multiple prior UC flares with similar symptoms to those at the presentation. Due to a history of cytomegalovirus (CMV) colitis six months prior, the patient was on secondary prophylaxis with valganciclovir. CT scan of the abdomen and pelvis revealed pan colonic mural thickening, associated intramural fat, and peri colonic adenopathy. A gastrointestinal PCR panel confirmed the presence of Salmonella. Patient was started on ceftriaxone. Although the patient did not report exposure to undercooked meats or eggs, or farm animals, she had consumed food prepared at a summer camp in Minnesota. Blood cultures were negative, but they were notably collected after 24 hours of antimicrobial therapy. Stool cultures identified pan-susceptible Salmonella enterica (subspecies enterica). A flexible sigmoidoscopy revealed mild active chronic colitis. Colon biopsy results showed negative results for CMV immunostaining, and CMV PCR was undetectable. During the hospitalization, the patient received intravenous ceftriaxone and was later switched to oral levofloxacin upon discharge, completing a two-week treatment course. At the one-month follow-up, the patient was noted to be doing well, without evidence of relapse.

Conclusion: Immunocompromised individuals face a greater risk of invasive non-typhoidal Salmonella (NTS) infections, which can spread and recur, resulting in high mortality. This case highlights the management of such patients with weakened immune systems and existing gastrointestinal issues.

Abstract #52: Severe Human Granulocytic Ehrlichiosis in an Immunosuppressed Host **Syeda Sahra, MBBS** | *Mayo Clinic*

Introduction: Ehrlichiosis is a zoonotic illness caused by various Ehrlichia species. E. chaffeensis causes human monocytic ehrlichiosis, while E. ewingii and E. muris eauclairensis (EME) lead to human granulocytic ehrlichiosis. It primarily

spreads through bites from infected ticks such as the lone star tick (Amblyomma americanum) and the blacklegged tick (Ixodes scapularis). High-risk groups, including transplant recipients and the immunocompromised, may experience severe complications such as renal failure and respiratory distress.

Case Description: A 55-year-old man with a history of liver transplant six months ago was admitted in May with symptoms including headache, blurred vision, and persistent malaise. His post-transplant course was complicated by multiple episodes of acute allograft rejection, the most recent of which was treated with anti-thymocyte globulin (ATG) the previous month.
Upon examination, he was jaundiced. Lab tests showed a low white blood cell count(1.2 x 10^9/L), lymphopenia(0.04 x 10^9/L), and transaminitis with aspartate aminotransferase (AST) 148 U/L, alanine aminotransferase (ALT) 88 U/L, and total bilirubin of 18.2 mg/dL.
Patient continued to decline clinically with worsening fever and mentation. An MRI brain ruled out acute cerebral lesions. PCR testing for tick-borne disease confirmed E. muris eauclairensis infection. Unfortunately, patient continued to decline and passed away despite addition of doxycycline. Autopsy revealed acute kidney injury, ischemic hepatic injury, hyaline membranes in the lungs and clinic congestion on histopathology.

Discussion: E. muris eauclairensis (EME), previously known as the Ehrlichia muris-like agent, is an emerging bacterium spread to humans through the bite of infected ticks. First isolated in 2009 from a resident of Eau Claire, Wisconsin, EME cases have mostly been reported in residents of Minnesota and Wisconsin. The young deer ticks, or nymphs, are particularly active during the spring and summer months, which aligns with the peak incidence of EME cases in May to July. Cellular immunity is essential for host defense. Administering anti-thymocyte globulin (ATG) raises the patient's risk of severe disease by depleting T-cells, causing B-cell apoptosis, and disrupting dendritic cell maturation and migration.

Conclusion: Impaired cellular immunity can lead to worse recovery and higher mortality in ehrlichiosis patients. Tick-borne disease suspicion should be heightened in high-risk areas.

Abstract #53: A Rare Case Presentation of Recurrent Porta Cath Associated Bloodstream Infection with *Gordonia polyisoprenivorans* in an Immune-compromised Host **Ayesha Samreen, MBBS** | *Mayo Clinic*

BACKGROUND: Gordonia species are gram positive ubiquitous aerobic actinomycetes, often misidentified as contaminants. Their slow growth makes quick identification difficult although 16s RNA sequencing have improved identification rates over years. Only a few handful cases have been reported in literature, although immunosuppression, hematologic malignancy and indwelling catheter are considered risk factors. No standardized treatment or duration recommendations exist because of its rarity, the choice of antimicrobial regimen is guided by in vitro susceptibility testing.

CASE PRESENTATION: Our patient is a 29-year-old young female with a complex medical history of autosomal recessive polycystic kidney disease (post bilateral native nephrectomies, and two failed kidney transplants), Caroli disease complicated by congenital hepatic fibrosis and recurrent ascending cholangitis on suppressive oral cefdinir (post liver transplant on chronic immunosuppression with mycophenolate, tacrolimus, and prednisone), splenectomy, hypogammaglobulinemia on monthly immunoglobulin infusions, recurrent clostridioides difficile colitis, who presented with persistent fever, nausea and right upper quadrant pain of five days duration, unresponsive to oral antibiotics prescribed as outpatient. Of note, she has a recent admission one month prior to current, for ascending cholangitis with bacteremia showing Gordonia Polyisoprenivorans from porta Cath and periphery, which was managed with line salvage (vancomycin lock solution), and linezolid for a two-week course with negative surveillance cultures a week later. Her physical examination showed right upper quadrant. Labs and abdominal imaging were unremarkable. Port-A-Cath blood cultures collected at admission were positive for gram-positive rods at 34 hours and peripheral cultures positive at 63 hours favoring Port-A-Cath involvement. These were finalized as Gordonia polyisoprenivorans on 16sRNA sequencing after five days. Meanwhile, she was treated with systemic vancomycin therapy and line removal was recommended by transplant infectious diseases, considering recurrence of this bacteremia and failed line salvage.

