939. Predicting Attributable Mortality in Pediatric Patients with Cancer Admitted to the Intensive Care Unit for Suspected Infection

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Session: P-53. Infections in Immunocompromised Individuals

Background. Infection and sepsis are important contributors to mortality in children with cancer. Although pediatric risk prediction scores have improved identification of children at high risk of death in the PICU, the value of these tests in immunocompromised children is unknown.

Methods. In this IRB-approved retrospective study performed at St. Jude Children's Research Hospital, we evaluated the performance of 4 pediatric risk scores, the Pediatric Risk of Mortality (PRISM), Pediatric Sequential Organ Failure Assessment (pSOFA), Quick Sequential Organ Failure Assessment (qSOFA) scores (using data available at 1, 6, 12 and 24 hours) and the Paediatric Index of Mortality 3 (PIM-3) score (at 1 hour), to predict attributable mortality (death ≤ 60 days without organ dysfunction recovery). Inclusion criteria: Age < 24 years, active cancer therapy (other than bone marrow transplantation), and admission to PICU between 2013 and 2019 with suspected infection (collection of a blood culture and initiation of antibiotic therapy). Scores were calculated using the worst value obtained for each variable. Score distributions were compared by the Mann-Whitney U test, and optimal cutoffs selected by maximizing Youden's index. An unadjusted p-value < 0.05 was considered statistically significant.

Results. Of 202 episodes of PICU admission for suspected infection in 168 participants, there were 12 attributable (6%) and 4 unrelated (2%) deaths. Demographic and cancer-related characteristics were not associated with mortality (Table 1). Of the 4 prediction scores, only the PRISM score at 24 hours was associated with mortality (P = 0.012; Table 2). For PRISM score ≥ 18, sensitivity was 58.3%, specificity was 81.6%, positive predictive value was 16.7%, and negative predictive value was 96.9% for attributable mortality.

Table 1. Risk factors for attributable mortality in pediatric patients with cancer admitted to the intensive care unit with suspected infection.

	Attributable mortality				
	Yes (n = 12)		No (n = 190)		P =
Characteristic	n	(%)	n	(%)	
Sex					0.76
Female	4	(33.3%)	79	(41.6%)	
Male	8	(66.7%)	111	(58.4%)	
Age, mean (SD)	13.4	(4.8)	11.4	(6.4)	0.29
Race					0.51
White	10	(83.3%)	137	(72.1%)	
Black	2	(16.7%)	33	(17.4%)	
'Mixed' or Other	0	(0%)	20	(10.5%)	
Malignancy group					0.36
Hematologic	9	(75%)	112	(58.9%)	
Solid Tumor	3	(25%)	50	(26.3%)	
Brain Tumor	0	(0%)	25	(13.2%)	
Other or multiple	0	(0%)	3	(1.6%)	
Malignancy status					1.0
Relapsed/Recurrent/Refractory	7	(58.3%)	86	(45.3%)	
Active	4	(33.3%)	86	(45.3%)	
Remission	1	(8.3%)	17	(8.9%)	
Not reported	0	(0%)	1	(0.5%)	
BMI percentile classification					0.22
Underweight	1	(8.3%)	13	(6.8%)	
Normal Weight	4	(33.3%)	93	(48.9%)	
Obese	3	(25%)	29	(15.3%)	
Very obese	4	(33.3%)	34	(17.9%)	
Not available	0	(0%)	21	(11.1%)	
ANC at presentation					0.060
<100	6	(50%)	94	(49.5%)	
100-<500	5	(41.7%)	26	(13.7%)	
≥500	1	(8.3%)	70	(36.8%)	

Table 2. Association between risk prediction scores and attributable mortality in pediatric patients with cancer admitted to the intensive care unit with suspected infection.

