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

Abstract

Allogeneic hematopoietic stem cell transplantation (alloHSCT) from mismatched unrelated donors (MMUD) carries high risks of non-relapse mortality (NRM) and graft-*versus*-host disease (GvHD). Post-transplant cyclophosphamide (PTCY) has emerged as an alternative to antithymocyte globulin (ATG) for GvHD prophylaxis. This single-center retrospective study compared PTCY (N=41) to high-dose ATG and low-dose ATG in 155 MMUD alloHSCT recipients. PTCY was associated with better overall survival with a 1-year overall survival of 78.7% *versus* 56.5% in the PTCY and high-dose ATG groups (*P*=0.007) and 64.8% in the low-dose ATG group (*P*=0.059), driven by a significant reduction in NRM (*P*=0.008), with a 1-year NRM in the PTCY group of 7.7% *versus* 24.4% in the high-dose ATG group (*P*=0.031) and 29.8% in the low-dose group (*P*=0.026). The relapse incidence was similar between the groups (17.5% *vs.* 25.7% and 16.2% for the PTCY, high-dose ATG and low-dose ATG groups, respectively; *P*=0.830), despite a better progression-free survival in the PTCY group (*P*=0.034) with 1-year progression-free survival being 78.4% compared with 50.0% in the high-dose ATG group (*P*=0.002) and 54.0% in the low-dose group (*P*=0.041). Day-100 grade II-IV and grade III-IV acute GvHD, as well as 1-year chronic GvHD and moderate/severe chronic GvHD were not significantly different. However, 1-year GvHD-related mortality was lower in the PTCY group (2.6% *vs*. 14.4% and 14.9% in the high- and low-dose ATG groups, respectively; *P*=0.018). Infection-related mortality was similar across groups, but cytomegalovirus and Epstein-Barr virus infections were less frequent with PTCY, a finding potentially linked to differences in immune reconstitution. Compared to high-dose and low-dose ATG, PTCY prophylaxis was associated with improved overall survival and progression-free survival as well as lower NRM in MMUD alloHSCT.

Introduction

Allogeneic hematopoietic stem cell transplantation (alloHSCT) is a crucial therapy for many hematologic malignancies. However, finding an HLA-matched sibling or unrelated donor can be challenging. When HLA-matched donors are unavailable, alternative donors, such as haploidentical or mismatched unrelated donors (MMUD), are viable options. Historically, mismatched alloHSCT has been associated with inferior outcomes, largely due to increased non-relapse mortality (NRM) and a higher incidence of graft-*versus*-host disease (GvHD).[1-4]

In vivo T-cell depletion using rabbit antithymocyte globulin (ATG) has become the standard of care for MMUD alloHSCT in Europe after randomized clinical trials demonstrated its efficacy in reducing the incidence of GvHD and improving transplant outcomes.[5-10] More recently, the use of post-transplant cyclophosphamide (PTCY) has emerged as a new prophylaxis for GvHD in haploidentical transplantation,[11,12] as well as in transplants from matched and mismatched unrelated donors, compared with standard prophylaxis without ATG.[13]

To date, only retrospective data comparing ATG to PTCY in MMUD alloHSCT are available. Some previous studies[14-16] suggested better outcomes with PTCY than with ATG, attributing the difference to reduced incidences of NRM and GvHD. However, these findings showed significant inconsistency with those of other studies,[17-20] precluding the

European Blood and Marrow Transplantation (EBMT) group from recommending a preference for either prophylactic regimen in their recent guidelines.[21] A recent large-scale EBMT retrospective study involving 2,123 patients (583 treated with PTCY, 1,540 with ATG) documented improved survival with PTCY, associated with reduced NRM, although without any difference in the incidence of GvHD.[22] However, these studies mainly used heterogeneous doses of ATG, with relatively low average doses, such as Thymoglobulin® (ATG-T) <6 mg/kg or ATG-Fresenius® (ATG-F) <35 mg/kg. High doses of ATG (ATG-T >7.5 mg/kg or ATG-F >35 mg/kg) were proposed in previous studies as a standard prophylaxis for MMUD transplants.[7,23] However, a comparison of PTCY with high-dose (HD) ATG has not yet been reported and it is currently unknown whether HD-ATG and PTCY lead to comparable outcomes. In this retrospective, single-center study, we compared the impact of GvHD prophylaxis using PTCY *versus* high or low doses of ATG in MMUD alloHSCT for hematologic malignancies.