CONCLUSION: Our case highlights the importance of recognizing this rare, but emerging pathogen in

immunocompromised hosts with an indwelling porta cath. Line salvage often results in treatment failure and its removal must be strongly considered

Abstract #54: Invasive Listeriosis in Immunocompromised Hosts- Retrospective Descriptive Study at a Tertiary Care Center in the United States **Ayesha Samreen, MBBS** | *Mayo Clinic*

BACKGROUND: Listeria monocytogenes can cause life threatening invasive infections and severely affects those that are immunocompromised. Unfortunately, there is lack of evidence in this group and our current therapeutic guidelines are based on limited data on effective therapy or treatment duration.

METHODS: We conducted a retrospective multicenter review at Mayo Clinic health system sites between 1980-2024 on microbiologically confirmed cases of invasive listeriosis in immunocompromised, non-pregnant patients. Kruskal–Wallis and chi square analyses were utilized as appropriate.

RESULTS: 28 adult patients were included, majority were female (n=15, 53.6%), median age at diagnosis was 70 years old (interquartile range (IQR):57.7.0-76.5). The most common group of patients were those with solid organ malignancy 7/28 (25%) and hematologic malignancy 7/28 (25%), followed by solid organ transplant recipients 6(21.4%), and bone marrow transplant recipients 2(7.1%). Six patients (21.4%) were on immunomodulating agents for autoimmune conditions. Blood cultures were positive in 22/25 patients (88%). The most common clinical syndrome diagnosed was bacteremia in 13(46.4%), followed by meningoencephalitis 11(39.3%), peritonitis in three (10.7%) and endocarditis in two (7.1%). Amongst confirmed neuro invasive cases, cerebrospinal fluid (CSF) analysis was done in 8/11 patients, with median values for CSF glucose being 42 mg/dl (IQR: 30.25 - 53.75), CSF white cell count 436 cells/mm3 (IQR: 134.5 - 1643.5), and protein 107 mg/dl (IQR: 92.25-184.75). When performed, imaging revealed rhombencephalitis in 2/7 patients.
In terms of definitive treatment, ten (35.7%) received monotherapy with ampicillin, whereas seven (25.0%), got combination therapy with ampicillin plus Bactrim, and six (21.4%) received ampicillin plus gentamicin; the median duration of therapy was 21 days (IQR: 14.0- 28.0). Ten (35.7%) patients needed critical care support on admission. Among neuro invasive cases, 36.4% (n=4) had residual neurological sequelae at the time of dismissal. All cause 90-day mortality was 14 .3% (n=5). There was no statistically significant difference in mortality among the different treatment modalities either monotherapy or combination (p= 0.56), baseline immunosuppressive state (p> 0.50), presence of bacteremia (p= 0.34) or clinical syndrome (p> 0.50).

CONCLUSION: We report a 90-day mortality (35.7%), which is higher compared to the average mortality in the general population (20-30%). This may be related to an altered T-cell mediated immunity in this cohort, thereby increasing the risk for infections with intracellular organisms such as listeria. We did not identify any clear risk factors for mortality, in terms of baseline disease, presentation or treatment, however, this may be due to low number of events. Prospective multicenter studies are recommended to better evaluate treatment options although its rarity makes evidence-based treatment guidelines difficult to establish.

Abstract #55: Clinical Experience with Gram-negative Blood-stream Infections in Pediatric HCT Recipients (2010-2023) **Hayley Scheerer, MD** | *St. Jude Children's Research Hospital*

Background: Gram-negative blood stream infections (GN-BSI) are a significant cause of morbidity and mortality worldwide. Immunocompromised patients, including pediatric hematopoietic cell transplant (HCT) recipients, are at increased risk of infection. Changing approaches to empiric antibiotics for febrile neutropenia and antibacterial prophylaxis practices may significantly alter the epidemiology of GN infections in this vulnerable population. Routine antibacterial prophylaxis in neutropenic HCT recipients was discontinued at St Jude in April 2017. We describe the epidemiology and clinical experience with GN-BSI in HCT recipients from 2010-2023 at St Jude Children's Research Hospital.

Methods: GN-BSI infections were identified via retrospective chart review in the 30 days pre-transplant, 100 days post autologous HCT and 365 days post allogeneic HCT. Statistical analysis was performed in RStudio (4.4.1).

Results: GN infections occurred in 24% (218/913) of all HCTs. GN-BSI occurred predominantly in allogeneic HCT

recipients (77.98%) compared to autologous transplant recipients (22.02%). Of the 218 episodes of GN-BSI, most were monomicrobial (71.10%) but nearly a third (28.90%) were polymicrobial. Enterobacteriaceae were the most commonly identified organisms (69.2%), followed by Pseudomonas aeruginosa (15.6%), and other Pseudomonas spp (6.0%). Neither 30-day (p=1) or 90-day all-cause mortality (p=0.378) were significantly different in the period prior to and after discontinuation of routine neutropenic antibacterial prophylaxis.