	Attributable mortality				
	Yes (n = 12)		No (n = 190)		P =
	Median	IQR	Median	IQR	
pSOFA score					
1 hour	8	(3;10)	5	(3;8)	0.18
6 hours	8.5	(4;11)	6	(3;8)	0.26
12 hours	9	(5;11)	7	(4;9)	0.45
24 hours	10	(6;14)	8	(7;10)	0.13
qSOFA score					
1 hour	1	(1;2)	1	(1;2)	0.23
6 hours	1.5	(1;2)	1	(1;2)	0.27
12 hours	2	(1;2)	1	(1;2)	0.20
24 hours	2	(1;3)	1	(1;2)	0.13
PRISM score					
1 hour	13.5	(4;18)	9	(8;13)	0.07
6 hours	13.5	(6;18)	11	(8;15)	0.19
12 hours	13.5	(8;20)	12	(8;15)	0.30
24 hours	18.5	(9;20)	12	(12;15.8)	0.01*
PIM-3	-2.6	(-6.1;-2.2)	-2.7	(-2.8;-2.4)	0.17

Conclusion. In children with cancer admitted to PICU with suspected infection, early pediatric risk prediction scores did not predict mortality. The PRISM score calculated at 24 hours did predict mortality but was relatively insensitive. Further research is needed to develop a risk score for immunocompromised children and to validate the 24 hour PRISM score in this population.

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940. The use of a commercially available CMV T Cell Immunity Panel to Assess the Risk of CMV Infections in Hematopoietic Cell Transplant Recipients with Low Level CMV Viremia

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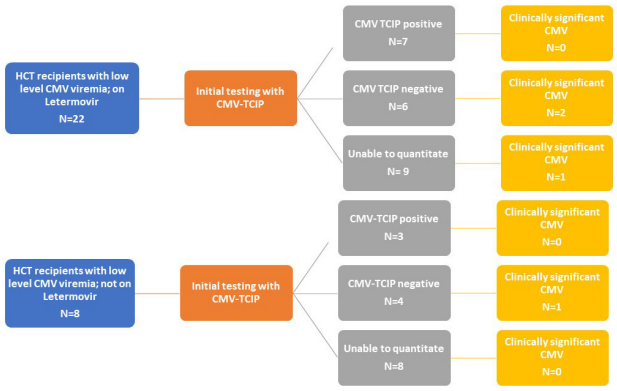
Session: P-53. Infections in Immunocompromised Individuals

Background. Cytomegalovirus (CMV) infections continue to be associated with increased morbidity and mortality in Hematopoietic Cell Transplant (HCT) recipients. Treatment of high risk patients with low level viremia may reduce overall duration of therapy and reduce complications. CMV T Cell Immunity Panel (TCIP) may help identify patients at high risk of CMV reactivation prior to developing clinically significant CMV infection (CS-CMVi). Our study aims to identify HCT recipients with low level CMV viremia who are at high risk of CMV reactivation with the use of CMV-TCIP while on or off letermovir for prophylaxis.

Methods. We enrolled in a prospective cohort study allogeneic HCT recipients (excluding cord blood transplantation) with low level of CMV viremia (viral load of < 1000 IU/ml) on no therapy, starting October 2019. CMV TCIP assay was performed at enrollment, weeks 1, 2, 3, 4, 6 and 8. CMV TCIP results were interpreted as negative or positive based on percentage of interferon gamma producing CD4+ or CD8+ CMV specific T cells. The primary endpoint was progression to a CS-CMVi. We are presenting the results of the first 30 patients with data up to 4 weeks from enrollment.

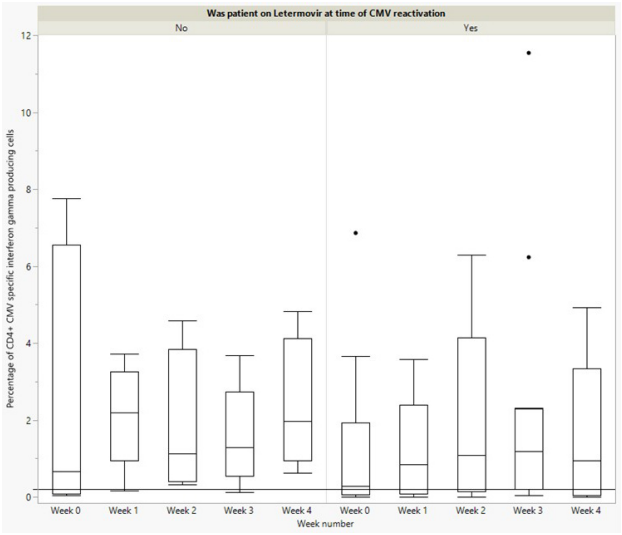
Results. Among the 30 patients, 73% were on letermovir for CMV prophylaxis. Majority of the patients were ≥ 40 years old (77%), male (63%), received transplant for AML (40%), were in complete remission at time of transplant (23%) and received cyclophosphamide (90%). The median time from transplant to enrollment was 77 days (IQR 37-172) (table 1). At enrollment, 10 (33%) patients had a positive CMV TCIP, 10 (33%) had a negative CMV TCIP, and 10 (33%) had an uninterpretable CMV TCIP result due to inability to quantify T cells (table 1). Four (13%) patients developed CS-CMVi; 3 of these patients had a negative TCIP and 1 had unquantifiable CMV TCIP (Figure 1). The mean percentage of CMV specific CD4+ and CD8+ interferon producing cells was 1.76% (SD 2.24) and 9.37% (SD 11.35) for those on letermovir and 2.09% (SD 2.05) and 3.97% (SD 5.24) off letermovir respectively (*P >0.05*) (Figure 2).

