

Post-transplant cyclophosphamide improves survival compared to antithymocyte globulin in HLA-mismatched unrelated donor stem cell transplantation

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Received: December 9, 2024.
Accepted: August 14, 2025.
Early view: August 28, 2025.

<https://doi.org/10.3324/haematol.2024.287157>

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Supplemental appendix

Table S1: Univariate analysis.

	OS		GRFS		PFS		NRM		CIR	
	HR [IC 95]	p.value	HR [IC 95]	p.value	HR [IC 95]	p.value	HR [IC 95]	p.value	HR [IC 95]	p.value
Age <45	0.5 [0.3 ; 0.7]	0.0003	0.6 [0.4 ; 0.9]	0.006	0.6 [0.4 ; 0.9]	0.02	0.4 [0.2 ; 0.8]	0.007	0.7 [0.4 ; 1.3]	0.2
MAC	0.7 [0.4 ; 1.1]	0.1	0.8 [0.5 ; 1.1]	0.2	0.7 [0.5 ; 1.1]	0.2	0.5 [0.3 ; 1.0]	0.04	0.9 [0.5 ; 1.6]	0.7
DRI	1.6 [1.0 ; 2.6]	0.03	1.4 [0.9 ; 2.1]	0.1	0.6 [1.1 ; 2.7]	0.01	1.0 [0.5 ; 1.9]	1	2.3 [1.3 ; 4.2]	0.004
HCT CI	0.4 [0.3 ; 0.7]	0.0003	0.6 [0.4 ; 1.0]	0.06	0.4 [0.3 ; 0.7]	0.0007	0.6 [0.3 ; 1.1]	0.08	0.4 [0.2 ; 0.8]	0.005
Group	2.1 [1.1 ; 4.0]	0.05	0.9 [0.5 ; 1.5]	0.9	2.2 [1.2 ; 4.1]	0.02	3.9 [1.4 ; 11.1]	0.01	1.7 [0.8 ; 3.7]	0.3
ATG HD	2.5 [1.1 ; 5.7]		1.0 [0.5 ; 2.1]		2.7 [1.2 ; 5.8]		4.7 [1.4 ; 15.7]		1.9 [0.7 ; 5.4]	
Ref										
PTCY										

Hazard ratios (HR) comparing Age (<45 vs. >45 years), MAC vs. RIC, DRI (high/very high vs low/intermediate), HCT-CI score (0-2 vs. ≥3) and treatment group (PTCY (ref) vs. LD ATG vs. HD ATG).

Table S2: Distribution of causes of death in each group and their variation over time.

Mortality at 1 year, n (%)	PTCY (n= 8)	HD (n=39)	LD (n=7)
Hemopathy	5 (62.5)	15 (38.5)	1 (14.3)
Infection	2 (25.0)	7 (17.9)	2 (28.6)
Bacterial	0 (0)	3 (7.7)	2 (28.6)
Fungal	1 (12.5)	1 (2.6)	0 (0)
Viral	1 (12.5)	3 (7.7)	0 (0)
GVHD	1 (12.5)	15 (38.5)	3 (42.9)
Other	0 (0)	2 (5.1)	1 (14.3)

All mortality causes, n (%)	PTCY (n= 11)	HD (n=52)	LD (n=13)
Hemopathy	7 (63.6)	24 (46.2)	6 (46.2)
Infection	2 (18.2)	9 (17.3)	2 (15.4)
Bacterial	0 (0)	3 (5.8)	2 (15.4)
Fungal	1 (9.1)	2 (3.8)	0 (0)
Viral	1 (9.1)	4 (7.7)	0 (0)
GVHD	2 (18.2)	16 (30.8)	4 (30.8)
Other	0 (0)	3 (5.8)	1 (7.7)

GVHD: Death related to GVHD; M = months; n = number of deaths; Analyses were conducted using a Fisher's exact test with significative p.value if p<0.05.

Table S3: Infectious complications at one year.

