2098: CMV INFECTION FOLLOWING HEMATOPOIETIC CELL TRANSPLANTATION WITH PTCY: OUTCOMES IN HAPLOIDENTICAL VERSUS MATCHED OR MISMATCHED DONOR ALLOGRAFTS

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INTRODUCTION

- Post-transplant cyclophosphamide (PTCy) is increasingly being used for prevention of graft-versus-host disease (GVHD) in matched unrelated donor (MUD), mismatched unrelated donor (MMURD), and haploidentical donor hematopoietic cell transplantation (HCT).
- PTCy has been associated with increased risk of viral infections including respiratory viruses, herpesviruses, and cytomegalovirus (CMV) infection after HCT.
- It remains unclear if the increased risk of viral infections is independent of donor allograft selection.
- This study evaluated the incidence of clinically significant CMV infection (CS-CMVi) following PTCy in patients who received MUD/MMURD allografts compared to haploidentical donor allografts.

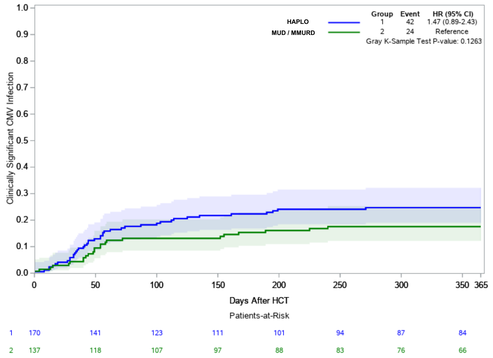
METHODS

- We performed a single-center retrospective study of adults undergoing HCT with PTCy between January 1, 2015 and July 1, 2021. Per institutional protocol, patients who were CMV seropositive (R+) received letermovir prophylaxis.
- CS-CMVi, defined as CMV viremia or disease requiring initiation of CMV therapy, was evaluated in two groups: haploidentical (n=170) and MUD/MMURD (n=137) allograft HCT recipients.
- CMV disease was defined according to criteria published by the Disease Definitions Working Group of the Cytomegalovirus Drug Development Forum.
- We assessed the incidence of CMV viremia, CS-CMVi, and CMV disease, as well as incidence of letermovir breakthrough infections and late CMV events after cessation of prophylaxis for one year following HCT.
- One-year Cumulative Incidence Functions were calculated based on time to CS-CMVi using dates of infection-free death, disease relapse, and repeat HCT as competing risks.

RESULTS

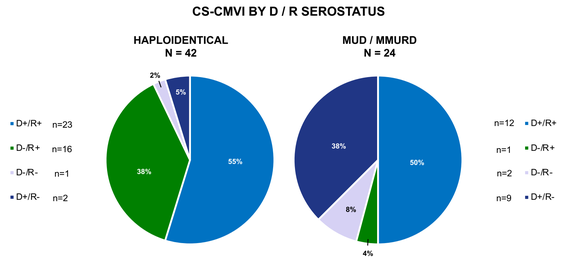
Baseline Characteristics	Haploidentical HCT n=170	MUD / MMURD HCT n=137
Demographics		
Age, median (range)	59 (19 – 77)	58 (21 – 78)
Male sex, no. (%)	103 (61)	74 (54)
Underlying Disease		
AML, no. (%)	69 (41)	51 (37)
MDS/MPN, no. (%)	39 (23)	35 (26)
ALL, no. (%)	19 (11)	24 (18)
NHL, no. (%)	19 (11)	10 (7)
HL, no. (%)	4 (2)	6 (4)
Other, no (%)	20 (12)	11 (8)
Transplant Characteristics		
Prior HCT		
Allogeneic	19 (11)	19 (14)
Autologous	9 (5)	4 (3)
Graft		
Peripheral blood	99 (58)	111 (81)
Bone Marrow	71 (42)	26 (19)
Conditioning		
Reduced Intensity	127 (75)	97 (71)
Myeloablative	43 (25)	40 (29)
HLA Match		
Fully Matched (10 of 10)	-	62 (45)
Mismatched (7, 8, or 9 of 10)	-	75 (55)
CMV Serostatus		
CMV D positive / R positive	59 (35)	47 (34)
CMV D positive / R negative	14 (8)	12 (9)
CMV D negative / R positive*	40 (24)	7 (5)
CMV D negative / R negative	55 (32)	71 (52)
Letermovir Primary Prophylaxis	66 (38)	54 (39)
CMV D positive / R positive	37 (22)	47 (34)
CMV D negative / R positive	26 (15)	7 (5)
Other**	3 (2)	0 (0)
Transplant Outcomes		
CRS Diagnosis	102 (60)	29 (21)
Acute GVHD	85 (50)	58 (42)
Grade 3 – 4	6 (4)	11 (8)
Tx ≥ 1 mg/kg Corticosteroids	48 (56)	29 (51)
Death	50 (29)	36 (26)
Days to Death, median (range)	223 (9 – 1795)	152 (10 – 1026)

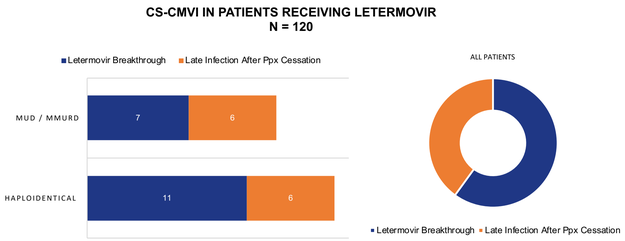
*Two patients were donor seronegative with indeterminate recipient serostatus
** Two CMV D negative / R negative patients and one CMV D positive / R negative patients received letermovir prophylaxis



CMV Outcomes	Haploidentical HCT n=170	MUD / MMURD HCT n=137	P-value
CMV Events			
CMV disease	1 (0.6)	1 (0.7)	-
CMV Viremia	68 (40)	50 (36)	0.557
Time to CMV Viremia, median (range)	29 (2 – 337)	29 (0 – 252)	-
CS-CMVi	42 (25)	24 (18)	0.162
Time to CS-CMVi, median (range)	44 (0 – 315)	49 (0 – 240)	-
CS-CMVi Risk group			
CS-CMVi in seropositive recipients	**39 (23)**	13 (9)	**0.002**
CS-CMVi in seronegative recipients	3 (2)	**11 (8)**	**0.012**
CMV Donor Status			
CS-CMVi with seropositive donor	25 (15)	21 (15)	0.874
CS-CMVi Infection Type			
Letermovir Breakthrough Infection	11 (6)	7 (5)	0.808
Infection After Letermovir Cessation	6 (4)	6 (4)	0.772
Not Receiving Letermovir	25 (15)*	11 (8)	0.077

*One patient with CS-CMVi was on the Letermovir versus Placebo study





DISCUSSION

- Despite the use of letermovir prophylaxis, high-risk (CMV R+) haploidentical recipients had a higher incidence of CS-CMVi than MUD / MMURD recipients (23% versus 9%; p=0.002), suggesting that haploidentical HCT may have increased risk for viral infections independent of PTCy, possibly related to impaired antigen presentation in the setting of HLA mismatch.
- For low-risk (CMV R-) recipients, there was a notably increased incidence of CS-CMVi in the MUD/MMURD cohort (8% versus 2%; p=0.012), that was driven primarily by D+/R- recipients. This raises the question of whether letermovir may benefit (CMV R-) patients when the donor is seropositive.
- Out of 120 patients who received letermovir, 25% developed CS-CMVi, with 60% of those cases due to breakthrough infection and 40% following cessation of letermovir. Further data is needed on the impact of delayed CMV-specific immunity related to letermovir use.

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