Figure 1. Breakdown of the 30 patients during the 4 week follow up period



Abbreviations: HCT: Hematopoietic cell transplantation; CMV: Cytomegalovirus; TCIP: T cell immunity panel

Figure 2. Box-plot of percentage of CD4+ CMV specific interferon producing cells over time. Threshold for positive result (0.2%) marked.



Abbreviations: CMV: Cytomegalovirus

Table 1. Baseline characteristics of patients enrolled

Baseline variables	Total (n=30)	CMV TCIP positive (n=10)	CMV TCIP negative (n=10)	CMV TCIP unquantifiable (N=10)
Age/years median (IQR)	54 (39-70)	51 (28-65)	56 (45-66)	46.5 (42-62)
Age >/= 40 years (%)	23 (77)	8 (80)	6 (60)	9 (90)
Gender (%):				
Male	19 (63)	5 (50)	4 (40)	8 (80)
Female	11 (37)	5 (50)	6 (60)	2 (20)
Race (%):				
Caucasian	14 (47)	3 (30)	5 (50)	6 (60)
African American	4 (13)	2 (20)	1 (10)	1 (10)
Hispanic	8 (27)	3 (30)	3 (30)	2 (20)
Other	4 (13)	2 (20)	1 (10)	1 (10)
Underlying cancer (%))				
Acute myeloid leukemia	12 (40)	3 (30)	4 (40)	5 (50)
Acute lymphoblastic leukemia	8 (27)	4 (40)	2 (20)	2 (20)
Non-Hodgkin's lymphoma	1 (3)	0 (0)	1 (10)	0 (0)
Myelodysplastic syndrome	5 (17)	2 (20)	2 (20)	1 (10)
Other	4 (13)	1 (10)	1 (10)	2 (20)
Cancer status at time of transplant (%):				
Complete remission	23 (77)	9 (90)	8 (80)	6 (60)
Partial remission	3 (10)	1 (10)	1 (10)	2 (20)
No remission	4 (13)	0 (0)	1 (10)	2 (20)
Type of transplant (%):				
Matched related donor	13 (43)	5 (50)	4 (40)	4 (40)
Matched unrelated donor	8 (27)	2 (20)	3 (30)	3 (30)
Haploidentical donor	9 (30)	3 (30)	3 (30)	2 (30)
Time from transplant to enrollment/ days Median (IQR)	77 (37-172)	133 (74-239)	72 (38-147)	41 (30-126)
Cell Source (%):				
Peripheral	27 (90)	2 (20)	9 (90)	10 (100)
Marrow	3 (10)	8 (80)	1 (10)	0 (0)
Discordant recipient-donor gender (%)	15 (50)	4 (40)	5 (50)	6 (60)
CMV serology at time of transplant (%):				
Donor positive	13 (43)	5 (50)	4 (40)	4 (40)
Recipient positive	27 (90)	10 (100)	7 (70)	10 (100)
Graft versus host disease prophylaxis (%):				
Cyclophosphamide containing regimen	26 (87)	8 (80)	9 (90)	9 (90)
Antithyroglobulin containing regimen	1 (3)	0 (0)	1 (10)	0 (0)
No cyclophosphamide/antithyroglobulin	3 (10)	2 (20)	0 (0)	1 (10)
Total body irradiation (%)	10 (33)	2 (20)	4 (40)	4 (40)
Graft versus host disease within 30 days of enrollment (%)	15 (50)	5 (50)	8 (80)	2 (20)
Graft versus host disease treatment within 30 days of enrollment (%):				
Systemic steroids	9 (30)	3 (30)	4 (40)	2 (20)
Ruxolotinib	2 (7)	2 (20)	0 (0)	0 (0)
Sirolimus	1 (3)	0 (0)	0 (0)	1 (10)
Vedolizumab	1 (3)	1 (10)	0 (0)	0 (0)
Tacrolimus	7 (23)	2 (20)	4 (40)	1 10)
Photopheresis	1 (3)	1 (10)	0 (0)	0 (0)
Itacitinib	1 (3)	0 (0)	1 (10)	0 (0)
Peak steroid dosing within 2 weeks of enrollment (%):				
>/=1 mg/kg/day prednisone equivalent	4 (13)	1 (10)	2 (20)	1 (10)
< 1 mg/kg/day prednisone equivalent	7 (23)	4 (40)	2 (20)	1 (10)
No steroids	19 (63)	5 (50)	6 (60)	8 (80)
CMV viral load at enrollment (%):				
<34.5- 136 copies/ml	24 (80)	10 (10)	7 (70)	7 (70)
137-500 copies/ml	5 (17)	0 (0)	2 (20)	3 (30)
500-1000 copies/ml	1 (80)	0 (0)	1 (10)	
On letermovir for CMV prophylaxis at time of enrollment (%)	22 (73)	7 (70)	6 (60)	9 (90)
Clinically significant CMV infection	4 (13)	0 (0)	3 (30)	1 (10)