Infectious complications at 1 year, n (%)	PTCY (n=41)	HD (n=93)	LD (n=21)	p- value
Invasive fungal infections	2 (4.9)	15 (16.1)	3 (14.3)	0.19
Median time in days (range min-max)	4.5 (1-9)	48 (5-253)	84 (53-228)	
Bacterial infections				
Fatal infection or requiring intensive care management	8 (19.5)	21 (22.6)	3 (14.3)	0.72
Median time (range min-max)	114.5 (0-300)	111 (9-336)	77 (10-125)	
EBV reactivation	3 (7.3)	45 (48.4)	7 (33.3)	<0.01
Median time in days (range, min-max)	93 (74-253)	45 (18-130)	46 (16-49)	
Lymphoproliferative syndrom	0	3	1	
Related mortality	0	2	1	
CMV infection	4 (9.8)	33 (35.5)	7 (33.3)	<0.01
Recipient positive serology #	4 (100)	27 (81.8)	7 (100)	
Median time in day (range min-max)	47 (31-79)	35 (12-147)	47 (27-144)	
Median number of treatment lines	1 (1-2)	1 (1-3)	1 (1-2)	
CMV disease	0	2	0	
Related mortality	0	1	0	
BK-virus symptomatic reactivation	15 (36.6)	17 (18.3)	3 (14.3)	0.04
Median time (range min-max)	41 (8-111)	36 (13-81)	43 (10-44)	
Related hospitalisation	2	4	2	
Respiratory virus (G≥ II)	1 (2.4)	5 (5.4)	0 (0)	0.59
SARS-COV2	1	0	0	
other (SRV, PIV3, H1N1)	0	5	0	
Grade II	0	2	0	
Grade III-IV	1	3	0	
Other virus (G≥ II)	7 (17.1)	15 (16.1)	1 (4.8)	0.44
Adenovirus	2	5	0	
HSV 1/2	2	6	0	
VZV	0	1	0	
HHV6 encephalite	2	0	1	
ParvoB19	1	2	0	
Norovirus	0	1	0	
Grade II	2	5	0	
Grade III-IV	5	10	1	
Incidence Other virus + Respiratory virus (G≥ II) at 1 year	8 (19.5)	20 (21.5)	1 (4.8)	0.2
Grade II	2	8	0	
Grade III-IV	6	13	1	

G= grade, grading based on common terminology criteria for adverse events V5.0 (CTCAE) of the US National Cancer institute; #: Among these patients, 3 patients in the PTCY group received prophylaxis with letermovir. The median time refers to the interval between the transplant and the onset of the infection. Analyses were conducted using a Fisher's exact test with significative p.value if p<0.05.