Methods

Eligibility criteria

This study involved patients aged ≥16 years with hematologic malignancies who underwent MMUD alloHSCT at our center between January 2010 and February 2024. Eligible patients had a single allele mismatch at HLA loci A, B, C, DRB1, or DQB1 and received ATG or PTCY as GvHD prophylaxis. Patients treated with other methods of T-cell depletion were excluded. The study adhered to the Declaration of Helsinki, with ethics approval (IRB00003888, project number 21-799). All patients provided informed consent to the retrospective use of their clinical and biological data.

Conditioning regimens and graft-*versus*-host disease prophylaxis

Conditioning regimens followed EBMT guidelines[24] and included myeloablative or reduced-intensity regimens. GvHD prophylaxis varied between groups. PTCY was administered at 50 mg/kg/day on days +3 and +4. ATG was administered in HD or low-dose (LD) regimens. HD regimens included Thymoglobulin® at 10 mg/kg (2.5 mg/kg/day from day -4 to day -1) or ATG-Fresenius® at 60 mg/kg (20 mg/kg/day from day -3 to day -1). LD regimens included Thymoglobulin® at 5 mg/kg (2.5 mg/kg on days -2 and -1) or ATG-Fresenius® at 30 mg/kg (10 mg/kg/day from day -3 to day -1). All patients also received cyclosporine A in combination with methotrexate for HD-ATG with myeloablative conditioning or with mycophenolate mofetil in all other cases.

Primary and secondary endpoints

The primary endpoint was 1-year overall survival (OS). Secondary endpoints included progression-free survival (PFS), severe GvHD-free and relapse-free survival (GRFS), cumulative incidence of relapse (CIR), NRM, and engraftment. The incidence of GVHD was assessed at day 100 for acute GvHD and at 1 year for chronic GvHD. OS was defined as time from transplantation to death from any cause. PFS referred to survival without relapse/disease progression, while GRFS was defined as survival without grade III-IV acute GvHD, moderate/severe chronic GvHD, or relapse. Relapse was indicated by ≥5% bone marrow blasts or re-appearance of the underlying disease. NRM was defined as death without relapse/progression. GvHD was graded using Mount Sinai Acute GVHD International Consortium[25] and National Institutes of Health[26] criteria for acute and chronic GvHD, respectively. Engraftment was characterized by achieving an absolute neutrophil count ≥0.5×10^9/L for 3 consecutive days and a platelet count ≥20×10^9/L for 7 consecutive days.

Immunophenotypic analysis of immune reconstitution

Immune reconstitution was assessed by flow cytometry on peripheral blood samples collected 3, 6, 12, and 18 months after alloHSCT. Blood cells were characterized using four-color flow cytometry. A minimum of 10,000 lymphocytes were analyzed using a FACS Canto II (BD Bioscience) and analyzed using FACS Diva software.

Statistical methods

Categorical and continuous variables were analyzed using Fisher exact and Kruskal-Wallis tests, respectively. The follow-up time was defined as the period between the day of alloHSCT and either the last follow-up or death. Survival probabilities (OS, PFS, GRFS) were calculated using the Kaplan-Meier method. Cumulative incidence functions were used to estimate CIR and NRM within a competing risk setting. Death and relapse were considered competing events in the GvHD study. Univariate analyses were performed using the log-rank test for OS, PFS, and GRFS, whereas the Gray test was applied for the others.[27] *P* values <0.05 were considered statistically significant. Multivariate analysis was performed with Cox proportional hazards models. Variables associated with clinical outcomes were selected after univariate analysis (*Online Supplementary Table S1*). The model included prophylaxis group (PTCY, LD-ATG, or HD-ATG), conditioning intensity, age (<45 or >45), Hematopoietic Cell Transplantation-specific Comorbidity Index (HCT-CI) score, and Disease Risk Index. One-year mortality incidences were calculated using a Gray and Fine model, considering different sources of mortality as competing events, with *P* values derived from the Gray test. Analyses were conducted with R software (version 4.1.2).[28]

Results

Cohort description

One-hundred and fifty-five patients receiving a MMUD

Table 1. Baseline characteristics of all patients and patients divided according to type of graft-*versus*-host disease prophylaxis.