Abbreviations: CMV: Cytomegalovirus; TCIP: T cell immunity panel; IQR: Interquartile range

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Conclusion. Our results demonstrate the value of the CMV TCIP in identifying high risk HCT recipients prior to developing CS-CMV infection.

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941. Isavuconazole Prophylaxis Against Invasive Fungal Infection: A Pooled Analysis with a Comparison of Posaconazole Delayed-release Tablet Prophylaxis

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Session: P-53. Infections in Immunocompromised Individuals

Background. There are limited data regarding the use of isavuconazole as primary antifungal prophylaxis against invasive fungal infection (IFI) among immunocompromised patients. Therefore, the purpose of this study was to assess efficacy and breakthrough IFIs of isavuconazole prophylaxis by a pooled analysis of the reported cases of isavuconazole prophylaxis with a comparison of cases of posaconazole delayed-release tablet prophylaxis.

Methods. Pubmed was searched for English-written articles published up to April 2021. Studies that reported cases of primary antifungal prophylaxis with isavuconazole or posaconazole delayed-release tablet in adults ≥ 18 years were reviewed. Breakthrough IFI was defined as the occurrence of proven or probable IFI while on prophylaxis.

Results. For overall isavuconazole prophylaxis, a total of 818 courses of prophylaxis was identified from 12 studies. Breakthrough IFIs were noted in 41 patients. The median duration of isavuconazole prophylaxis of these patients before the diagnosis of IFI was 17 days. The most common breakthrough IFI was candidiasis (34.1%), followed by aspergillosis (24.4%) and mucormycosis (12.2%). Sixteen patients died (39.0%). Among patients with hematologic malignancies or hematopoietic stem cell transplantation, isavuconazole prophylaxis (404 courses) was compared with posaconazole delayed-release tablet prophylaxis (1952 courses). The incidence rate of breakthrough IFIs was higher in the cohort of isavuconazole prophylaxis (24 patients of 404 courses) than in the cohort of posaconazole delayed-release tablet prophylaxis (44 patients of 1952 courses). Aspergillosis (40.9%) was the most common breakthrough IFI in the cohort of isavuconazole prophylaxis among patients with hematologic malignancies or hematopoietic stem cell transplantation, followed by candidiasis (27.3%) and mucormycosis (18.2%).

Conclusion. Although isavuconazole is licensed to treat aspergillosis and mucormycosis, breakthrough IFIs including aspergillosis, mucormycosis, and candidiasis may occur while on isavuconazole prophylaxis. Therefore, further studies are needed to define the benefits and risks of isavuconazole prophylaxis.

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942. Pulmonary Infections in Intestinal Transplant Recipients with Preexisting Pulmonary Nodules

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Session: P-53. Infections in Immunocompromised Individuals

Background. Pulmonary nodules in asymptomatic patients could represent latent pulmonary infections. Intestinal transplant (ITx) recipients with preexisting pulmonary nodules might be at higher risk for pulmonary infections. However, data is lacking.

