Conclusions: The Vira-ome tool, designed to detect pathogenic viruses using cfDNA data, performed well both on simulated and clinical samples with a majority of results confirmed by qPCR. Our results emphasize how computational predictions can complement clinical diagnostic approaches.

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Pjp Breakthrough Rates in Pediatric Allo-HSCT Patients Receiving a 2 Days per Week Sulfamethoxazole/Trimethoprim (SMX/TMP) Prophylaxis Regimen

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Introduction: Pneumocystis jiroveci pneumonia (PJP) is a serious complication for allo-HSCT recipients. Incidence has been reported up to 1 to 6% with a more recent report from CIBMTR data in allo-HSCT recipients of all ages demonstrating an incidence of 0.63% with prophylaxis. Current SMX/TMP prophylaxis guidelines do not specify the optimal days per week dosing regimen.
Objectives: To identify efficacy of 2.5mg/kg bid dosing two days per week and incidence of PJP pneumonia.
Methods: We conducted a retrospective chart review of all pediatric allo-HSCT patients ages 0 to 21 years from July 1, 2007 through June 30, 2019. SMX/TMP regimen was 2.5 mg/kg/dose bid at the start of conditioning through day -2 and then resumed Sat/Sun on day+28 (if engrafted) until 6 months off immunosuppression.
Results: We evaluated 118 cases of allo-HSCT in 114 patients. Two transplants received treatment dose SMX/TMP for other reasons and were excluded. Regimens included SMX/TMP prophylaxis (N=90), pentamidine (N=25), and atovaquone (N=1). There was one case of PJP pneumonia in a patient receiving SMX/TMP prophylaxis for an overall incidence of 0.86% and an incidence of 1.1% in the SMX/TMP prophylaxis group. The break-through case occurred day + 198 concurrently with Aspergillus pneumonia in a leukemia patient s/p cord blood transplant with GVHD and a history of BK, adenovirus, Candida, and multiple bacterial infections. This patient died on day +214 due to ARDS.
Conclusion: Current recommendations for PJP prophylaxis lack specific details regarding the optimal number of days per week. This pediatric specific analysis suggests that a SMX/TMP regimen of 2.5 mg/kg/dose bid at the start of conditioning through day -2 with a restart Sat/Sun on day+28 (if engrafted) until off immunosuppression for 6 months is efficacious relative to historical data. Unfortunately, patients with evidence of very severe T-cell dysfunction such as our breakthrough case may remain at risk despite a prophylactic regimen. Future collaborative multi-institutional studies should include specific details regarding dosing regimens.

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Impact of HHV-6 in Recipients of Ex Vivo T-Cell Depleted Hematopoietic Cell Transplant

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Introduction: Recipients of ex-vivo T-cell depleted (TCD) ($CD34^+$ selected) hematopoietic cell transplant (HCT) are at increased risk for infections by double-stranded DNA viruses. TCD HCT recipients at Memorial Sloan Kettering Cancer Center were routinely screened for HHV-6 by plasma PCR between 2012 and 2016. The objectives of our study were to 1) report the incidence of persistent HHV-6 viremia and disease 2) identify risk factors of persistent HHV-6 viremia; 3) examine the association between persistent HHV-6 viremia and overall survival (OS) at 1-year post-HCT.
Methods: Recipients with TCD HCT between 2012 and 2016 routinely screened for HHV-6 by plasma PCR were reviewed retrospectively. $CD34^+$ selection was performed by the CliniMACS CD34 Reagent system (Miltenyi Biotec, Germany). HHV-6 viremia was defined as $\geq$1 HHV-6 viral load (VL) >limit of quantification. Persistent HHV-6 viremia was defined as $\geq$2 consecutive measurements of VL $\geq$500 copies/mL through day +100 post-HCT, death, relapse, and second transplant whichever occurred first. Cox proportional model was used to examine the risk factors of persistent HHV-6 viremia. One-year OS was estimated by Kaplan-Meier method.
Results: Of 312 patients, 59% were male and median age was 55 years (range, 22-73). 67% had acute leukemia and myelodysplastic syndrome and 18% had mismatched donors. 55% developed HHV-6 viremia. Eighty-three (27%) had persistent HHV-6 viremia with a median duration of 67 days (interquartile range [IQR], 56-75) (Figure 1). Mismatched donor (P=0.04) and recipient CMV seronegativity (R-) (P=0.04) were associated with persistent HHV-6 viremia. Of 83 patients with persistent HHV6 viremia, 23 (28%) had max VL $\geq$10,000 copies/mL and 7 (8%) developed HHV-6 disease (encephalitis 1, pneumonitis 4, and organizing pneumonia 2). Maximum VL with HHV-6 disease was a median VL 71,700 copies/mL (IQR, 8,211-123,500). Persistent HHV-6 viremia was associated with lower absolute lymphocyte counts (ALCs) up to 1-year post-HCT (figure 2) and lower 1-year OS (P=0.02) (figure 3).
Conclusion: 27% of TCD HCT recipients developed persistent HHV-6 viremia. Mismatched donor and CMV R- were associated with persistent HHV-6 viremia. Among patients with persistent HHV-6 viremia, 8% developed HHV-6 disease. Persistent HHV-6 viremia was associated with lower ALCs and OS at 1-year post-HCT.

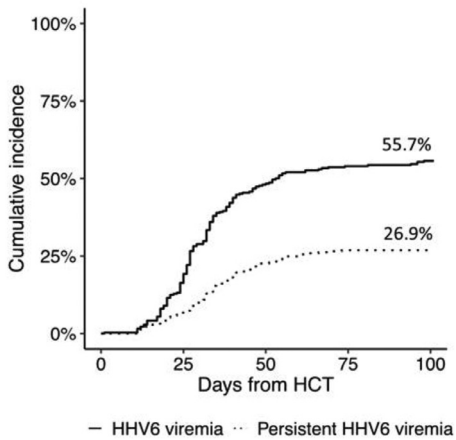

Figure 1. The cumulative incidence of HHV-6 viremia and persistent HHV-6 viremia.