Characteristics	All N=155	PTCY N=41	HD-ATG N=93	LD-ATG N=21	*P*
Follow-up, months, median (IQR)	52.4 (18.6-97.2)	19.4 (11.3-30.5)	91.4 (59.9-127.6)	73.0 (24.1-85.0)	<0.01
Year of alloHSCT, median (range)	2016 (2010-2024)	2022 (2018-2024)	2013 (2010-2022)	2016 (2011-2019)	<0.01
Period of alloHSCT, N (%) 2010-2014 2015-2019 2019-2024	 63 (40.6) 47 (30.3) 45 (29.0)	 0 (0.0) 3 (7.3) 38 (92.7)	 59 (63.4) 27 (29.0) 7 (7.5)	 4 (19.0) 17 (81.0) 0 (0.0)	-
Age, years, mean (range)	47.1 (15.5-66.6)	47.5 (22.5-64.9)	43.5 (15.5-66.6)	50.1 (16.3-66.5)	0.08
Patient gender, N (%) Female Male	 59 (38.1) 96 (61.9)	 19 (46.3) 22 (53.7)	 31 (33.4) 62 (66.7)	 9 (42.9) 12 (57.1)	0.37
Female donor to male recipient, N (%)	30 (19.4)	6 (14.6)	19 (20.4)	5 (23.8)	0.65
D/R CMV serological status, N (%) Neg/neg Pos/neg Pos/pos Neg/pos	 33 (21.3) 30 (19.4) 53 (34.2) 39 (25.2)	 8 (19.5) 7 (17.1) 17 (41.5) 9 (22.0)	 22 (23.7) 17 (18.3) 30 (32.3) 24 (25.8)	 3 (14.3) 6 (28.6) 6 (28.6) 6 (28.6)	0.80
Letermovir prophylaxis in CMV-positive recipients, N (%)	29 (31.5)	23 (88.5)	5 (9.3)	1 (8.3)	<0.01
ECOG score, N (%) 0 1 2	 112 (72.3) 36 (23.2) 7 (4.5)	 25 (61.0) 12 (29.3) 4 (9.8)	 73 (78.5) 17 (18.3) 3 (3.2)	 14 (66.7) 7 (33.3) 0 (0.0)	0.11
HCT-CI, N (%) 0 1-2 ≥3	 56 (36.1) 68 (43.9) 31 (20.0)	 14 (34.1) 20 (48.8) 7 (17.1)	 31 (33.3) 44 (47.3) 18 (19.4)	 11 (52.4) 4 (19.1) 6 (28.6)	0.16
Second HSCT, N (%)	4 (2.5)	1 (2.4)	1 (1.1)	2 (9.5)	0.06
Leukemias and related disorders, N (%) Acute lymphoblastic leukemia Acute myeloid leukemia Chronic myeloid leukemia Myelofibrosis MDS MPN/MDS	118 (76.1) 28 (18.0) 65 (41.9) 3 (1.9) 14 (9.0) 19 (12.3) 3 (1.9)	35 (85.4) 3 (7.3) 19 (46.3) 0 (0.0) 0 (0.0) 11 (26.8) 2 (4.9)	81 (87.1) 23 (24.8) 32 (34.4) 3 (3.3) 13 (14.0) 7 (7.5) 3 (3.2)	19 (90.5) 2 (9.5) 12 (57.1) 0 (0.0) 1 (4.8) 3 (14.3) 1 (4.8)	0.89
Lymphomas, N (%) B-cell lymphoma T-cell lymphoma Hodgkin lymphoma Others	20 (12.9) 5 (3.1) 10 (6.5) 3 (1.9) 2 (1.3)	6 (14.6) 1 (2.4) 5 (12.2) 0 (0.0) 0 (0.0)	12 (12.9) 4 (4.4) 5 (5.4) 1 (1.1) 2 (2.2)	2 (9.5) 0 (0.0) 0 (0.0) 2 (9.5) 0 (0.0)	0.89
Disease Risk Index, N (%) Low Intermediate High Very high	 22 (14.2) 80 (51.6) 46 (29.7) 7 (4.5)	 7 (17.1) 19 (46.3) 12 (29.3) 3 (7.3)	 15 (16.1) 49 (52.7) 27 (29.0) 2 (2.2)	 0 (0.0) 12 (57.1) 7 (33.3) 2 (9.5)	0.32
Complete remission at transplant, N (%)	100 (64.5)	28 (68.3)	60 (64.5)	12 (57.1)	0.69
HLA mismatch, N (%): Class I mismatch A/B/C Class II mismatch DR/DQ	 135 (87.1) 86/20/29 30 (12.9) 3/17	 34 (82.9) 23/5/6 7 (17.1) 1/6	 83 (89.3) 51/11/21 10 (10.8) 2/8	 18 (85.7) 12/4/2 3 (14.3) 0/3	0.81
Stem cell source, N (%) Bone marrow PBSC	 4 (2.5) 151 (97.4)	 1 (2.4) 40 (97.6)	 2 (2.2) 91 (97.8)	 1 (4.8) 20 (95.2)	0.74

Continued on following page.

