

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

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## 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

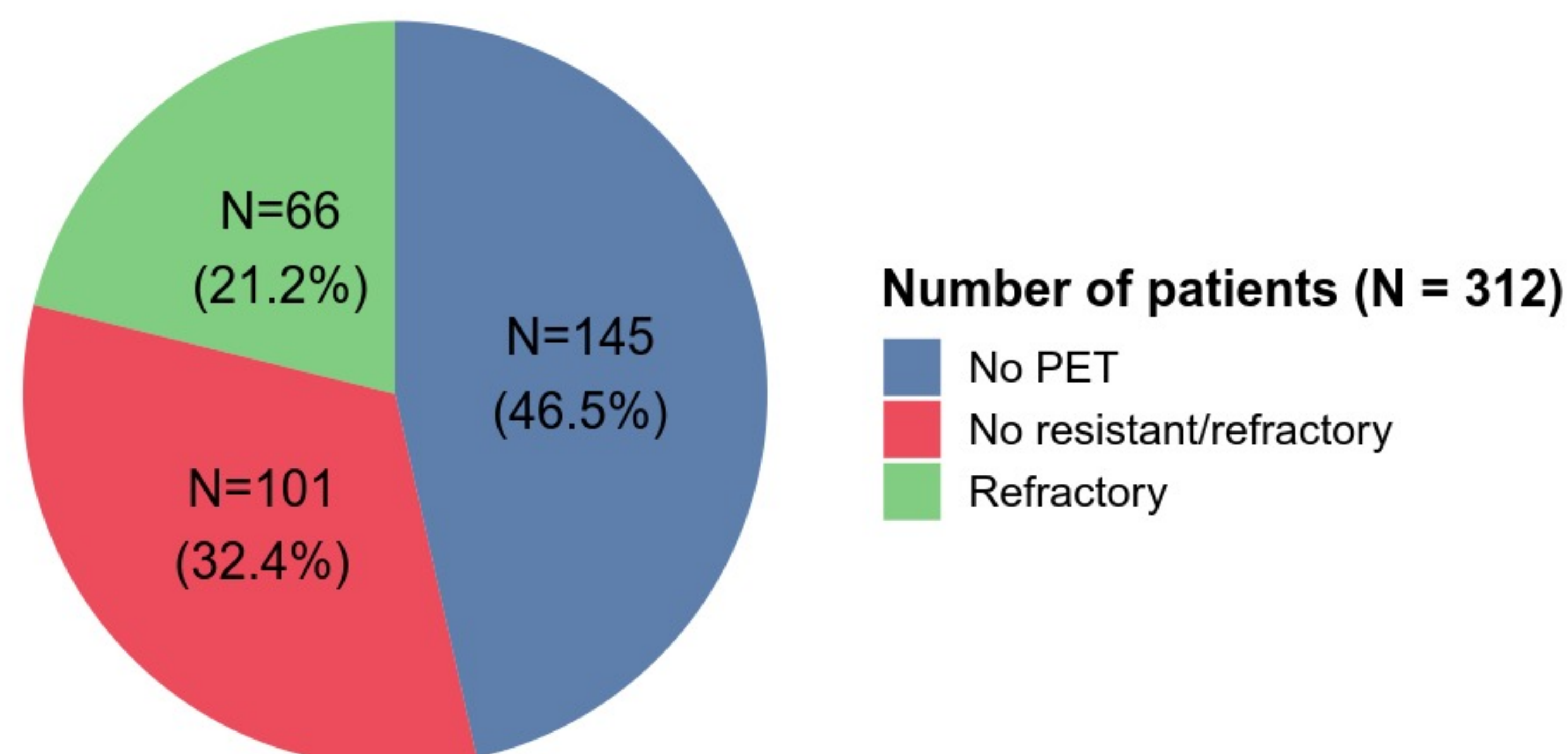
- Retrospective review of CMV seropositive (R+) recipients of first marrow or peripheral blood HCT from 1/2014 - 12/2017.
- Clinically significant (cs)- CMV was defined any level viremia treated with preemptive therapy (PET)
- Refractory CMV was defined as failure to achieve >1 log<sub>10</sub> decrease 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