Conclusions: The incidence of BSI in our population was consistent with previously reported incidence in pediatric HCT recipients with majority of infections occurring in allogeneic HCT recipients. Polymicrobial infection was more commonly seen than described in the literature. Although not significant, 90-day all-cause mortality was higher (12.87% vs 8.55%) prior to discontinuing routine prophylaxis. Additional analyses will be performed to further describe GNBSI episodes, including clinical severity, to adjust for mortality outcomes.

Abstract #56: Bloodstream Infection and Risk for Plasma Cell Neoplasms: A Large Population-based Cohort Study
Adam Stewart, MBBS, MPH | *Massachusetts General Hospital*

Background: Although infectious complications of patients with plasma cell neoplasms are common, invasive infections may be the first prompt to investigate their occult presence. This study aimed to quantify the risk for subsequent diagnosis of a plasma cell neoplasm following bloodstream infection (BSI).

Methods: Population-based surveillance was conducted in Queensland, Australia during 1 January 2000 to 31 December 2019. Statewide databases were used to identify patients with incident plasma cell neoplasms (plasmacytomas, multiple myeloma, and plasma cell leukemia) diagnosed within one-year following BSI.

Results: After exclusion of 800 subjects who had incident BSI following a diagnosis of a plasma cell neoplasm, a cohort of 90 individuals who had BSI within the year preceding diagnosis of plasma cell neoplasm and 95,753 patients with BSI without this malignancy were included. The time to diagnose a plasma cell neoplasm was a median 114 (31-221) days after index BSI, and 11 subjects had more than one incident BSI within the year prior to this diagnosis. The overall incidence of plasma cell neoplasms among those with incident BSI was 93.9 per 100,000 population annually. Development of BSI was associated with a 13-fold increased risk for diagnosis of plasma cell disorder (IRR; 12.9; 95% CI, 10.3-15.8; p<0.001). The increased risk following BSI was elevated for both sexes, with a magnitude of risk higher in females (IRR; 14.0; 95% CI, 9.8-19.4) as compared with males (IRR; 11.8; 95% CI, 8.9-15.5). Streptococcus pneumoniae BSI was associated with the highest risk for subsequent diagnosis of a plasma cell neoplasm (RR; 4.2; 95% CI; 2.4-7.3).

Conclusions: The presence of a BSI, particularly with S. pneumoniae, is a marker for occult plasma cell neoplasms in a small but significant number of patients. Further studies are warranted to identify occult neoplastic disease investigation strategies for patients with incident BSIs.

Abstract #57: Donor-derived Tuberculosis in Three Solid Organ Transplant Recipients
Paulina Vega, MD | *Fred Hutch Cancer Center*

Background: Donor-derived tuberculosis (TB) is a rare complication following solid-organ transplant (SOT) and TB screening is not a current transplant prerequisite for most donors. Donor-derived TB usually presents sooner than reactivation TB and the most common finding is fever.

Case Presentation: We present three cases of donor-derived TB in the recipients of two kidneys and one liver from the same donor, who presented with unexplained fevers occurring 5-6 weeks after transplantation. All three patients failed initial antibacterial therapy, leading to further testing which isolated Mycobacterium tuberculosis by culture and molecular studies. All recipients successfully received TB therapy but had significant morbidity and prolonged hospital stay.

Conclusion: Donor-derived TB should be among the differential diagnoses of unexplained fever in SOT recipients within three months of transplantation. Stricter screening algorithms should be implemented for donors with epidemiologic risk of TB.

Abstract #58: Factors Associated with Antimicrobial Utilization in Solid Organ Transplant Recipients: A Next Step in Further Understanding Antimicrobial Stewardship in the Solid Organ Transplant Population **Emily Wong, MD** | *University of Texas Southwestern Medical Center*

Background: To provide antimicrobial benchmarking, the CDC optimized the National Healthcare Safety Network (NHSN) as a method for institutions to report antimicrobial utilization (AU). The data generated can provide actionable initiatives for antimicrobial stewardship programs. Herein, we describe inpatient AU in solid organ transplant (SOT) recipients during the first six months post-transplant and factors associated with AU.

Methods: We conducted a retrospective single-center cohort study of all the first adult SOT recipients at our institution from 2010 and 2019 using merged data from the OPTN Standard Transplant Analysis and Research files and the electronic health record. Inpatient AU during the first six months post-transplant was calculated as days of therapy per 1000 days using NHSN definitions. Organ-specific multiple linear regression models identified baseline factors associated with AU.

Results: 1845 SOT recipients were included (293 heart, 531 kidney, 426 liver, and 595 lung). Total inpatient AU varied by transplant type: heart 560.55, kidney 285.16, liver 622.32, and lung 1111.23. During the study period, AU decreased in heart, liver, and kidney transplant recipients and increased in lung transplant recipients. AU was highest for vancomycin, piperacillin-tazobactam, levofloxacin, and meropenem. In heart transplant recipients, year of transplant, A-blood group, hospitalization acuity, infection requiring IV antibiotics within two weeks prior to transplant, and ischemic time were associated with AU. In Lung transplant recipients, age, LAS, and ischemic time were associated with AU. For liver transplant recipients, the year of transplant was the only variable associated with AU. In kidney transplant recipients, the year of transplant, functional status at transplant, ischemic time, and type of insurance were associated with AU.

Conclusion: SOT recipients at our institution had substantial AU in the first 6 months post-transplant, and organ-specific baseline predictors were associated with AU. The data generated could aid in implementing antimicrobial stewardship interventions to optimize utilization.