Characteristics	All N=155	PTCY N=41	HD-ATG N=93	LD-ATG N=21	*P*
Conditioning intensity, N (%) Myeloablative Reduced intensity	 68 (43.9) 87 (56.1)	 19 (46.4) 22 (53.7)	 40 (43.0) 53 (57.0)	 9 (42.9) 12 (57.1)	0.93
Total body irradiation, N (%)	31 (20.0)	1 (2.4)	28 (30.1)	2 (9.5)	<0.01
In vivo T-cell depletion, N (%) ATG-T 5 mg/kg ATG-T 10 mg/kg ATG-F 30 mg/kg ATG-F 60 mg/kg PTCY 100 mg/kg	 19 (12.3) 66 (42.6) 2 (1.3) 27 (17.4) 41 (26.5)	 0 (0.0) 0 (0.0) 0 (0.0) 0 (0.0) 41 (100.0)	 0 (0.0) 66 (71.0) 0 (0.0) 27 (29.0) 0 (0.0)	 19 (90.5) 0 (0.0) 2 (9.5) 0 (0.0) 0 (0.0)	<0.01
GvHD prophylaxis, N (%) CSA+MTX CSA+MMF	42 (27.1) 113 (72.9)	0 (0.0) 41 (100.0)	41 (44.1) 52 (55.9)	1 (4.8) 20 (95.2)	<0.01

N: number; PTCY: post-transplant cyclophosphamide; HD-ATG: high dose of antithymocyte globulin; LD-ATG: low dose of antithymocyte globulin; IQR: interquartile range; alloHSCT: allogeneic hematopoietic stem cell transplantation; ATG-T: thymoglobulin; ATG-F: ATG-Fresenius; D/R : donor/recipient; CMV: cytomegalovirus; Neg: negative; Pos: positive; ECOG: Eastern Cooperative Oncology Group; HCT-CI: Hematopoietic Cell Transplant-specific Comorbidity Index; MDS: myelodysplastic syndrome; MPN/MDS: hematologic disorder between myeloproliferative neoplasm and myelodysplastic syndrome; HLA: human leukocyte antigen; PBSC: peripheral blood stem cells; CSA: cyclosporine A; MTX: methotrexate; MMF: mycophenolate mofetil. Analyses were conducted using a Fisher exact test and a Kruskal-Wallis test. *P* values <0.05 are considered statistically significant.

alloHSCT for a hematologic malignancy were included. Among them, 41 patients received PTCY-based prophylaxis (PTCY group), 93 patients received HD-ATG (HD group) and 21 patients received LD-ATG (LD group). The patients' characteristics, presented in Table 1, were comparable across groups in terms of age, sex and disease type, with a majority having acute leukemia. Disease Risk Index was high or very high in more than one-third of cases. No differences were identified in the prevalence of cytomegalovirus (CMV) and Epstein-Barr virus (EBV) infections or ABO matching. Most patients underwent a peripheral blood stem cell transplant. HLA mismatches were mainly in class I. Due to the recent adoption of PTCY as GvHD prophylaxis, transplant year differed significantly (median: 2021 *vs*. 2014 and 2016 for the PTCY, HD and LD groups, respectively, *P*<0.01) and the median [interquartile range] follow-up times were significantly different across groups (19.4 [11.3-30.5], 91.4 [59.9-127.6], and 73.0 [24.1-85.0] months for the PTCY, HD, and LD groups, respectively, *P*<0.01). Lastly, GvHD prophylaxis in the PTCY and LD groups was almost exclusively based on cyclosporine A and mycophenolate mofetil, compared with usage in 55.9% of patients in the HD group.

