affected by antacids. Maribavir increases tacrolimus exposure by 51% and does not affect voriconazole.

Conclusions: Maribavir has low risk for DDI. Inhibitors of CYP3A4 and/or P-gp may increase maribavir exposure, but dose adjustment of maribavir is not necessary. Potent inducers of CYP3A4 and P-gp decrease maribavir exposure, necessitating maribavir dose increase. Maribavir may increase exposure of immunosuppressants, such as tacrolimus. Therefore, monitoring of concomitant immunosuppressants' blood concentration should be considered at initiation, co-administration, and discontinuation of maribavir. Maribavir is not expected to interact with other concurrent medications.

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Toxicities of CMV Preemptive Therapy in the First 100 Days after Allogeneic Hematopoietic Cell Transplantation (HCT): A Real-World Study at Memorial Sloan Kettering Cancer Center (MSKCC)

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Background: Cytomegalovirus (CMV) is the most common viral infection after HCT. Current antivirals used for preemptive therapy (PET) effectively prevent CMV disease, but their use is limited by toxicities. We examined real-world utilization patterns of PET and associated toxicities in HCT recipients at high risk (HR) and low risk (LR) for CMV through day (D) 100 post HCT.

Methods: Adult, CMV-seropositive first bone-marrow or peripheral blood HCT recipients from January 1, 2015 through December 31, 2017, routinely monitored by quantitative CMV PCR (Taqman, Roche) were analyzed**.** PET utilization including types and sequence of antivirals, dose and duration, and reasons for discontinuation through D 100 were extracted from medical records. HR included T-cell depleted HCT or conventional mismatched or haploidentical HCT. All other were LR. Descriptive statistics are reported.

Results: Of 232 patients (pts), 121 (52%) received PET including 40 LR and 81 HR. PET started at a median 35 D post HCT [HR vs. LR: 32 vs. 39, P<0.0001]. CMV viral load (VL) at PET initiation was <137 IU/mL in 23 pts; and median of 475 IU/ml in 98 pts. Valganciclovir was the most common 1st PET (55%), followed by foscarnet (26%) and ganciclovir (19%). 65 pts completed planned 1st PET regimen; 33.1% discontinued 1st PET due to either clinical toxicity (20.7%) or lack of virologic response (12.4%). Subsequently, 2nd and 3rd PET agents were administered to 46.1% and 20.7% of pts respectively. Median duration of PET was 37 days [HR vs. LR: 41 vs. 30.5, P=0.011].

Conclusions: Valganciclovir was the preferred first line PET agent. HR pts had earlier initiation and longer PET duration. 1st PET discontinuation/change due to clinical or laboratory defined toxicity occurred commonly with similar frequency between HR and LR. Our findings support the need for more effective and safer PET alternatives for HCT recipients.

Characteristics	Overall (N = 121)	Low Risk (N = 40)	High Risk[1] (N=81)	P-value[2]
1st PET Agent				
Time to initiation of PET agent from index HCT (in days), median (IQR)	35.0 (28.0 - 42.0)	39.0 (35.0 - 52.0)	32.0 (26.0 - 39.0)	< 0.001
Quantifiable VL at PET initiation (>137 IU/ml), n (%)	98 (81.0%)	36 (90%)	62 (77%)	0.089
Viral load at PET initiation (in IU/ml), median (IQR)[3]	475.0 (312.5 - 1376.0)	471.0 (337.3 - 960.3)	698.0 (308.3 - 1478.0)	0.409
Types of 1st PET regimen				
Use of Valganciclovir, n (%)	66 (54.5%)	16 (24%)	50 (61.7%)	0.033
Duration of Valganciclovir (in days), median (IQR)	17.0 (11.2 - 31.0)	17.0 (14.0 - 19.5)	18.0 (10.0 - 31.8)	0.899
Use of Ganciclovir, n (%)	23 (19.0%)	14 (35%)	9 (11.1%)	0.003
Duration of Ganciclovir use, median (IQR)	14.0 (7.0 - 17.5)	11.5 (7.0 - 15.8)	15.0 (13.0 - 20.0)	0.141
Use of Foscarnet , n (%)	32 (26.4%)	10 (31%)	22 (27.2%)	0.800
Duration of Foscarnet use (days), median (IQR)	14.0 (11.0 - 21.2)	14.5 (10.3 - 21.5)	14 (11.3- 20.3)	0.826
Reason for 1st discontinuation of PET (as per physician's judgement), n (%)	121 (51.9%)	40 (32.2%)	81 (74.3%)	0.248
Completion of treatment regimen	65 (53.7%)	24 (60%)	41 (50.6%)	
Clinical Toxicity	25 (20.7%)	7 (17.5%)	18 (22.2%)	
Nephrotoxicity	8 (32%)	4 (57.1%)	4 (22.2%)	
Myelosuppression	13 (52.0%)	2 (28.6%)	11 (61.1%)	
Other Toxicities[4]	4 (16%)	1 (14.3%)	3 (16.7%)	
Lack of virologic response	15 (12.4%)	3 (7.5%)	12 (14.8%)	
Death[5]	2 (1.7%)	2 (5%)	0 (0%)	
Other[6]	14 (11.6%)	4 (10%)	10 (12.3%)	
Laboratory-based toxicity events for 1st PET[7]				
Myelosuppression for (Val)Ganciclovir (N= 89)				
Neutropenia	19 (21.3%)	7 (17.5%)	12 (14.8%)	0.745
Thrombocytopenia	10 (11.2%)	5 (12.5%)	5 (6.2%)	0.295
Leukopenia	20 (22.5%)	7 (17.5%)	13 (16.0%)	0.890
Nephrotoxicity for Foscarnet (N= 32)				
Increase in Serum Creatinine (≥ 2x)	4 (12.5%)	1 (10.0%)	3 (13.6%)	1.000
Aggregate use of PET during 100 days post-HCT				
Number of patients who received 2nd PET[8]	107 (46.1%)	34 (27.4%)	73 (67.6%)	<.0001
Number of patients who received 3rd PET	48 (20.7%)	13 (10.5%)	35 (32.4%)	<.0001
Duration of any PET agents (days), median (IQR)	37.0 (26.0 - 51.0)	30.5 (22.8 - 42.3)	41.0 (28.0 - 60.0)	0.011