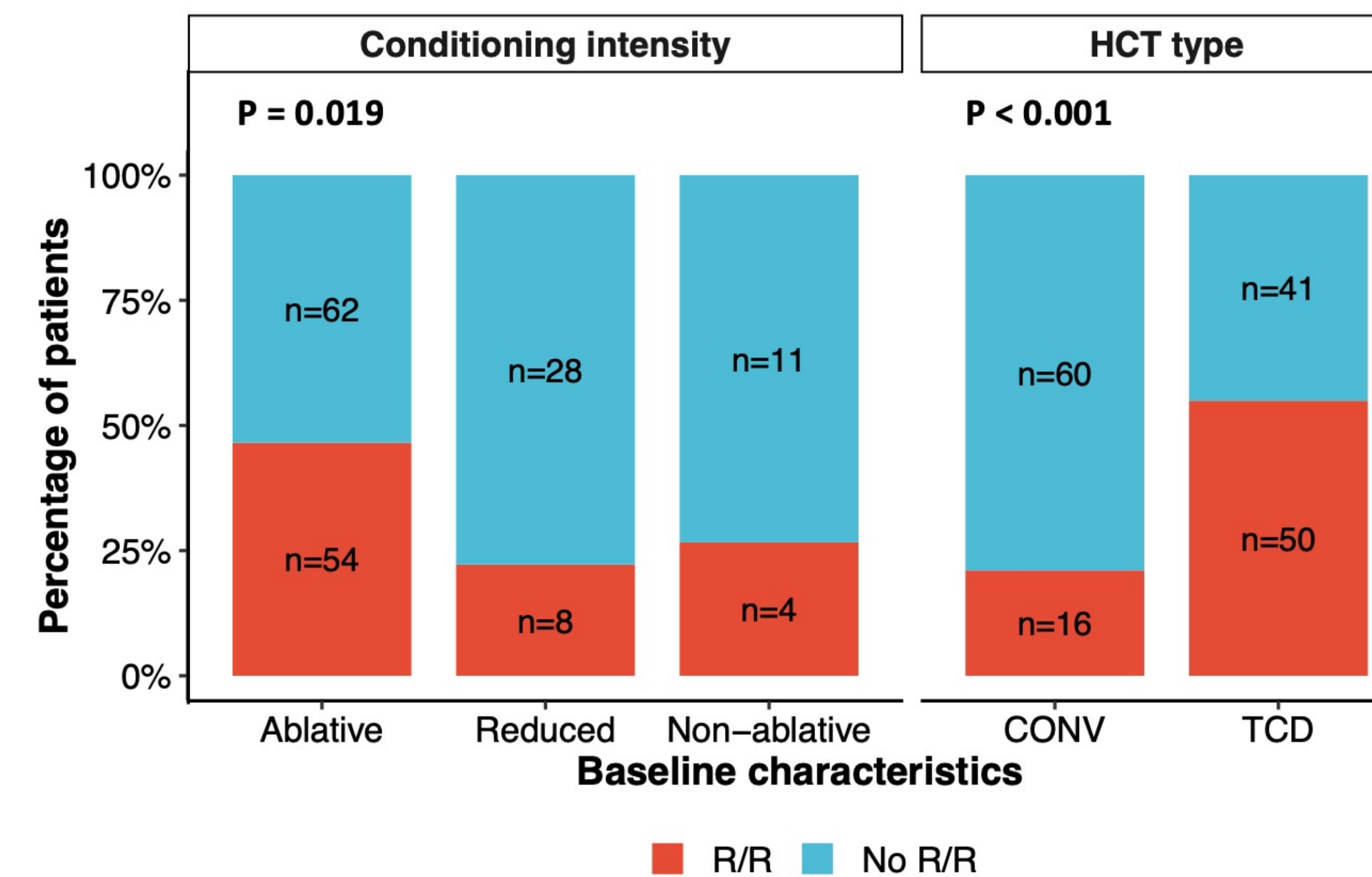
Of 312 CMV R+, 167 (53.6%) pts developed clinically significant (cs)-CMV viremia including 66 (21.2%) pts with R/R and 101 (32.4%) with no R/R CMV. Resistant CMV occurred in 6 patients (9% of R/R).