Survival analyses

PTCY was associated with better OS (*P*=0.049, log-rank test) with the 1-year OS being 78.7% and 56.5% in the PTCY and HD groups, respectively (*P*=0.007) and 64.8% in the LD group (*P*=0.059). PFS was also better in the PTCY group than in the HD and LD groups (*P*=0.034, log-rank test) with the 1-year PFS being 78.4%, 50.0% (*P*=0.002) and 54.0% (*P*=0.041), respectively. This improvement may be attributed to a significant reduction in NRM (*P*=0.008, Gray test), with a lower 1-year NRM observed in the PTCY group than in either the HD group (7.7% *vs*. 24.4%, *P*=0.031) or the LD group (7.7% *vs*. 29.8%, *P*=0.026). The CIR was not significantly different between the three groups (17.5%, 25.7% and 16.2% in the PTCY, HD and LD groups, respectively, *P*=0.830) (Figure 1, Table 2). Specific comparison between the HD and LD groups revealed no significant differences at 1 year in OS, PFS, NRM or CIR.

A multivariate Cox analysis adjusted for age (≤45 *vs*. >45 years), conditioning regimen intensity (myeloablative *vs*. reduced intensity, Disease Risk Index (low/intermediate *vs*. high/very high), and HCT-CI score (0-2 *vs*. ≥3) confirmed these findings (Table 3). After adjustment, ATG prophylaxis was still associated, independently of the dose, with increased mortality (hazard ratio [HR] HD-ATG: 2.47, *P*=0.008, and LD-ATG: 2.41, *P*=0.033), with higher NRM (HR HD-ATG: 4.34, *P*=0.006, and LD-ATG: 4.28, *P*=0.018) and with lower PFS (HR HD ATG: 2.44, *P*=0.006, and LD ATG: 2.46, *P*=0.023) compared to PTCY.

Impact of post-transplant cyclophosphamide on engraftment and graft-*versus*-host disease

Among the 155 patients, primary graft failure occurred in nine cases: six in the HD group (6.5%) and three in the LD group (14.3%). Mean neutrophil recovery times were similar across the PTCY, HD, and LD groups, averaging 24.3 days (standard deviation [SD] 5.1), 22.9 days (SD 5.3), and 22.3 days (SD 14.8), respectively (*P*=0.51). By contrast, platelet recovery was significantly slower in the PTCY group (31.8 days [SD 23.9]) than in the HD (24.0 days [SD 15.5]) and LD (20.8 days [SD 15.7]) groups (*P*=0.04).

GvHD incidences are reported in Figure 2. No significant differences were observed between the PTCY, HD, and LD groups in day-100 cumulative incidences of grade II-IV acute GvHD (65.9%, 52.8%, and 47.6%, respectively; *P*=0.346) or grade III-IV acute GvHD (17.1%, 22.7% and 29.4%, respectively; *P*=0.257). The high incidence of acute GvHD was mainly due to grade II cases, particularly in the PTCY group. Similarly, 1-year incidences of chronic GvHD (35.1%, 29.5%, and 37.8%; *P*=0.854) and moderate/severe chronic GvHD (24.2%, 15.9%, and 27.0%; *P*=0.959) were comparable across groups. ATG dose was not significantly associated with differences in grade II-IV or grade III-IV acute GvHD or the incidence of chronic GvHD incidence. Similarly, the rates of GRFS at 1 year showed no significant differences (40.6%, 32.2%, and 16.7% for the PTCY, HD, and LD groups, respectively; *P*=0.064).

Mortality analysis and contributing factors

The causes of mortality are detailed in *Online Supplementary Table S2*. Overall, 11 (26.8%), 52 (55.9%), and 13 (61.9%) patients died in the PTCY, HD, and LD groups, respectively. At 1 year, hematologic disease remained the leading cause of mortality in the PTCY and HD groups, with no significant differences between the groups (13.7%, 19.2%, and 5.4%;