Fungal Disease

Abstract #59: Breakthrough *Fusarium solani* Aortitis with Neurovascular Complications Following Posaconazole Prophylaxis **Alaa Atamna, MD** | *Beilinson Hospital, Israel*

A 64-year-old patient who presented with relapsed AML after he had stem cell transplanted 4 years ago. Daunorubicin and cytarabine (3+7) protocol and Midostaurin for 14 days were started. Posaconazole prophylaxis was started too. At day 21 of neutropenia he presented with fever and skin nodule on the right arm, blood cultures were negative, serum galactomannan and cryptococcal antigen were negative too. A culture from a skin specimen grew Fusarium solani. Liposomal amphotericin B (L-AmB) 5mg/kg and voriconazole (loading dose IV 6 mg/kg q12 hours x 2 doses, then 4 mg/kg IV q12 hours) were started. One week later, he experienced shortness of breath and chest pain, a CT angiography was done and excluded pulmonary embolism, however, an abnormal aortic wall with irregular and thickened wall of the ascending aorta and the aortic arch was demonstrated compatibile with aortitis. While on therapy, he developed stroke with carotid inflammation and cerebral infarcts per brain imaging. In response, the L-Amb dose was increased (7.5mg/kg) with subsequent neurological improvement, the fever and skin nodules subsided. As the F. Solani isolate had high MICs for all triazoles, the patient continued to receive L-AmB only and was discharged home with L-AmB monotherapy. While at home, he experienced severe myalgias, arthralgia,due to electrolyte disturbances.
The isolate was sent to Innsbruck Medical University, Austria, for further characterization and susceptibility to novel antifungals as more convenient maintenance therapy. The isolate was found to be susceptible to fosmanogepix (MIC 0.125) and olorofim (MIC 0.008-0.062). Therefore, the patient started olorofim as a compassionate treatment (loading dose 150mg twice at day 1, then 90mg twice daily. Before starting Olorofim, and after 4 months on L-AmB treatment, a PET CT was done showing no FDG uptake in the aorta. During olorofim treatment, the patient was fully active, with no new signs of neurologic impairment, no breakthrough mold infections. His liver enzymes were normal throughout the treatment period.
Unfurtunately, after 2 months of olorofim therapy, the patient suffered an AML relapse. As the prognosis was not

favourable, the patient went to palliative care programm, and olorofim was suspended. Three weeks after, the patient presented with febrile neutropenia, skin rash on the face, upper and lower limbs. Ear-nose-throat evaluation raised the suspesion for fungal involvement of the nasal concha as the mucosa was pale. Blood, skin and nasal concha specimens cultures' all grew Fusarium solani. Unfortunately, the patient died several weeks after due to progression of the underlying disease.
The reference laboratory in Innsbruck confirmed susceptibility to olorofim (MIC 0.032) of F. solani isolated from the new sites of infection.

Abstract #60: Characterization of Solid Organ Transplant Recipients with Positive T2Candida Panel Presenting with Suspected Invasive Candidiasis **Megha Jagannathan, MD** | *Henry Ford Hospital*

Background: There is limited data describing T2Candida® Panel (T2Candida) use in solid organ transplant recipients (SOTr) with suspected invasive candidiasis (IC). The study aimed to evaluate the clinical characteristics and outcomes of SOTr with positive T2Candida testing.

Methods: This is a retrospective study of hospitalized SOTr who underwent T2Candida testing for suspected IC between 2015-2024. Demographics, comorbidities/risk factors, transplant characteristics, microbiology data, and outcomes of patients with positive T2Candida were evaluated.

Results: Of the 326 SOTr who underwent T2Candida testing, 43 (13.2%) had a positive result. Median age was 62 years, and 51% were female. Median Charlson comorbidity index was 6 [4-7]. Common risk factors for IC included indwelling vascular catheter (77%), broad-spectrum antibiotic use (77%), and hospitalization within prior 30-days (56%). Sixteen-percent of patients received rejection treatment within 90-days of presentation. Median time from transplant to positive T2Candida was 172 [27-1872] days. Most patients were liver (42%), kidney (19%), and lung transplant recipients (14%). Thirteen (30.2%) SOTr had concomitant isolation of Candida spp. in blood and/or sterile cultures (T2Candida/IC group), whereas 30 (69.8%) did not (T2Candida-alone group). Patients in both groups presented with sepsis/septic shock and/or imaging suspicious of intracavitary abscess, except one in the T2Candida/IC group and three in the T2Candida-alone group. T2Candida positive for C parasilopsis (n=10) was observed only in the T2Candida-alone group. Most patients in both groups received empiric antifungals. Overall, 90-day mortality was 49%. Readmission rates for relapsed infection or death were comparable in both groups (p=0.46).

Conclusions: Positive T2Candida test was mostly observed in liver transplant recipients. Clinical features and outcomes were similar in T2Candida/IC and T2Candida-alone groups. The frequent detection of C parapsilosis in the T2Candida-alone group needs further evaluation. Additional studies are needed to evaluate the role of T2 and rapid diagnostics to improve outcomes of SOTr with IC.

Abstract #61: Fungal Infections and Treatment Outcomes in STAT1 and STAT3 Gain-of-Function Mutations: A Case Series **Valerie Jaroenpuntaruk, MD** | *Mayo Clinic*

Background: STAT1 and STAT3 Gain of Function (GOF) mutations are immunodeficiencies associated with immune dysregulation and increased susceptibility to fungal infections. This study evaluates clinical characteristics, fungal organisms, and therapeutic responses in these populations.