Methods. This retrospective study included adult patients that underwent intestinal transplantation (ITx) from 5/2016 to 5/2020. Chest computed tomography (CT) scans performed within 12 months prior of ITx were obtained to evaluate for preexisting pulmonary nodules. Screening for endemic mycoses, *Aspergillus*, *Cryptococcus* and latent tuberculosis infection (LTBI) performed within 12 months prior ITx was obtained. We assessed for worsening pulmonary nodules, and fungal and mycobacterial infections during the 1st year post-transplant. Survival at one year post-transplant was also assessed.

Results. Forty-three patients underwent ITx. Twenty-three (53%) were Female. Median age was 46 years (range: 18-67). Chest CT scans were performed in 36(84%) patients prior to ITx. Preexisting pulmonary nodules were found in 30 (83%) of the patients. All were asymptomatic. Nodules were not calcified in 10 (33%) patients, calcified in 4 (13%), some calcified and some not calcified in 4 (13%) and unclear in 12 (40%). All the patients screened negative for fungi [*Coccidioides* antibody (Ab) was done in 15 (50%) patients, *Blastomyces* Ab and Histoplasma Ab in 7 (23%) each, *Histoplasma* urine antigen (Ag) and *Aspergillus* serum galactomannan in 3 (10%) each, and *Cryptococcus* serum Ag in 10 (33%) patients]. QuantiFERON-TB (QFT) was negative in 35 (81%) patients, positive in 2 (5%) and indeterminate in 6 patients (14%). QFT-Gold In-Tube was replaced to QFT-Plus in 3/2019. Post-transplant worsening of pulmonary nodules was noted in 12 (40%) patients and bronchoscopy was performed in six of them. Note that only 1 (3%) of the patients that had pre-existing pulmonary nodules developed a pulmonary infection (invasive pulmonary aspergillosis diagnosed 33 days after ITx). Our cohort survival at one year post-transplant was 79%.

Conclusion. Preexisting pulmonary nodules was common in our ITx cohort. However, only one case of pulmonary infection was noted among those who had pre-existing pulmonary nodules. Clinical monitoring is essential.

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943. Epidemiology of Actinomycosis in a Tertiary Care Cancer Center

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Session: P-53. Infections in Immunocompromised Individuals

Background. Actinomyces are human commensals with significant pathogenic potential. The aim of this study was to determine the epidemiology of Actinomycosis in a tertiary care cancer center and identify species most commonly associated with invasive disease.

Methods. We retrospectively reviewed all patients referred to our institution with suspected or documented solid or hematological malignancies and positive cultures for Actinomyces species from July 2007 to June 2020 (13 years). Species identification was performed by VITEK® automated system (bioMerieux Inc.). Probable invasive actinomycosis was defined as cases with consistent clinical presentation, suggestive radiographic findings, and a positive culture from a nonsterile site, but lack of histopathological confirmation. Proven invasive actinomycosis was defined as the presence of consistent clinical symptoms, suggestive radiographic findings, a positive culture and histopathological confirmation, or cultures from sterile site without histopathological confirmation. Contaminants were considered positive cultures from sterile or non-sterile site without evidence of disease.

Results. Of 233 cases with positive cultures 194 (83.3%) were considered contaminants and 39 (16.7%) diagnostic of invasive actinomycosis. Of 39 cases of invasive actinomycosis, 64% were documented in patients with solid tumors, 13% in hematological malignancy and 23% among individuals without proven malignancy, 25 (64%) were probable and 14 (36%) proven. Of patients with proven/probable actinomycosis 27 (69%) had polymicrobial growth. Abdominopelvic was the most frequent site of invasive actinomycosis. A. odontolyticus was the most common species isolated (41%) followed by A. meyeri (28%) in patients with invasive disease, and A. odontolyticus (42%) among contaminants.

Conclusion. The majority of positive cultures for Actinomyces species were considered contaminants. In our cohort Invasive actinomycosis affected mainly patients with solid tumors. Abdominopelvic was the most common site of invasive disease. Species most commonly associated with invasive actinomycosis were A. odontolyticus followed by A. meyeri with A. israelii isolated less frequently.

Disclosures. **All Authors**: No reported disclosures

944. CMV Peak Viral Load, Recurrence, Duration, and Outcomes in Kidney Transplant Recipients

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Session: P-53. Infections in Immunocompromised Individuals

Background. Cytomegalovirus (CMV) infection continues to cause morbidity in kidney transplant recipients, despite prophylaxis and pre-emptive therapy. Predictors