Notes:
1. High risk for CMV group included patients that received T-cell depleted or haploidentical HCT, or HCT from a mismatched donor. The rest of the patients were classified into the low risk group.
2. Statistical differences in characteristics between high and low-risk individuals were identified using chi-square test for categorical variables and Mann-Whitney rank-sum test for continuous variables
3. Among patients with quantifiable VL (>137 IU/ml)
4. Other toxicities included drug fever, electrolyte dyscrasias, and GI symptoms.
5. Causes of death included: progression of hematologic disease.
6. Other reasons for PET discontinuation included insurance coverage-related, switch between oral and IV medication forms due to intolerance of IV PET and hospital discharge respectively, change to cidofovir/CMX-001 to cover concurrent adenoviremia, dose modification as per renal function.
7. Laboratory myelosuppression was defined as follows: 250% decrease in ANC, PLT, and WBC count from baseline for neutropenia, thrombocytopenia, and leukopenia respectively, at the time of PET agent discontinuation. Laboratory nephrotoxicity was defined as ≥ 2 times increase in creatinine from baseline, at the time of PET agent discontinuation.
8. Changes in PET type and/or dose of same PET agent were imputed as PET change.

Abbreviations: HCT: allogenic stem-cell transplant; PET: preemptive anti-viral therapy; SD: standard deviation; VL: CMV viral-load; GI: gastrointestinal tract

Figure 1. PET utilization and outcomes among HCT who received PET

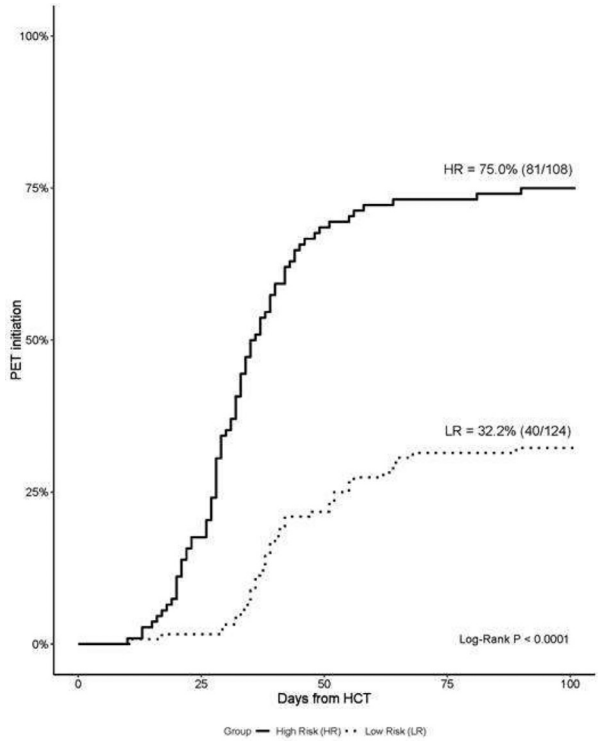

Figure 2. Cumulative incidence of 1st PET in the first 100 days post-HCT

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Use of the Quantitative Karius® Plasma Next Generation Sequencing Cell-Free Pathogen DNA Test to Detect and Monitor Cytomegalovirus Infection in Allogeneic Stem-Cell Transplant Recipients

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Background: Allogeneic stem-cell transplant (allo-SCT) recipients are at risk of developing severe CMV infection. The pre-