Risk factors and outcomes of Refractory and/or Resistant Cytomegalovirus (CMV) infection after Allogeneic Hematopoietic Stem Cell Transplantation

Eleni Karantoni[1], Yiqi Su[1], Anat Stern[1], Phaedon D. Zavras[1], Sergio Giralt[2,3], Miguel-Angel Perales[2,3], Genovefa A Papanicolaou[1,2]

1 Infectious Disease Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, NY
2 Department of Medicine, Weill Cornell Medical College, Cornell University, New York, NY
3 Adult Bone Marrow Transplantation Service, Memorial Sloan Kettering Cancer Center, New York, NY

Objectives

The epidemiology of CMV end-organ disease (EOD) after Hematopoietic cell transplant (HCT) in the era of preemptive therapy (PET) is defined. In contrast, less data exists on refractory and/or resistant (R/R) CMV.

We report on :

1) the incidence
2) risk factors
3) outcomes of R/R CMV by 1-year post HCT

Methods

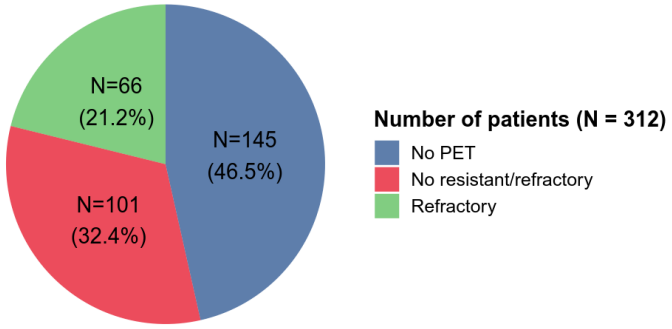
- Retrospective review of CMV seropositive (R+) recipients of first marrow or peripheral blood HCT from 1/2014 - 12/2017.
- Clinically significant (cs)- CMV was defined any level viremia treated with preemptive therapy (PET)
- Refractory CMV was defined as failure to achieve >1 log10 decrease in CMV viral load (VL) and having VL >1,000 IU/mL after ≥14 day of PET.
- Resistant CMV required genotypic confirmation of resistance mutation(s) in UL54 and/or UL97 genes.
- Patients (pts) were followed through 1-year post HCT and were categorized in two mutually exclusive groups as R/R and no R/R.
- Univariable and multivariable logistic models were used to identify risk factors for R/R CMV.

Results

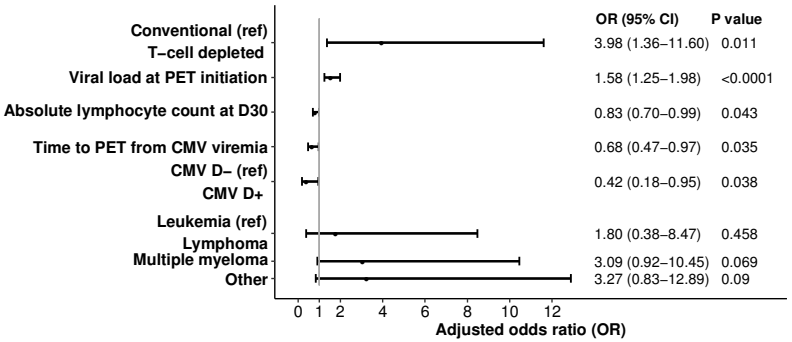
Of 312 CMV R+, 167 (53.6%) pts developed clinically significant (cs)-CMV viremia including 66 (21.2%) pts with R/R and 101 (32.4%) with no R/R CMV. Resistant CMV occurred in 6 patients (9% of R/R).

Among 167 pts with cs-CMV, 91 (54.5%) received ex vivo T cell depleted (TCD) HCT; 40 (24.0%) had mismatched donor; and 26 (15.6%) had multiple myeloma. 66/167 (39.5%) pts developed refractory CMV (6 pts also had resistant CMV).

cs-CMV occurred earlier in the R/R group: median (IQR) days 21.5 (17.2-27.8) vs 26 (19-32) for no RR (p=0.031).



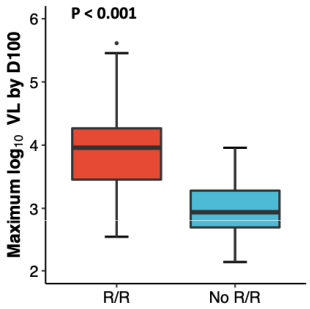
Multivariable Predictors for R/R CMV



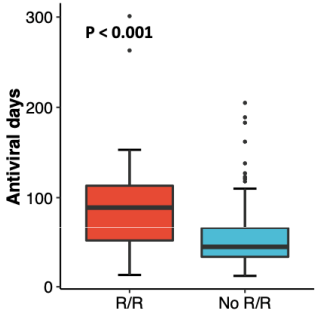
TCD and viral load at PET initiation (incremental of 500 IU/mL) are risk factors of CMV refractory.

ALC at D30 (incremental of 0.2 K/mcL), time to PET from CMV viremia (incremental of 5 days) and donor CMV positive (D+) were protective for CMV refractory

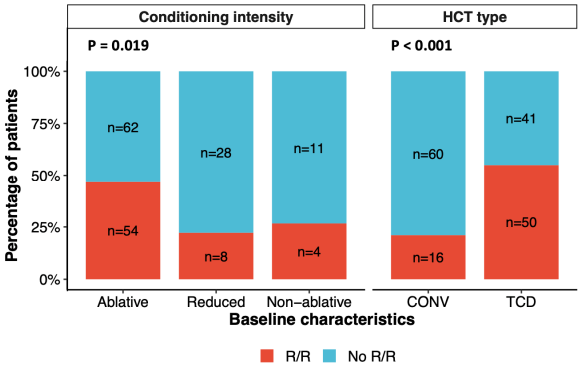
R/R had higher Maximum CMV viral load (VL)



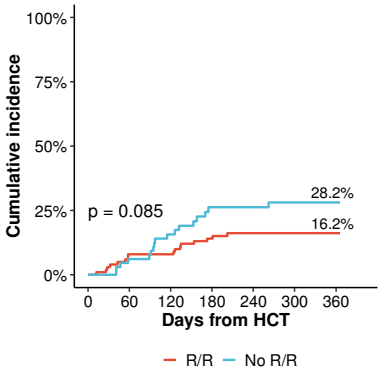
R/R used more CMV antiviral-days



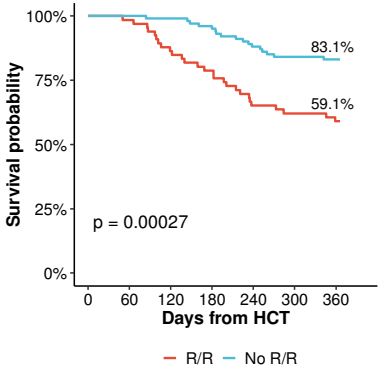
R/R was more frequent in myeloablative conditioning and T-cell depleted HCT type



CMV end-organ disease occurred more frequently in the R/R group



1-Year overall survival was worse in R/R



Overall survival at 1 year was 59.1% for R/R compared to 83.1% for no R/R group

Conclusions

- Refractory and/or resistant CMV occurred in 39.5% of PET recipients.
- T-cell depletion and higher CMV VL at PET initiation were risk factors for R/R CMV in multivariable model.
- CMV seropositive donor, Absolute Lymphocyte Count at D30 and time to PET from CMV viremia were protective.
- R/R CMV was associated with more EOD and worse overall survival.