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).

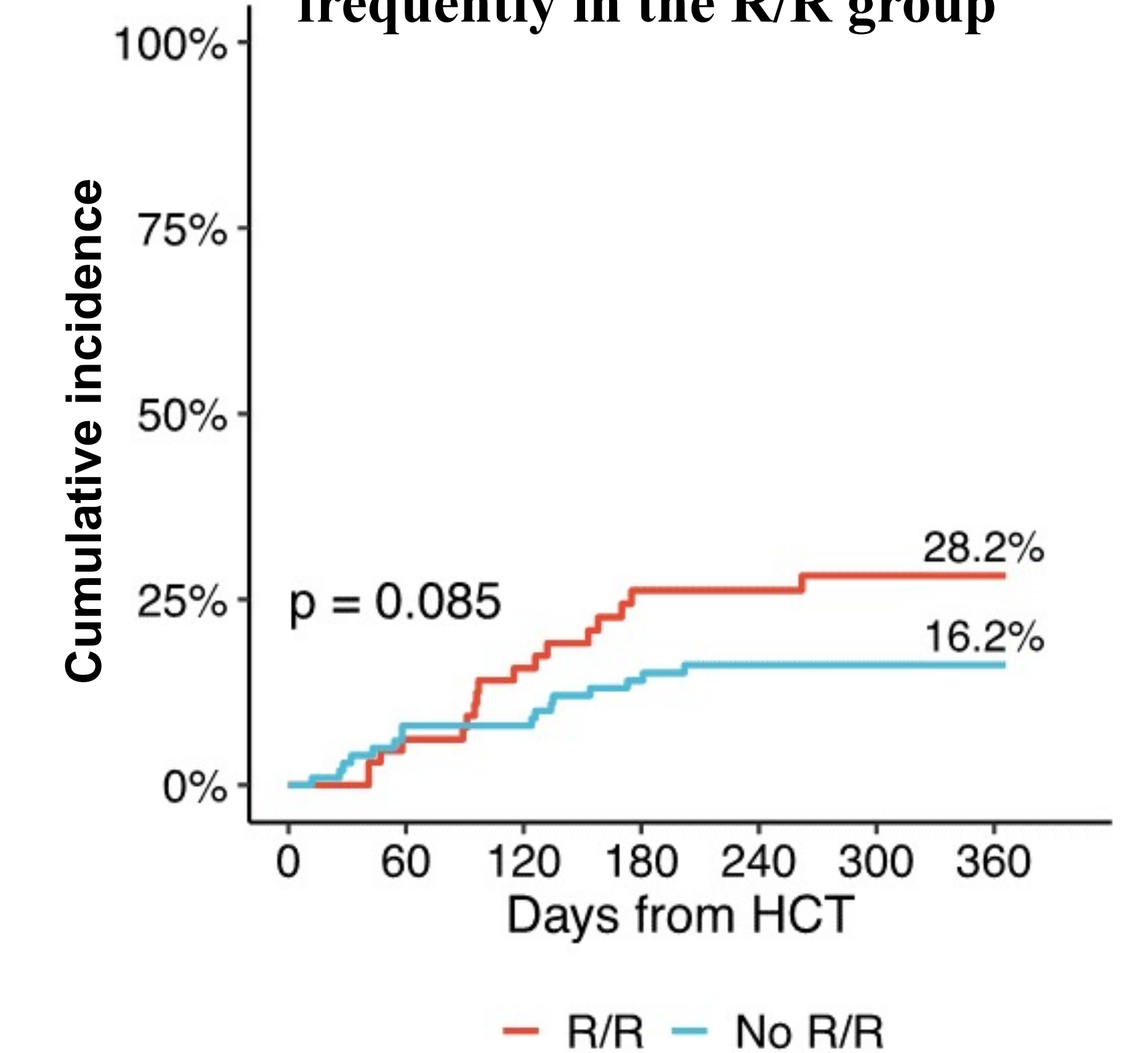
cs-CMV occurred earlier in the R/R group: median (IQR) days 21.5 (17.2-27.8) vs 26 (19-32) for no RR (p=0.031).