Methods: A retrospective review of patients with STAT1 and STAT3 GOF mutations was conducted. Data included fungal infection types, diagnostic methods, antifungal treatments, and immune profiles.

Results: Nine patients with STAT1 (n=5) and STAT3 (n=4) GOF mutations were included. The average age at genetic testing was 21.7 years for STAT1 (4 females, 1 male), with symptom onset in infancy, and 37.9 years for STAT3 (1 female, 3 males), with symptom onset in childhood.
STAT1 GOF patients commonly presented with chronic mucocutaneous candidiasis (oral/esophageal) and tinea spp. Pulmonary infections were observed in those with the c.1154C>T (p.Thr385Met) mutation, primarily due to Pneumocystis jirovecii pneumonia and Cryptococcus spp. One case of disseminated histoplasmosis was reported in a patient with the c.1310C>T (p.Thr437Ile) mutation. STAT3 GOF patients experienced oropharyngeal candidiasis and onychomycosis, both responsive to antifungal treatment, while those with the c.832C>T (p.Arg278Cys) mutation had no

fungal infections.
Diagnostic methods included bronchoalveolar lavage, beta-glucan assays, antigen titers, and tissue cultures. Immunological analysis revealed low IgA/IgM levels, reduced CD4 counts, and cytokine dysregulation (elevated IL-10 and IL-18). STAT1 GOF patients required combination antifungal therapies, often with maintenance or repeat courses, while STAT3 GOF patients received antifungals as needed. Adjunctive immunomodulation (ruxolitinib) improved autoimmune manifestations and infection control in STAT1 GOF patients.

Conclusion: Fungal infections in STAT1 and STAT3 GOF mutation patients pose diagnostic and therapeutic challenges. Early interventions, such as hematopoietic stem cell transplantation and JAK inhibitors, can be considered but require individualized management. This cohort underscores the importance of personalized approach, combining aggressive antifungal therapy with tailored immunomodulation, with further studies needed to optimize outcomes in this immunocompromised population.

Abstract #62: Aspergillus Galactomannan Assay in Bloody Bronchoalveolar Lavage Fluid: Investigating Factors Associated with False-Positive Results **Mabel Jiminez, MD, MPH** | *Fred Hutch Cancer Center*

Background: Patients with bloody bronchoalveolar lavage (BAL) samples occasionally yield unexpected positive Aspergillus galactomannan (GM) results, which are often presumed to be false positives. Blood components, such as hemoglobin or red blood cell (RBC) components, may interfere with the assay's optical density index (ODI) readings. We hypothesized that bloody BAL samples would be associated with higher GM-ODI values and an increased likelihood of false-positive GM results.

Methods: This retrospective cohort study evaluated adult patients with hematologic malignancies or recipients of hematopoietic cell transplants (HCT) who underwent diagnostic bronchoscopy with BAL at Fred Hutchinson Cancer Center between July 2020 and July 2024 and had a positive Aspergillus GM. Medical records were reviewed, and data were abstracted into an electronic database. Cases were classified as probable/proven invasive pulmonary aspergillosis (IPA), false-positive, or indeterminate using EORTC/MSGERC criteria. The primary aim was to assess the association between Aspergillus GM results and amount of blood in BAL fluid using RBC count.

Results: Analysis of 69 BAL samples revealed no significant correlation between RBC count and Aspergillus GM ODI values across the full cohort (correlation coefficient: -0.007, 95% CI: -0.386 to 0.374, p = 0.973). Even after removing an outlier, the correlation coefficient was 0.201 (95% CI: -0.202 to 0.546, p = 0.324). Among patients with diffuse alveolar hemorrhage (DAH), the correlation between RBC count and GM ODI values remained weak and statistically insignificant (correlation coefficient: -0.164, 95% CI: -0.816 to 0.672, p = 0.726).

Conclusion: The lack of a significant correlation between Aspergillus GM and BAL RBC count suggests that RBC count alone is not a reliable predictor of false-positive GM results. If blood in BAL influences GM-ODI, interference may be mediated by other blood components, such as hemoglobin. These findings highlight the need for controlled experiments to elucidate the mechanisms underlying false-positive results.

Abstract #63: Post-transplant Outcomes in Kidney Transplant Recipients with Invasive Fungal Infections Prior vs. After Emergence of SARS-CoV2 **Lucy Li, MD** | *Johns Hopkins University*

Background: Invasive fungal infections (IFIs) are a serious complication in kidney transplant recipients (KTRs). Given pandemic-related care changes and potential compounding effects of COVID-19 infection, we sought to determine whether the emergence of SARS-CoV2 contributed to worsened transplant outcomes associated with IFIs.
Methods: We performed a retrospective study of adult KTRs transplanted at JHH 2012-2018 followed through 5/2023. IFI diagnoses were based on EORTC/MSGERC criteria. KTRs with and without IFIs were matched 1:1 on time-post-KT and followed until all-cause graft loss (ACGL), a composite outcome of allograft failure and mortality. We estimated cumulative incidence of ACGL prior vs. after SARS-CoV2 emergence in 2/2020 and assessed the association between IFI and ACGL pre vs. during SARS-CoV2 pandemic using Cox regression with an interaction term adjusting for age, transplant risk, and cardiovascular disease.

