Patrick Derigs[1], Maria-Luisa Schubert[1], Paul Schnitzler[1], Carsten Müller-Tidow[1], Peter Dreger[1], Michael Schmitt[1]

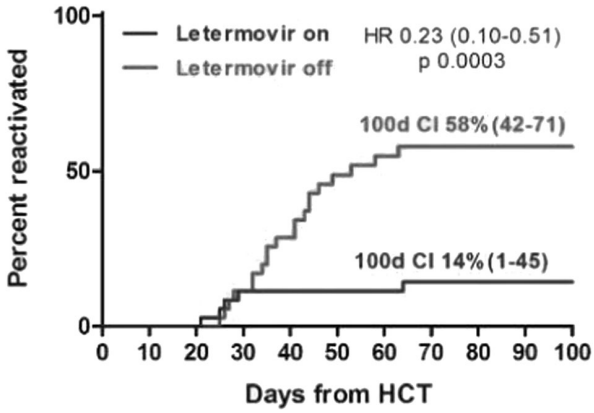
[1]Heidelberg University Hospital, Heidelberg, Germany,

Background: Reactivation of cytomegalovirus (CMV) still contributes substantially to morbidity and mortality after allogeneic hematopoietic cell transplantation (alloHCT). Recently, letermovir became available as the first drug approved in Europe for prophylaxis of CMV reactivation in seropositive patients who have undergone alloHCT. Letermovir is neither myelo- nor nephrotoxic, and significantly reduced the incidence of CMV reactivation in a pivotal phase III trial (NEJM 2017;377:2433). Therefore we adopted letermovir prophylaxis according to the label as standard policy in our institution: In seropositive recipients letermovir was initiated after engraftment and continued until day +100 or CMV reactivation. The aim of the present study was to investigate if the favorable trial results could be reproduced under real-world conditions.

Methods: The study cohort consisted of the first seropositive 35 patients who received letermovir prophylaxis at our institution (between March and August 2018). These were compared with a control cohort transplanted between August 2017 and March 2018 before the advent of letermovir. Study and control cohorts were matched for CMV donor/recipient sero-status, underlying disease and donor type source of stem cells and application of ATG. CMV viremia was monitored by a quantitative PCR twice a week during the inpatient period and weekly thereafter. Patients reactivating CMV prior to engraftment were not considered as event in both groups.

Results: No major side effects of letermovir intake were observed. With altogether 5 reactivation events, the cumulative rate of CMV reactivation on day +100 was 14% (95%CI 1-45%) in the letermovir cohort and thus significantly lower than in the control group (20 events, 58% (95%CI 42-71%); HR 0.23 (0.10-0.51); p=0.0003). The median time to reactivation was 53 days for the control group and not reached for the letermovir group. The cumulative number of days on valganciclovir before d +100 was 151d for the 35 letermovir patients vs 689d for the 35 control patients. There were no hospitalizations for foscavir administration in the letermovir group compared to 5 hospitalizations in the control group. There were 2 deaths before d +100 in the letermovir group (one PD, one NRM) and 3 deaths in the control group (all PD).

Conclusions: This observational study confirms the safety and efficacy of letermovir for the prophylaxis of CMV reactivation in seropositive patients after alloHCT in a real-world setting. Our results are in good concordance with the phase III trial. Although letermovir appeared to reduce the need for therapeutic valganciclovir and foscavir tremendously, larger samples with longer follow-up are needed to assess the impact of letermovir prophylaxis on non-relapse and overall mortality as well as on resource consumption.



[[P407 Image] 1. Cumulative incidence of CMV reactivation by letermovir prophylaxis (n=35 per cohort)]

Disclosure: Patrick Derigs, Maria-Luisa Schubert and Paul Schnitzler have nothing to declare.

Carsten Müller-Tidow, Peter Dreger and Michael Schmitt are members of a national advisory board of MSD Germany.

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CMV outcomes and health care resource utilization in CMV-seropositive (R+) hematopoietic stem cell transplant (HCT) recipients managed with pre-emptive therapy (PET)

Jiaqi Fang[1], Phaedon D. Zavras[1], Yiqi Su[1], Amit D. Raval[2], Yuexin Tang[2], Miguel-Angel Perales[3,4], Sergio Giralt[3,4], Genovefa Papanicolaou[1,4]

[1]Memorial Sloan Kettering Cancer Center, Infectious Disease Service, New York, NY, United States, [2]Merck & Co., Inc., Kenilworth, NJ, United States, [3]Memorial Sloan Kettering Cancer Center, Bone Marrow Transplant Service, New York, NY, United States, [4]Weill Cornell Medical College, Cornell University, New York, NY, United States

Background: CMV viremia occurs in 40%-80% of CMV R + HCT recipients. PET use has reduced the risk of CMV end-organ disease (EOD) and associated mortality; However, PET use may lead to substantial antiviral use and healthcare resource utilization. Limited real-world data are available on the outcomes of PET. Therefore, we aimed to examine CMV outcomes (EOD, resistance), CMV-related

mortality by Day (D)180 and healthcare resource utilization between PET and No-PET groups among CMV R+ recipients undergoing first HCT.