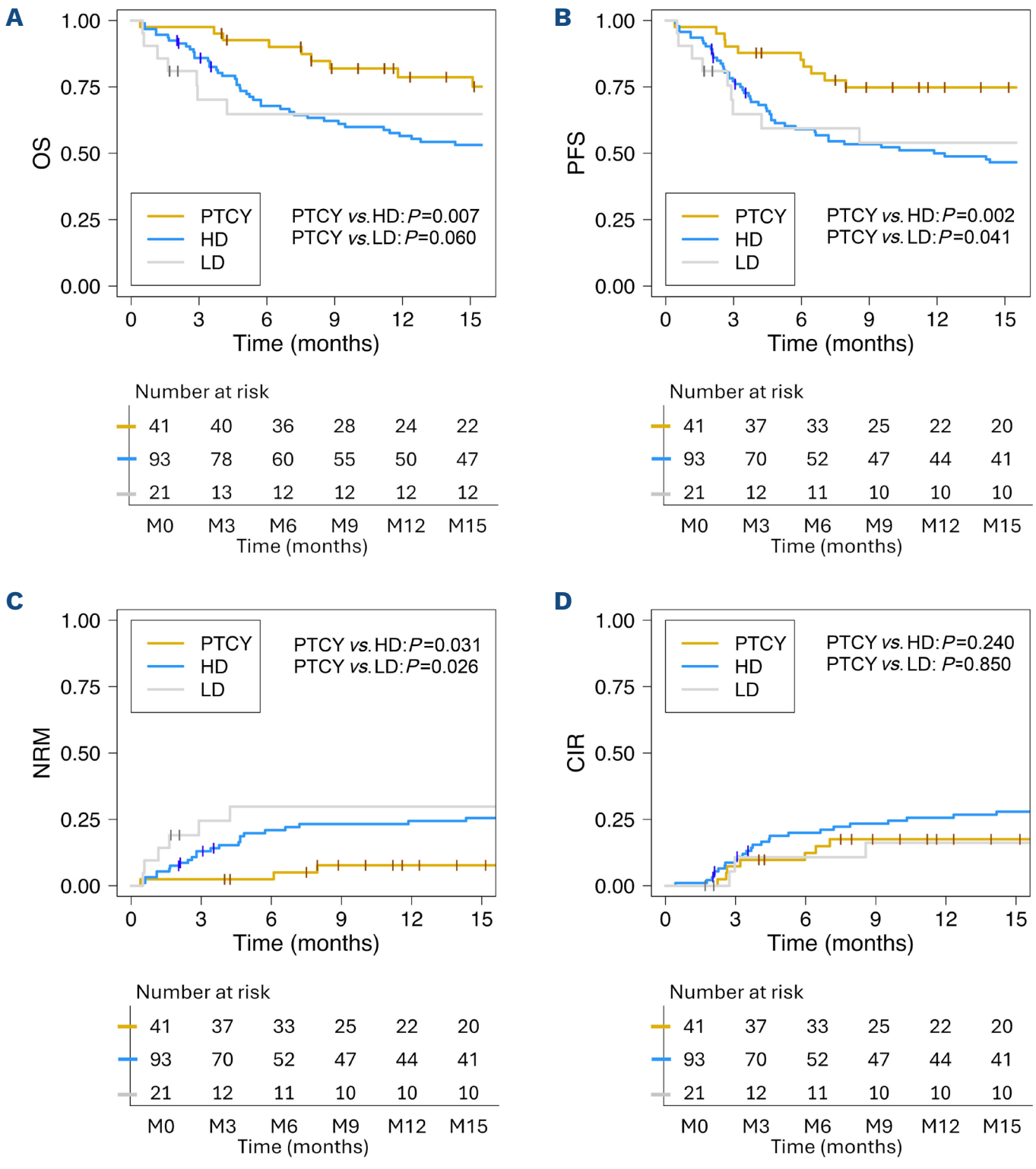

Figure 1. Main survival and relapse outcomes of the three groups. (A) Overall survival. (B) Progression-free survival. (C) Non-relapse mortality. (D) Cumulative incidence of relapse. Statistical analyses were performed at 1 year using a log-rank test, except for non-relapse mortality and cumulative incidence of relapse, for which the Gray test was used, with death and relapse as competing events. *P* values <0.05 are considered statistically significant. OS: overall survival. PTCY: post-transplant cyclophosphamide; HD: high-dose antithymocyte globulin; LD: low-dose antithymocyte globulin; PFS: progression-free survival; NRM: non-relapse mortality; CIR: cumulative incidence of relapse.

P=0.712). Infection-related mortality, occurring outside the context of active GvHD, was similarly comparable across the groups (5.1%, 7.5% and 9.5%; *P*=0.432).