Results: Among 1453 KTRs, 79 (5.4%) had proven/probable IFIs of which 12 occurred after emergence of SARS-CoV2. Yeast were the majority of IFIs (50/79) overall, but mold (5/12) and yeast (6/12) were equally represented among IFIs occurring after the emergence of SARS-CoV2. Pre-pandemic ACGL occurred in 66% (44/67) of KTRs with IFIs vs. 31% (414/1338) of KTRs without IFIs (log-rank p<0.001). During the pandemic, ACGL occurred in 75% (9/12) of KTRs with IFIs vs. 31% of KTRs without IFIs (log-rank p<0.001). KTRs with IFIs had a 2-fold greater ACGL risk (aHR 2.05, 95% CI 1.17-3.57, p=0.012) pre-pandemic and a 5.5-fold greater ACGL risk (aHR 5.54, 95% CI 1.17-26.24, p<0.01) during the pandemic. The ACGL risk associated with IFIs changed after the emergence of SARS-CoV2 (p-interaction term <0.001).

Conclusion: KTRs with IFIs had higher rates of ACGL during the pandemic, and molds constituted a greater proportion of the IFIs during the pandemic. The emergence of SARS-CoV2 may have shifted the epidemiology of IFIs among KTRs, leading to increased ACGL.

Abstract #64: Cryptococcal Laryngitis Associated with Inhaled Medical Cannabis Use in a Multiple Myeloma Patient
Christopher Marino, MD | *University of Pittsburgh Medical Center*

Background: Cryptococcal laryngitis is a rare infection that can be acquired from direct inhalation of fungal organisms and often associated with inhaled corticosteroids. Whereas inhaled cannabis use is a recognized risk factor for pulmonary aspergillosis, there is not a clear association between inhaled cannabis use and cryptococcal infections.

Case Presentation: A 46-year-old woman with multiple myeloma on daratumumab, pomalidomide, and dexamethasone and a history of daily inhaled medical cannabis use presented with a two-month history of progressive dysphonia, right-sided throat pain, and new-onset headache. Laryngoscopy revealed an irregular, white, exophytic mass involving the laryngeal surface of the epiglottis and aryepiglottic fold. Biopsy of the lesion demonstrated encapsulated yeast forms on mucicarmine stain and cultures grew Cryptococcus neoformans. Cerebrospinal fluid (CSF) culture also grew Cryptococcus confirming disseminated cryptococcal infection with meningeal and laryngeal involvement. The patient was treated with three weeks of liposomal amphotericin B and flucytosine followed by high-dose fluconazole. Her dysphonia and sore throat resolved, and laryngoscopy showed no residual mass after one month of therapy. We hypothesized that the cryptococcal infection originated from her inhaled cannabis. Three patient cannabis products, each from different dispensaries, were cultured. While all samples yielded growth of molds including Aspergillus, Fusarium, and Penicillium, one sample yielded colonies of Cryptococcus. Illumina whole genome sequencing was performed on Cryptococcus isolates from the cannabis and the clinical laryngeal and CSF cultures. These isolates were confirmed to be genomically identical C. neoformans var. grubii, and genetically distinct from comparative Cryptococcus isolates of two unrelated patients (>69 single nucleotide polymorphisms).

Conclusion: Cryptococcal laryngitis should be considered in immunocompromised patients with progressive hoarseness or throat pain. This case provides evidence linking cryptococcal laryngitis to inhaled cannabis use. Further research exploring fungal infection risk with cannabis use will guide safer practice of cannabis use in immunocompromised patients.

Abstract #65: Microsporidiosis Following Solid Organ Transplantation: A Case Series
Jack McHugh, MBBS | *Mayo Clinic*

Background: Microsporidiosis, traditionally associated with advanced HIV, is increasingly recognized in solid organ transplant (SOT) recipients. This series provides a comprehensive review of its clinical features, treatment, and outcomes in this population.

Methods: A retrospective case series of microsporidiosis in SOT recipients at Mayo Clinic, Rochester (2000–2024) was conducted using laboratory codes. Demographics, clinical presentations, immunosuppression regimens, microbiologic findings, treatments, and outcomes were collected.

Results: The series comprised 9 patients (mean age: 53.6 years; range: 16-68), male (n = 6, 67%), with microsporidiosis diagnosed post-transplantation. Eight followed renal transplantation, and one involved a heart transplant recipient.

Enterocytozoon bieneusi was identified in six (67%), two were caused by Encephalitozoon species, and one case was caused by Anncaliia algerae. Enteritis was the sole manifestation in seven (78%) and was diagnosed with stool polymerase chain reaction (PCR). Disseminated disease by E. cuniculi and Anncaliia algerae occurred in two patients. Diagnosis was made via direct visualization on pathologic specimens and confirmed with PCR. Six patients (67%) had well water exposure prior to symptom onset. Symptoms resolved in one enteritis case where mycophenolate mofetil (MMF) was held; nitazoxanide administered alone (n=2) or in conjunction with reduction in immunosuppression (n=3). In both cases where nitazoxanide was administered alone, the patient had initial improvement before recrudescence; infection resolved only after stopping MMF. Disseminated disease was cured with an 8-week course of albendazole in one case (E. cuniculi); in the case of Anncaliia algerae, the patient had a profound and persistent neutropenia associated with aplastic anemia and died of disseminated disease despite multi-drug therapy.