Methods: We conducted a retrospective cohort study of adults, CMV R+ recipients of first peripheral blood or marrow allograft at MSKCC identified from March 2013 through December 2017. Data was extracted from electronic medical records and HCT databases. CMV+ recipients were monitored weekly by quantitative PCR assay starting on D14 through D180 post HCT. Use of antiviral therapy for CMV viremia defined PET. High CMV risk (HR) comprised T-cell depleted (TCD) HCT by CD34+-selection regardless of donor HLA match or conventional HCT from mismatched or haploidentical donors; Low risk (LR) included conventional HCT from matched related donors. CMV EOD was scored by standard criteria. CMV resistance mutations were confirmed by sequencing (Viracor-Eurofins). Length of stay (LOS) for HCT admissions and readmissions were identified through D180. Stratified analyses were performed to examine outcomes by PET use and CMV risk.

	Overall PET (n=208)	Overall No-PET (n=160)	P-value	Low CMV Risk PET (n=58)	Low CMV Risk No-PET (n=118)	P-value	High CMV Risk PET (n=150)	High CMV Risk No-PET (n=42)	P-value
LOS for admission for HCT in days, mean (SD)	34.3(18.6)	29.9 (15.5)	**0.0001**	36.0(22.1)	30.7 (17.6)	**0.02**	33.3 (16.7)	27.7 (6.4)	**0.02**
Number of patients with readmission(s), (%)	112 (53.8%)	53 (33.1%)	**0.00005**	34 (58.6%)	39 (33.1%)	**0.001**	78 (52.0%)	14 (33.3%)	**0.03**
Number of readmissions, (%)	180 (100%)	78 (100%)		53 (100%)	57 (100%)		127 (100%)	21 (100%)	
CMV	40 (22.2%)	0 (0%)	N/A	4 (7.5%)	0 (0%)	N/A	36 (28.3%)	0 (0%)	N/A
Non-CMV Infections	41 (22.8%)	21 (26.9%)		12 (22.6%)	18 (31.6%)		29 (22.8%)	3 (14.3%)	
GvHD	15 (8.3%)	6 (7.7%)		8 (15.1%)	4 (7.0%)		7 (5.5%)	2 (9.5%)	
Other	84 (46.7%)	51 (65.4%)		29 (54.7%)	35 (61.4%)		55 (43.3%)	16 (76.2%)	
Readmission rate (per 1,000 patient-days)	5.2	3.1	**0.00006**	5.5	3.0	**0.002**	5.1	3.2	**0.04**
Readmission LOS (per 1,000 patient-days)	93.4	54.2	N/A	95.6	53.4	N/A	92.6	56.3	N/A

[[P408 Table] 1. Hospital length of stay (LOS) and readmissions by CMV risk category and receipt of PET]

Results: Of 368 patients including 76 LR and 192 HR (81.3% TCD), 273 (74%) patients developed CMV viremia; 208 (56.5%) patients started PET with an average of 36 days post HCT (including 33% and 78% of LR and HR respectively). By D180, 17 (4.7% of entire cohort or 8% among PET group) patients developed EOD (gastrointestinal disease in 12, retinitis in 1, pneumonitis and encephalitis in 2 patients each); Among PET group 7 (3.4%) patients developed CMV resistance: (val)Ganciclovir 5 patients, Cidofovir 1 patient and Cidofovir+Foscarnet 1 patient. Overall, PET group had longer mean LOS for HCT (34.3 vs 29.9 days, p=0.0001) and higher rates of readmission (5.2 vs 3.1, p=0.00006). Similar findings were observed in stratified analysis by CMV risk (Table). 40 (22.2%) of readmissions in PET group were associated with CMV. By D180, CMV accounted for 17% of infection-related deaths.

Conclusions: Among PET group, nearly 1 in 12 patients developed CMV EOD; PET use was associated with longer inpatient stay and greater rates of readmissions compared to no PET use. Findings highlights the need for improved strategies for CMV management.

Clinical Trial Registry: NA

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Impact of CMV prophylaxis on rates of rehospitalization in adult CMV seropositive allogeneic HSCT recipients: Experience from the letermovir phase 3 clinical trial

Shahrul Mt-Isa[1], Hong Wan[2], Cyrus Badshah[2], Valerie Teal[2], Randi Leavitt[2], Jonathan Schelfhout[2]

[1]MSD Ltd, Hoddesdon, United Kingdom, [2]Merck & Co., Inc., Kenilworth, NJ, United States

Background: In a Phase III randomized, double-blind, placebo-controlled study of CMV-seropositive post-HSCT recipients, letermovir prophylaxis significantly reduced the incidence of clinically significant CMV infection through week 24. The objective of this research was to assess the impact of CMV prophylaxis on rates of rehospitalization in adult CMV seropositive allogeneic HSCT recipients from the letermovir phase 3 clinical trial.

Methods: Rehospitalization was recorded as an exploratory endpoint in the clinical trial at end of treatment (Week14), time of primary endpoint (Week24) and through an extended follow-up period (Week48). CMV-related rehospitalization was assessed in the trial. Prespecified analyses describe the observed rates of rehospitalization for the letermovir and placebo groups at the specified times. Fine-Gray cumulative incidence function(CIF) regression models were used to explore the rate of all-cause, and CMV-related rehospitalization accounting for the competing risk of mortality. A multiple linear regression model