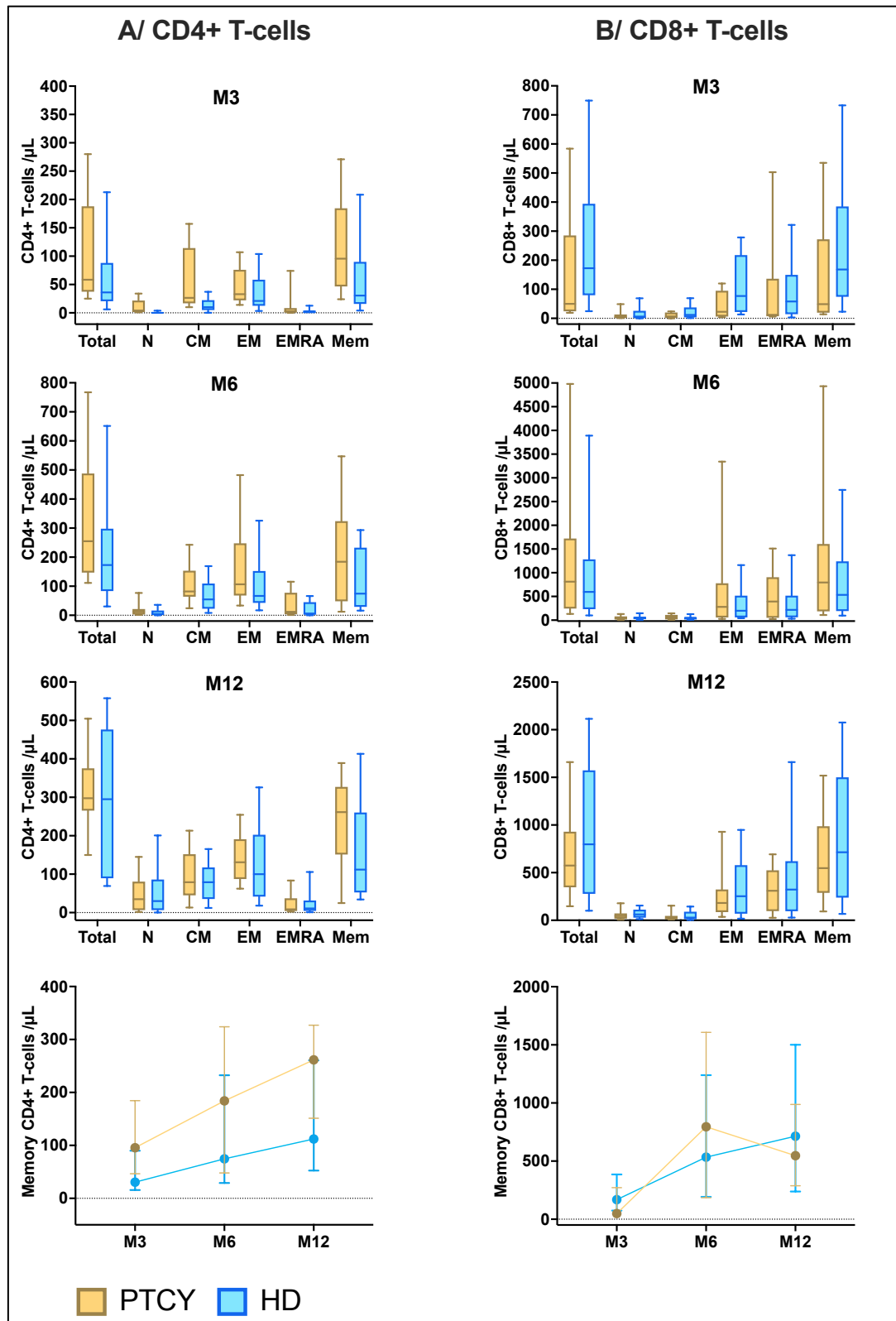


Figure S1: Study of effector T Cell subpopulations over time.

A: Effector CD4+ T-Cell Subpopulations. B: Effector CD8+ T-Cell Subpopulations

The box plots represent the median and interquartile range, as well as values between the 10th and 90th percentiles. The curves represent the median and associated interquartile ranges over time. M: months; N: naive T-cells (CD45RA+CCR7+); CM: central memory T-cells (CD45RA-CCR7+); EM: effector memory T-cells (CD45RA-CCR7-); EMRA: effector memory RA+ T-cells (CD45RA+CCR7+); Mem: total of memory T cells. *significant p.value if $p < 0.05$.

Table S4: Characteristics of patients explored in terms of immune reconstitution at 3 months post transplantation.

Characteristics, n (%)	PTCY n=34	HD n=62	LD n=13	p.value
Median year of transplant (IQR)	2022 (2021-2023)	2013 (2012-2017)	2016 (2015-2017)	<0.01
Median age (IQR)	50.1 (37.0-59.6)	41.3 (26.9-55.2)	59.1 (35.7-63.3)	0.02
Patient gender				
Female	16 (47.1)	21 (33.9)	6 (53.9)	0.37
Male	18 (52.9)	41 (66.1)	7 (46.1)	
Donor female to male	5 (14.7)	11 (17.7)	3 (23.1)	0.77
CMV+ recipient status	20 (58.8)	35 (56.5)	8 (61.5)	>0.99
ECOG >1	4 (11.8)	1 (1.6)	0 (0)	0.07
HCT-CI ≥ 3	6 (17.6)	13 (21.0)	3 (23.1)	0.88
Second HSCT:	1 (2.9)	0 (0)	1 (7.7)	0.08
Leukemias	19 (55.9)	45 (72.6)	10 (76.9)	0.20
Other myeloid disorders	8 (23.5)	11 (17.7)	2 (15.4)	
Mature lymphoid disorders	7 (20.6)	6 (9.7)	1 (7.7)	
Disease Risk Index: High and very high	11 (32.4)	19 (30.7)	6 (46.1)	0.54
CR status:				
CR	24 (70.6)	48 (77.4)	10 (76.9)	0.77
Not in CR	10 (29.4)	14 (22.6)	3 (23.1)	
Stem Cell Source:				
Bone Marrow	1 (2.9)	1 (1.61)	0 (0)	>0.99
PBSCs	33 (97.1)	61 (98.4)	13 (100)	
Conditioning Intensity:				
MAC	14 (41.2)	32 (61.6)	4 (30.8)	0.33
RIC	20 (58.8)	30 (48.4)	9 (69.2)	
TBI	1 (2.9)	20 (32.3)	2 (15.4)	<0.01
CMV reactivation	2 (5.9)	24 (38.7)	4 (30.8)	<0.01
EBV reactivation	3 (8.2)	31 (50.0)	5 (38.5)	<0.01
aGVH II-IV	23 (67.6)	33 (53.2)	6 (46.2)	0.28
aGVH III-IV	4 (11.8)	6 (9.7)	3 (23.1)	0.37

IQR: interquartile range; CR: complete remission; MAC: myeloablative conditioning; RIC: reduce intensity conditioning; TBI: total body irradiation; aGVH: acute GVH. Analyses were conducted using a Fisher's exact test or a Kruskal-Wallis test with significant p.value if $p < 0.05$.