Conclusion: Microsporidiosis should be considered in the differential diagnosis for chronic diarrhea following SOT. Reducing immunosuppression remains the cornerstone of treatment; further research is needed to assess efficacy of nitazoxanide. Patients should be advised to properly filter well water, when appropriate.

Abstract #66: All that Glitters is Not Cancer: Unexpected Diagnosis of a Skin Lesion in a Patient with Metastatic Melanoma **Gabriel Motoa Cardona, MD** | *Massachusetts General Hospital; Brigham and Women's Hospital*

Background: Phaeohyphomycosis is a deep fungal infection caused by dematiaceous fungi, typically affecting the immunocompromised. We report an unusual case in an elderly patient with metastatic melanoma.

Case: A female in her 80s with metastatic melanoma arising from the right plantar surface underwent excision and 13 cycles of adjuvant nivolumab. This was complicated by pneumonitis, treated with steroids, and immune checkpoint inhibitor (ICI)–induced hepatitis, managed with tacrolimus, mycophenolate, and prednisone. She presented with a firm, non-tender, 3.5 cm x 5 cm subcutaneous plaque on her left calf, initially suspected to be metastatic melanoma. PET/CT showed a new linear cutaneous uptake along the left calf. Skin biopsy revealed a deep fungal infection consistent with phaeohyphomycosis. The patient, from the northeastern US and a gardening enthusiast, denied any recent or remote penetrating trauma to the left calf.
She was initially treated with voriconazole 200 mg orally twice daily. Beta-D-glucan was elevated (217 pg/mL; reference <60 pg/mL), and was later switched to posaconazole due to phototoxicity and difficulty achieving therapeutic voriconazole levels with increasing doses. Plastic surgery deemed debridement unfeasible due to concerns about poor wound healing.
Fungal culture grew Exophiala spp (MIC for voriconazole was 0.5 mcg/mL, 0.06 mcg/mL for posaconazole). After 5 months of therapy, the lesion flattened with no drainage or tenderness, and Beta-D-glucan became negative. Antifungal therapy was discontinued. One month later, the patient remained asymptomatic with no worsening of the skin lesion, though it remained hyperpigmented but without nodularity. Beta-D-glucan remained negative, and PET/CT showed resolution of the focal FDG uptake.

Conclusions: This case emphasizes the importance of considering fungal infections in immunocompromised patients with skin lesions, even without apparent trauma. The diagnosis of Exophiala spp. with histopathology alone is challenging, underscoring the importance of fungal cultures and susceptibility testing for optimal therapy.

Abstract #67: Optimizing Liposomal Amphotericin B in Patients on Extracorporeal Membrane Oxygenation Utilizing Therapeutic Drug Monitoring **Shiv Patel, MD** | *Medical College of Wisconsin*

Background: Liposomal amphotericin B (L-AMB) dosing is difficult in patients requiring extracorporeal membrane oxygenation (ECMO) due to pharmacokinetic changes from sequestration into the ECMO circuitry and overall, from critical illness. We present 2 cases of L-AMB use while on ECMO in patients who have histoplasmosis- or blastomycosis-induced acute respiratory distress syndrome (ARDS). Amphotericin peak levels for therapeutic drug monitoring (TDM) were collected from the central venous line (CVL), pre-oxygenator, post-oxygenator, and arterial line along with trough levels in the CVL. These were interpreted based on the goal maximum concentration of 83 ug/mL from amphotericin package insert.

Case Presentation: The first case is of a 53-year-old man with immunosuppression for focal segmental glomerulosclerosis who presented with ARDS secondary to pulmonary histoplasmosis. He was started on venovenous ECMO and L-AMB at 5 mg/kg/day along with oral itraconazole. L-AMB was increased the next day to 10 mg/kg/day to achieve appropriate levels. TDM obtained before dose increase and 4 days after dose increase demonstrated arterial amphotericin peaks of 77.14 ug/mL and 78.75 ug/mL, respectively. After 7 days of L-AMB, he was decannulated from ECMO. He improved and was discharged home.

The second case is a 27-year-old woman who presented with ARDS secondary to pulmonary blastomycosis. She was started on ECMO (venovenous then veno-veno-arterial) and L-AMB at 10 mg/kg/day. TDM obtained 8 days later demonstrated an arterial amphotericin peak of 96.61 ug/mL. After 30 days of L-AMB, she was decannulated from ECMO and eventually discharged to a facility. Itraconazole was not started until after decannulation.

Conclusions: In these cases, both patients on ECMO achieved similar pharmacokinetic parameters with 10 mg/kg/day compared to 5 mg/kg/day in non-ECMO patients. TDM can be considered to help guide L-AMB dosing in ECMO.

Abstract #68: Infectious Dermatologic Disease in Displaced Populations: A Systematic Review of Trends and Proactive Measures **Nadia Siddiqui** | *University of Washington*

Background: The global refugee population faces significant health challenges, including a high burden of infectious dermatologic diseases. These issues are compounded by climate change and diverse environmental exposures during migration. This review synthesizes existing research to identify gaps, effective interventions, and trends in the burden of infectious cutaneous diseases among displaced populations.

Methods: This systematic review adhered to PRISMA guidelines, evaluating 9,292 articles. Studies addressing infectious cutaneous diseases in forcibly displaced populations were included. After full-text screening, 46 publications met the inclusion criteria. Data were analyzed to identify disease prevalence, treatment patterns, and contextual factors.