GvHD-related mortality (either directly or facilitated by GvHD) was significantly lower in the PTCY group (2.6% *vs*. 14.4% and 14.9%; *P*=0.023), potentially explaining the reduced NRM observed in this group. While rates of severe acute and chronic GvHD were similar among the groups, the PTCY group exhibited fewer cases of grade IV acute GvHD (2.6% *vs*. 15.3% and 14.9%; *P*=0.019). Additionally, the incidence of corticosteroid-refractory GvHD was lower in the PTCY group (22.2% *vs*. 38.0% and 50.0%). One-year OS of patients with corticosteroid-refractory GvHD was 85.7% in the PTCY group (N=7), 31.6% in the HD group (N=19) and 40.0% in the LD group (N=5) (*P*=0.15). This result could be limited by the low number of patients with corticosteroid-refractory GvHD; however, it suggests that the reduced GvHD-related mortality may be due to the recent access to ruxolitinib, which was predominantly used as standard second-line therapy in the PTCY group (*vs*. <15% in the ATG groups). Notably, ruxolitinib use was associated with a significantly lower 1-year NRM in patients with acute GvHD requiring at least second-line therapy (21.4% *vs*. 51.9%, *P*=0.044, in a combined analysis of all study groups).

Adverse events

The occurrence of complications, particularly infections, was analyzed at 1 year (*Online Supplementary Table S3*). No significant differences were found in the incidence of severe bacterial infections, defined as fatal sepsis or those requiring intensive care management, between groups (19.5%, 22.6%, and 14.3% for the PTCY, HD, and LD groups, respectively; *P*=0.72). Although the difference was not statistically significant, fungal infections were more frequent in the HD and LD groups than in the PTCY group (4.9% *vs*. 16.1% and 14.3%; *P*=0.19).

A substantial difference was observed in the spectrum of viral infections. EBV reactivation, defined as an increasing EBV viremia >4 log IU/mL confirmed 1 week apart and requiring preemptive treatment, was significantly less common in the PTCY group than in the HD and LD groups (7.3% *vs*. 48.4% and 33.3%, respectively; *P*<0.01). Despite its rarity, EBV-positive lymphoproliferative disease occurred in three patients in the HD group and one patient in the LD group, with high associated mortality (75%, 3/4 patients). Similarly, CMV infections, defined as an increasing CMV viremia >3 log IU/mL confirmed 1 week apart and requiring preemptive treatment, were more frequent in ATG-treated groups (9.8% *vs*. 35.5% and 33.3%; *P*<0.01 for PTCY, HD, and LD, respectively). However, this difference may have been influenced by the more frequent use of letermovir prophylaxis in CMV-positive recipients within the PTCY group (88.5% *vs*. 9.3% and 8.3% in the HD and LD groups, respectively). Conversely, symptomatic urinary BK virus reactivation was more common in the PTCY group, affecting 15 patients (36.6%) compared to 17 patients (18.3%) in the HD group and three patients (14.3%) in the LD group (*P*=0.04). Eight patients required hospitalization (2 in the PTCY group, 4 in the HD group, and 2 in the LD group), and four underwent urological interventions in the operating room (2 in the PTCY group, 1 in the HD group, and 1 in the LD group).

No significant differences were observed in the incidence of thrombotic microangiopathy, sinusoidal obstruction syndrome, or severe acute renal failure (grade 3 or 4 as per Common Terminology Criteria for Adverse Events [CTCAE] v5.0) (*data not shown*). Cardiovascular compli-

Table 2. Univariate analyses of 1-year outcomes by treatment group.

Outcomes at 1 year, % (95% CI)	All N=296	PTCY N=41	HD-ATG N=93	LD-ATG N=21	*P*
Overall survival	63.5 (56.1-71.8)	78.7 (66.4-93.1)	56.5 (47.1-67.8)	64.8 (46.7-89.8)	0.049
Progression-free survival	57.0 (49.5-65.6)	74.8 (62.4-89.7)	50.0 (40.6-61.5)	54.0 (35.7-81.6)	0.034
Cumulative incidence of relapse	22.3 (15.6-29.1)	17.5 (5.5-29.5)	25.7 (16.5-34.8)	16.2 (0.0-33.6)	0.830
Non-relapse mortality	20.7 (14.2-27.2)	7.7 (0.0-16.2)	24.4 (15.4-33.3)	29.8 (9.0-50.7)	0.008
GRFS	32.6 (25.7-41.2)	40.6 (27.5-60.1)	32.2 (23.8-43.6)	16.7 (6.0-46.5)	0.064
Acute GvHD II-IV[#]	55.6 (47.7-63.5)	65.9 (51.0-80.7)	52.8 (42.5-63.0)	47.6 (25.5-69.7)	0.346
Acute GvHD II-IV[#]	22.0 (15.5-28.6)	17.1 (5.4-28.8)	22.7 (14.1-31.3)	29.4 (8.9-49.9)	0.257
Chronic GvHD	32.0 (24.3-39.7)	35.1 (19.1-51.1)	29.5 (19.9-39.1)	37.8 (14.3-61.3)	0.854
Chronic GvHD M/S	19.5 (13.0-26.1)	24.2 (10.0-38.5)	15.9 (8.2-23.5)	27.0 (5.6-48.4)	0.959