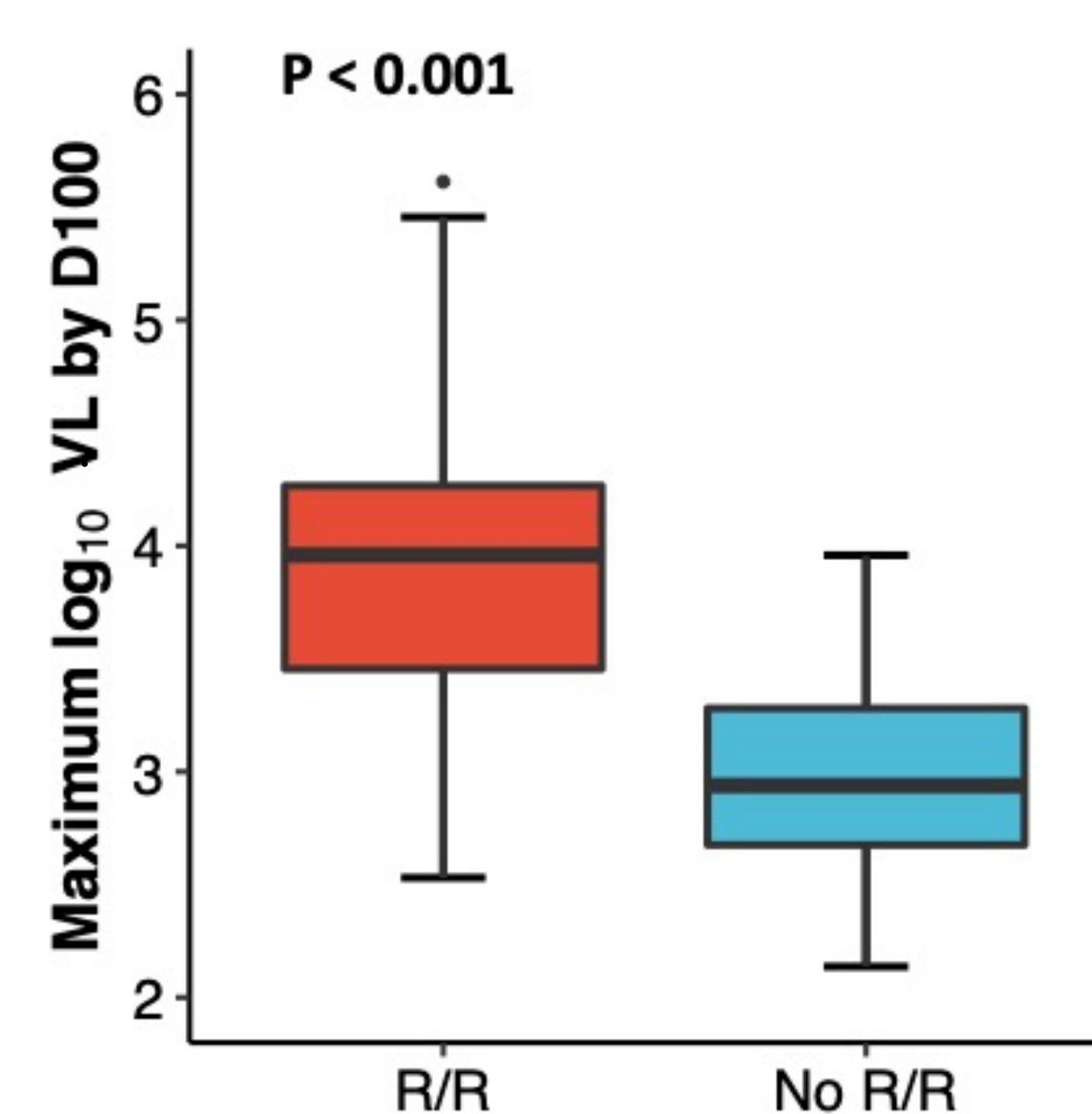
### R/R was more frequent in ablative conditioning and T-cell depleted HCT type