Results: The most frequently addressed diseases included cutaneous leishmaniasis (CL), scabies, fungal infections, and leprosy. CL was the most extensively studied, with attention to its transmission dynamics and treatment challenges. Scabies, prevalent in overcrowded refugee camps, was associated with secondary bacterial infections. Fungal infections, particularly tinea capitis, were notable among groups of refugees. While dermatitis was frequently mentioned, its non-infectious subtypes highlight the importance of distinguishing between infectious and non-infectious etiologies.
Few studies directly addressed the role of climate change, with limited evidence linking environmental changes to shifts in the epidemiology of CL. Treatment barriers, such as drug resistance and inadequate healthcare access, were prevalent in refugee camp settings. Publication trends showed increased focus on migration-related infectious dermatoses following the Syrian refugee crisis, with studies conducted in refugee camps, community clinics, and hospitals.

Conclusions: This review highlights the compounded impact of displacement on infectious dermatologic diseases. Gaps remain in addressing climate change as a variable and ensuring equitable access to care for displaced populations. Targeted surveillance, improved healthcare access, and integrated strategies are essential to mitigate these challenges and improve outcomes for vulnerable populations.

Abstract #69: A Case of a Rare Disseminated Dimorphic Fungal Infection in a Kidney Transplant Recipient **Rebecca Unterborn, MD** | *University of Colorado*

Background: Primarily affecting immunosuppressed hosts, Emergomyces canadensis is a dimorphic fungus that has recently emerged in North America. Mortality is quoted at 50%. With its tendency to present as disseminated disease combined with its propensity to mimic other organisms in the laboratory, >75% of patients are misdiagnosed with tuberculosis or other fungal infections.

Case Presentation: A 63-year-old male with history of kidney transplant in 2021 for hypertensive nephropathy on tacrolimus, mycophenolate, and prednisone, presented with ten days of dyspnea, cough, and widespread papular rash. Laboratory studies were notable for pancytopenia and acute kidney injury (creatinine 5.72 mg/dL, baseline 2.5 mg/dL).

Blood CMV, EBV, HSV and VZV PCRs were undetectable. Serum beta-D-glucan, Blastomyces and Coccidiomycosis antibody panels were negative. Aspergillus galactomannan was positive. Histoplasma urine and serum antigens were positive at 4.62ng/mL and 1.88ng/mL respectively. Histopathology of a skin papule biopsy noted abundant yeast forms, consistent with Histoplasma capsulatum. CT chest and abdominal ultrasound showed right upper lobe pulmonary nodules and hepatosplenomegaly. Voriconazole was started on hospital day two and liposomal amphotericin was added on hospital day four for presumed disseminated histoplasmosis. He subsequently developed respiratory failure and encephalopathy requiring intubation. He died on hospital day eight following family decision to transition to comfort-focused care. Post-mortem, skin biopsy and fungal blood cultures returned positive for Emergomyces canadensis, identified via DNA sequencing.

Conclusion: Prompt identification of Emergomycosis is challenging due to cross-reactivity with fungal antigens (i.e. Histoplasma, beta-D-glucan, galactomannan), similar morphology to other dimorphic fungi, and clinical similarity to tuberculosis. PCR or sequencing is the diagnostic gold-standard. While no treatment guidelines exist, literature suggests amphotericin improves mortality, often followed by at least twelve months of itraconazole with extension if immunosuppression cannot be augmented. With increasing prevalence of transplantation and expanded use of immunosuppressive medications, Emergomyces should be considered in an immunosuppressed host with disseminated infection.

Abstract #70: *Pneumocystis jirovecii* Pneumonia Following Bispecific Monoclonal Antibodies in Patients with Relapsed or Refractory Multiple Myeloma: A Systematic Review and Meta-analysis **Karan Srisurapanont, MD** | *Chiang Mai University, Thailand*

Background: Routine prophylaxis against *Pneumocystis jirovecii* pneumonia (PJP) in patients with relapsed/refractory multiple myeloma (R/R MM) treated with bispecific antibodies (BsAbs) is suggested by various international guidelines. However, the evidence supporting the recommendation is currently limited. This systematic review and meta-analysis aimed to assess the prevalence of PJP and the benefits of PJP prophylaxis in this population.

Methods: We searched PubMed, Scopus, and Embase up to November 28, 2024. Observational studies and clinical trials reporting the prevalence and/or mortality rate of PJP among patients with R/R MM treated with BsAbs were included. The relative risk (RR) of PJP was compared between patients receiving PJP prophylaxis and those who did not. The outcomes were pooled using random-effects meta-analysis and presented with 95% confidence intervals (CIs). The certainty of evidence regarding PJP prophylaxis was evaluated using the Grading of Recommendations Assessment, Development, and Evaluation approach.

Results: A total of nine studies involving 846 patients with R/R MM treated with BsAbs were included. The BsAbs in these studies targeted B-cell maturation antigen (BCMA), G-protein-coupled receptor, class C, group 5, member D (GPRC5D), and Fc Receptor Homolog 5 (FcRH5). The prevalence of PJP was 3.43% (95% CI 2.39–4.89%). Grade 3-4 infections accounted for 83.74% (95% CI 55.26-95.55%) of all PJP infections. The mortality rate of PJP was 25.00% (95% CI 6.30–62.29%). Evidence of low certainty suggested that PJP prophylaxis reduced the risk of PJP (RR 0.26, 95% CI 0.07–0.96).

Conclusions: PJP is an uncommon but devasting infectious complication in patients with R/R MM receiving BsAbs. Our findings support routine PJP prophylaxis in this population.