DONOR-SPECIFIC HLA MISMATCH: HAPLOIDENTICAL VERSUS MISMATCHED UNRELATED DONOR HEMATOPOIETIC CELL TRANSPLANTATION WITH PTCY

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Introduction

Direct comparative analysis of haploidentical and mismatched unrelated donor (MMUD) transplant outcomes with post-transplant cyclophosphamide (PTCy), while accounting for HLA is lacking.

Methods

- We compared haploidentical (n=659) and MMUD (n=138) HCT with PTCy.
- HLA mismatches were classified using high-resolution typing, including Class I peptide-binding motif (PBM), *DPB1* T-cell epitope, and B-leader matching.
- "Absence of PBM-mismatched" includes donor-recipient pairs matched within the same PBM group or unidirectional mismatched in the host-versus-graft (HVG) direction.
- HLA-*DPB1* mismatches were classified according to TCE group; donor-recipient pairs with non-permissive GVH mismatch were labeled as "*DPB1* non-permissive mismatched" while all others were categorized as "no *DPB1* non-permissive mismatch"
- HLA-DRB1 and –DQB1 pairs were classified based on mismatches in the GVH vector.
- B-leader was categorized as matched or mismatched.

Results

Baseline Characteristics	Haplo (n=659)	MMUD (n=138)	P
Recipient age, (median [Q1-Q3]), years	52 [37-61]	53.5 [42.5-62]	.042
Recipient age, years n, (%)			.369
≤ 52	341 (51.7)	65 (47.1)	
> 52	318 (48.3)	73 (52.9)	
Donor age, years (median [Q1-Q3])	34 [24.5-43]	35 [27.2542.75]	.482
Disease, n (%)			
AML/MDS	384 (58.3)	76 (55.1)	.092
ALL	99 (15)	14 (10.1)	
Other	176 (26.7)	48 (34.8)	
Disease stage, n (%)			1.0
Low/Intermediate	427 (64.8)	90 (65.2)	
High/Very High	232 (35.2)	48 (34.8)	
Conditioning intensity, n (%)			.214
MAC	409 (62.1)	94 (68.1)	
RIC/NMA	250 (37.9)	44 (31.9)	
Graft type, n (%)			<.001
Bone marrow	466 (70.7)	64 (46.4)	
Peripheral blood	193 (29.3)	74 (53.6)	
HCT-CI, n (%)			.214
0	120 (18.2)	34 (24.6)	
1-2	190 (28.8)	38 (27.5)	
≥ 3	349 (53)	66 (47.8)	
D/R CMV, n (%)			.018
Neg/Neg	85 (12.9)	21 (15.2)	
Neg/Pos	196 (29.7)	54 (39.1)	
Pos/Neg	52 (7.9)	15 (10.9)	
Pos/Pos	326 (49.5)	48 (34.8)	
Time to HCT, months, n (%)			.298
<6	179 (27.2)	29 (21)	
6-12	166 (25.2)	40 (29)	
>12	314 (47.6)	69 (50)	
Year of HCT, n (%)			.202
< 2019	324 (49.2)	59 (42.8)	
≥ 2019	335 (50.8)	79 (57.2)	
Follow-up (median [95% CI]), months	54.53 (50-64)	24.3 (21-49)	<.001

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Results

In the MMUD group:

- The absence of HLA *A*-peptide PBM mismatching was associated with worse overall survival (OS) (HR 1.87, 95% CI 1.04–3.37, p=.037) and non-relapse mortality (NRM: HR 3.27, 95% CI 1.26–8.47, p=.015).

In the haploidentical group:

- *DPB1* non-permissive mismatch correlated with poorer OS (HR 1.50, 95% CI 1.13–1.98, p=.004) and NRM (HR 1.80, 95% CI 1.27–2.55, p=.001)
- B-leader mismatch increased NRM (HR 1.39, 95% CI 1.05–1.85, p=.023).

❑There was no independent association between donor type or individual HLA factors and relapse.

❑Grade III-IV acute GVHD: effects of donor type and donor age varied by disease.

❑AML/MDS: MMUD recipients had higher risk without statistical significance: (HR 5.3, 0.89-31.6, p=0.67)

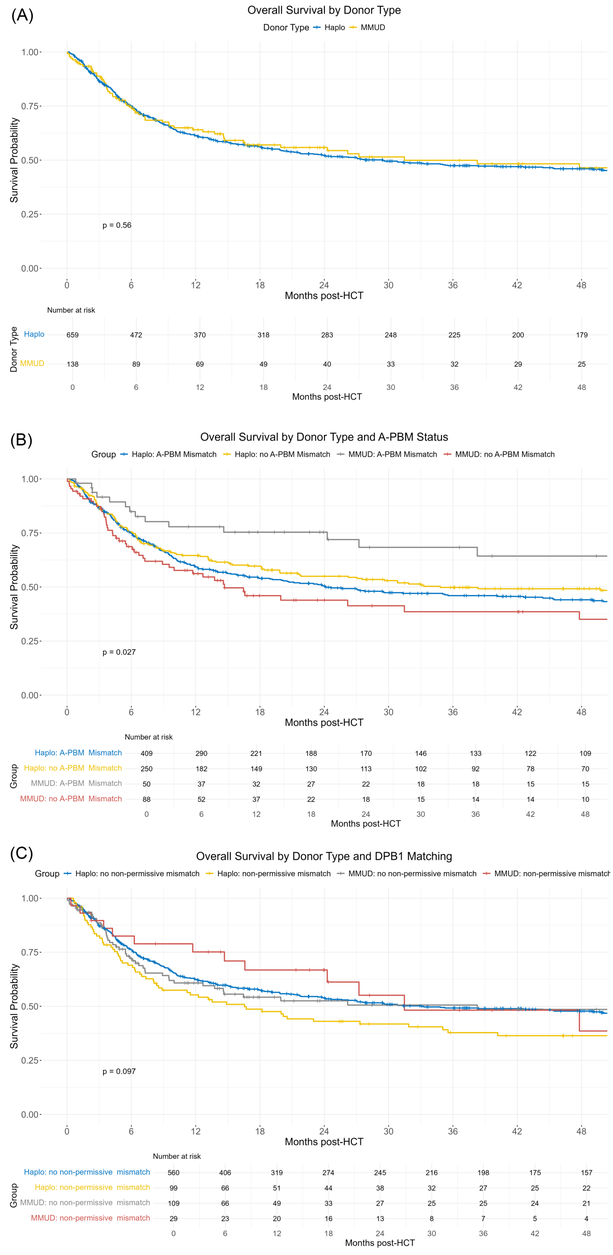


Figure 1: Kaplan-Meier estimate of OS **(a)** by donor type **(b)** by donor type and HLA-A matching status **(c)** by donor type and HLA-DPB1 matching status

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