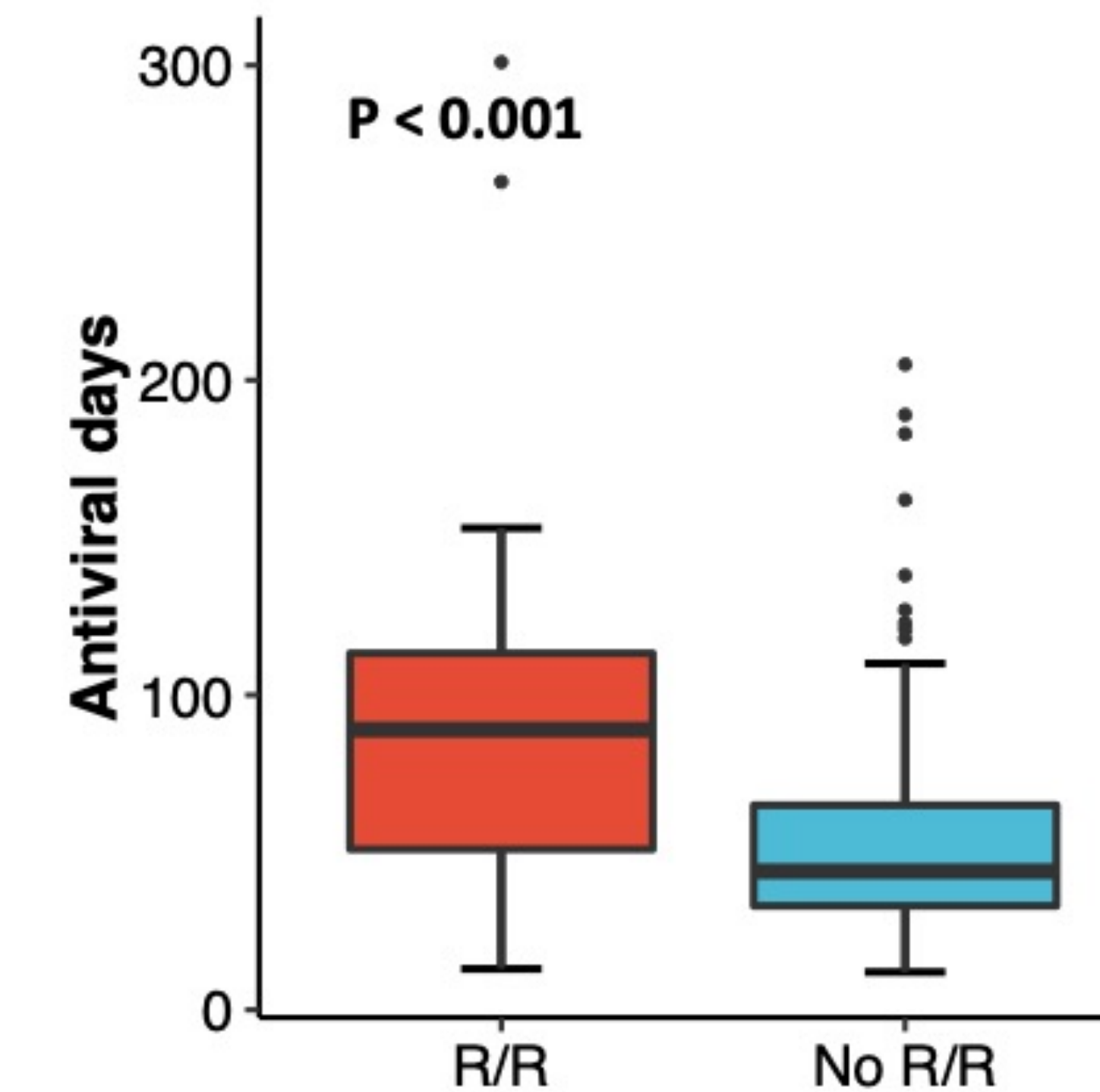
### CMV end-organ disease occurred more frequently in the R/R group



