CMV Outcomes and Health Care Resource Utilization in CMV-seropositive (R+) Hematopoietic Stem Cell Transplant (HCT) Recipients Managed with Pre-emptive Therapy (PET)

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INTRODUCTION

- CMV viremia occurs in 40% - 90% of CMV R+ recipients and is associated with increased overall mortality after hematopoietic cell transplantation (HCT) [1].
- Risk factors for CMV reactivation after HCT include T-cell depletion, allograft from HLA-mismatched and graft-versus-host disease (GvHD) [1].
- Pre-emptive therapy (PET) has reduced the risk of CMV end-organ disease (EOD) [2] and associated mortality; However, it may lead to substantial antiviral use along with its toxicities and higher healthcare resource utilization. Limited real-world data exists about CMV outcomes and healthcare resource utilization with PET.
- Established benchmarks of CMV outcomes and HCRU in the era of PET are required to perform cost benefit analyses of novel interventions for CMV.

OBJECTIVES

- To report rates of CMV end-organ disease (EOD), CMV antiviral resistance, CMV-related mortality and rates of readmission and hospital length of stay (LOS) by day+180 in a contemporary cohort of HCT recipients in major Cancer Center in New York City.

METHODS

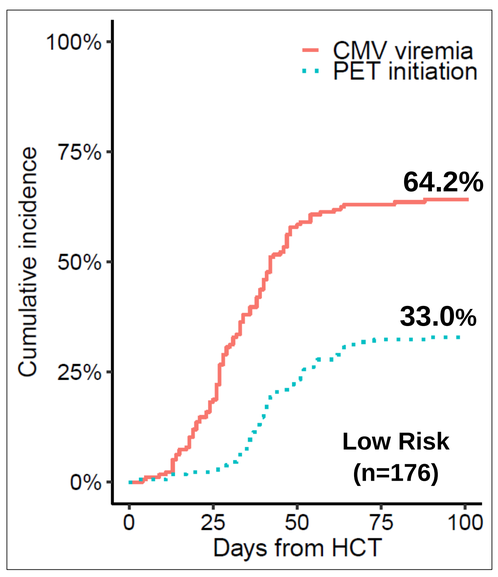
- **Study Design**: Retrospective cohort study
- **Study Population**: CMV R+ adult recipients of first peripheral blood or marrow allograft at MSKCC from March 2013 to December 2017.
- **CMV monitoring:** CMV+ recipients were monitored weekly by quantitative PCR assay starting on day 14 through day 180 post HCT and treated pre-emptively. CMV EOD was scored by the standard criteria. CMV resistance mutations were confirmed by sequencing (Viracor-Eurofins).
- The **follow-up period** was until day 180 post-HCT or death, whichever occurred first.
- **PET group**: Receipt of pre-emptive antiviral therapy for CMV viremia.
- **CMV RISK**: High CMV risk (HR) comprised recipients of conventional HCT from mismatched or haploidentical donors or recipients of T-cell depleted (TCD) HCT regardless of donor HLA match. Low CMV risk (LR) included conventional HCT from matched related donors.
- **Healthcare resource utilization** was measured as length of stay (LOS) for incident admission, readmission rate per 1000 patient-day and number of patients required readmission by day 180 post HCT.
- **Risk-Stratified analyses** were performed to examine outcomes by PET use and CMV risk.

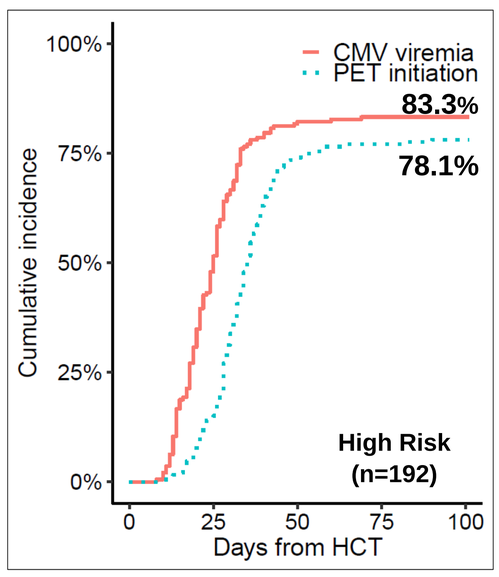
RESULTS

Among 368 CMV R+ recipients included in this study, over half of the recipients were male with an average age of 55.9 years.

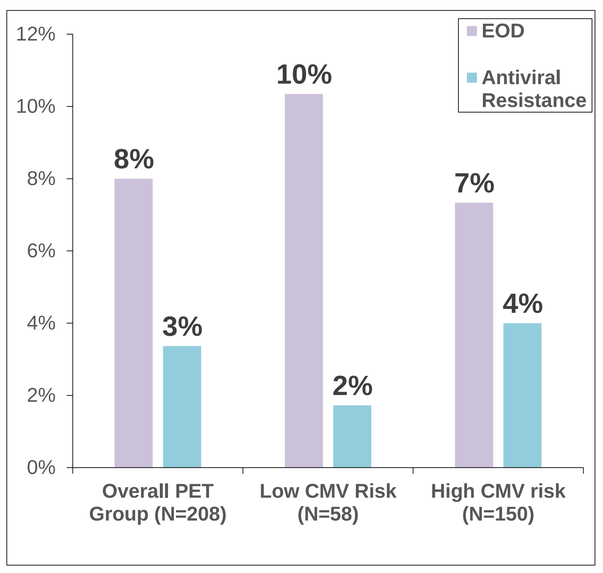
Clinical Characteristics	Overall N=368	%
Underlying Disease		
Leukemia	186	51%
Lymphoma	51	14%
Other	131	36%
HLA match		
Matched related donor	117	32%
Matched unrelated donor	192	52%
Mismatched (related or unrelated)	59	16%
Stem cell source		
Peripheral blood	319	87%
Bone Marrow	49	13%
Conditioning regimen		
Myeloablative	226	61%
Reduced intensity	111	30%
Ex vivo T-cell depletion	156	42%
CMV Risk		
High	192	52%
Low	176	48%

High risk patients had higher incidence, earlier onset of CMV viremia and earlier initiation of PET compared with low risk patients.