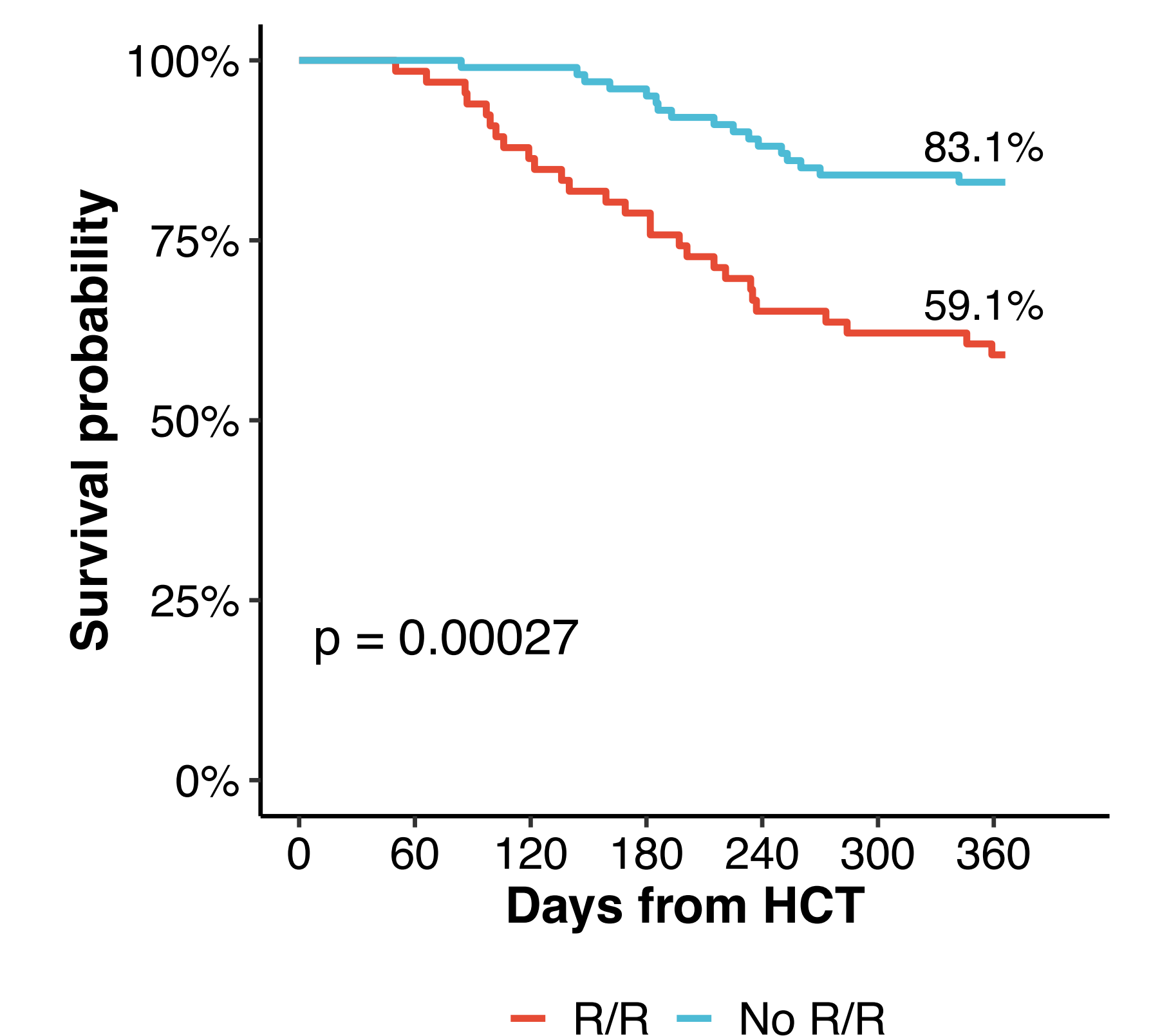
### R/R had higher Maximum CMV VL



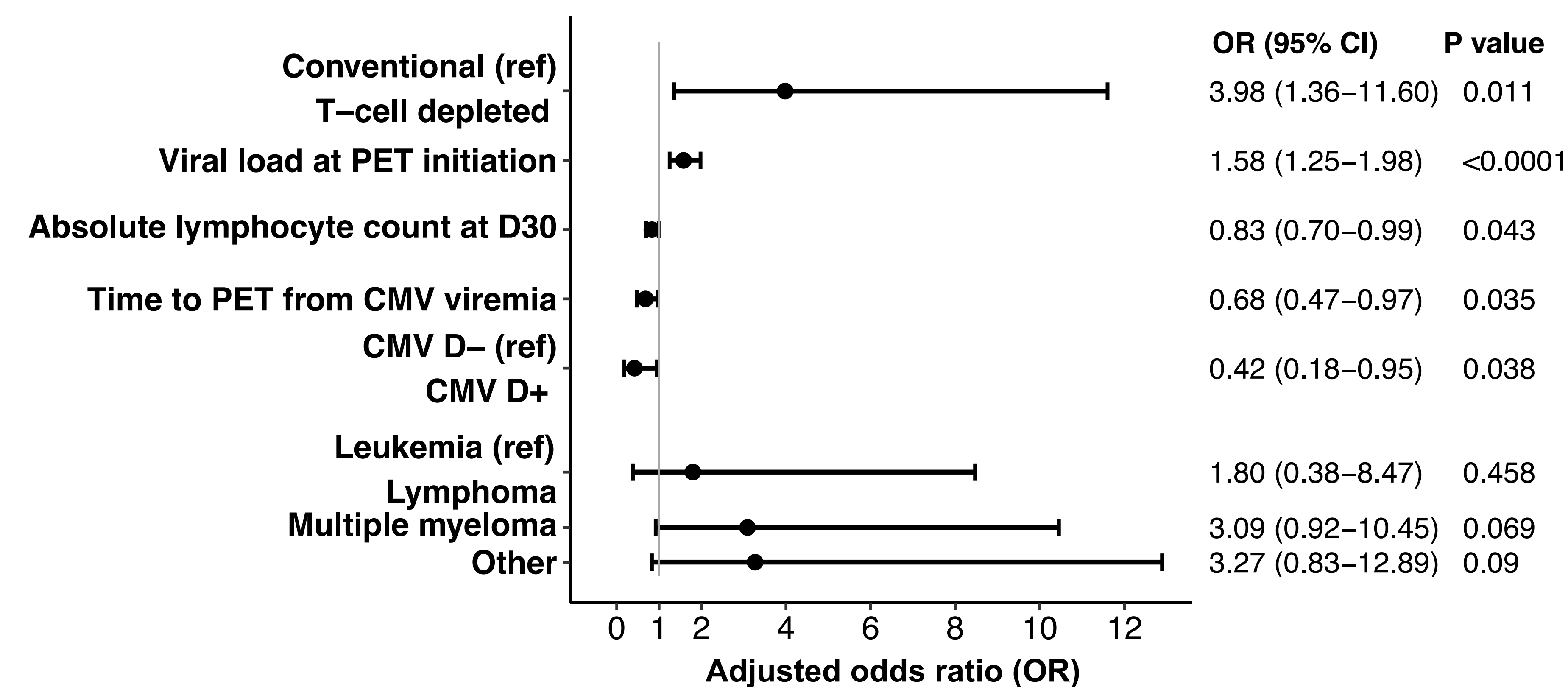
### R/R used more CMV antiviral- days



### 1-Year overall survival was worse in R/R



### 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

## 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.

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