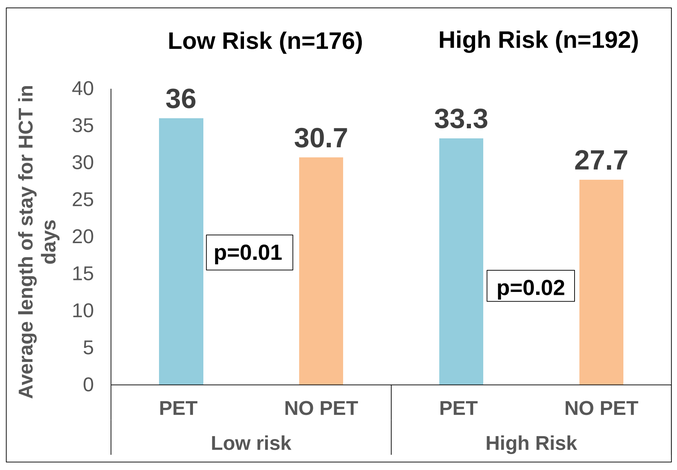


CMV outcomes (End organ disease, antiviral resistance) at day+180 among PET group

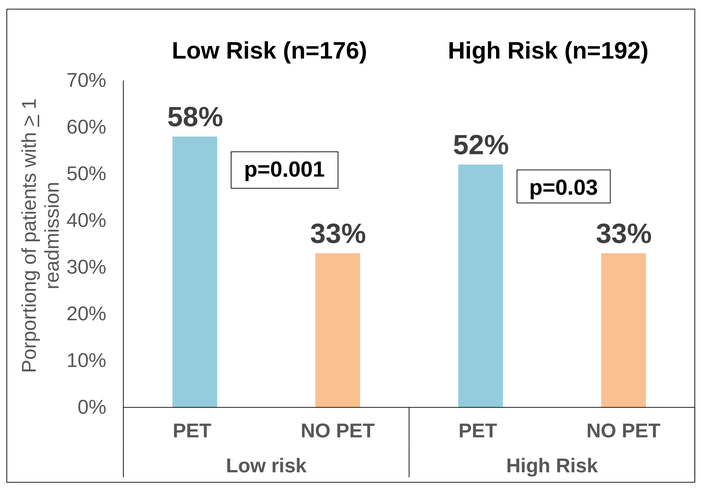


- 17 patients developed EOD (gastrointestinal disease in 12, retinitis in 1, pneumonitis and encephalitis in 2 patients each);
- 7 patients developed CMV resistance: (val)Ganciclovir 5 patients, Cidofovir 1 patient and Cidofovir+Foscarnet 1 patient.

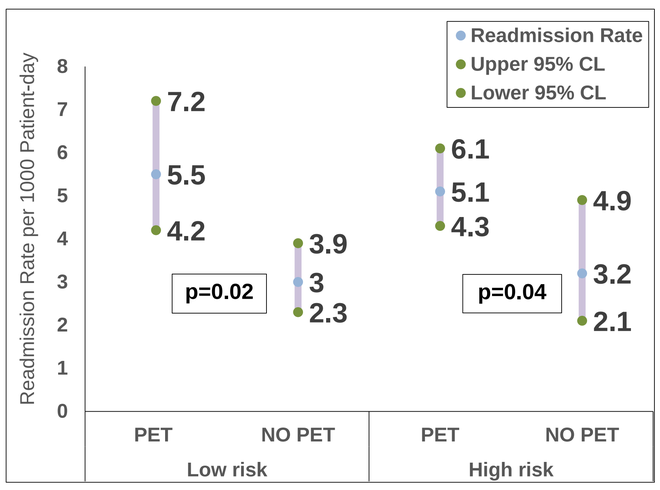
Patients in PET group had longer inpatient stays for HCT admission than patients in NO PET group



A greater proportion of patients within the PET group required readmission



Overall, PET group had higher rates of readmission



CONCLUSION

- 4.5% of CMV R+ recipients developed CMV EOD by day+180. Two thirds of CMV EOD cases occurred in high risk group.
- 3% of patients that received PET (4% among high risk group) were identified to have CMV resistance mutations by day+180.
- CMV related mortality was 1.5% among high risk group by day+180.
- PET was associated with higher healthcare resource utilization (HCRU) including longer inpatient stays for HCT (p=0.0001), higher rates of readmission (p<0.001) and higher proportion of patients required readmission (p<0.001) by day+180.
- Our real-world data highlights the need for improved management strategies for CMV in HCT recipients.

DISCLOSURE

- The study was funded by a grant from Merck & Co., Inc

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2. de la Camara R. CMV in hematopoietic stem cell transplantation. *Mediterr J Hematol Infect Dis*. 2016;8 e2016031.

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