[#]Data at day 100. Statistical analyses were performed at 1 year, except for acute graft-*versus*-host disease (GvHD), which was analyzed at day 100, using a log-rank test for overall survival, progression-free survival and GRFS, and a Gray test for the other outcomes. Statistical significance was defined as *P*<0.05. 95% CI: 95% confidence interval; PTCY: post-transplant cyclophosphamide; HD-ATG: high-dose antithymocyte globulin; LD-ATG: low-dose antithymocyte globulin; GRFS: severe GvHD-free/relapse-free survival; M/S: moderate or severe.

cations were reported in 15 patients: seven (17.1%) in the PTCY group, eight (8.6%) in the HD group, and none (0%) in the LD group (P=0.11). The primary complication was left ventricular dysfunction, resulting in heart failure episodes in eight patients (5 in the PTCY group and 3 in the HD group). Among these, six patients recovered left ventricular function to levels exceeding 50% within 6 months (4 in the PTCY group and 2 in the HD group).

Impact of graft-*versus*-host disease prophylaxis on immune reconstitution

Immune reconstitution was evaluated through peripheral blood lymphocyte immunophenotyping at 3, 6, 12, and 18 months after alloHSCT in 106 patients (34 PTCY, 62 HD, and 13 LD) (Figure 3). These patients' characteristics are described in *Online Supplementary Table S4*. At 3 months (Table 4), the median $CD8^+$ T-cell count was significantly lower in the PTCY group than in the HD and LD groups (median: 52.5/μL *vs*. 176.0/μL and 245.0/μL, respectively; P<0.01). $CD4^+$ T-cell counts did not differ, resulting in a higher CD4/CD8 ratio in the PTCY group (1.26 *vs*. 0.23 and 0.25; P<0.01). Over time, from 6 to 18 months, this difference in the CD4/CD8 ratio narrowed with similar results across the three groups. No significant differences were observed in B- and NK-cell counts across the groups.

A detailed analysis of effector T-cell phenotypes comparing PTCY and HD groups (excluding the LD group because of the limited sample size) showed a tendency toward higher counts of memory $CD4^+$ T cells, particularly central memory T cells, beginning at 3 months after transplantation and persisting at 1 year (*Online Supplementary Figure S1*). These differences were not observed in $CD8^+$ T-cell subpopulations, which demonstrated similar reconstitution across the groups.

Discussion

In this study, we analyzed outcomes in patients who received PTCY or ATG as GvHD prophylaxis following alloHSCT from a MMUD. Compared to both HD-ATG and LD-ATG, PTCY was associated with superior OS and PFS, along with significantly lower NRM at 1 year. The rates of acute and chronic GvHD, relapse, and GRFS were comparable across the three groups. However, GvHD-related mortality was significantly reduced in the PTCY group compared to the ATG groups, contributing to the observed reduction in NRM. In the literature,[14-17,19,20] the use of PTCY has been associated with a decrease in the incidence of total and severe acute GvHD in three studies[14-16] but with no differences in extensive chronic GvHD. Batipaglia *et al.*[14] also reported a decrease in GvHD-related mortality at 2 years (24% *vs*. 9%) but most of these studies did not show an improvement in OS. A recent large EBMT registry study retrospectively compared 1,540 patients given ATG and 583 given PTCY.[22] At 2 years, the PTCY group exhibited better OS (65.7% *vs*. 55.7%; P<0.01) and PFS (64.9% *vs*. 57.2%; P<0.01) related to a reduction in NRM (18% *vs*. 26.2%, P=0.03) without a difference in relapse or acute or chronic GvHD rates. These results are consistent with those of our study in which

Table 3. Survival outcomes in multivariate Cox analysis.

Risk factor	HR (95% CI)	*P*
Overall survival		
PTCY	1	NA
HD-ATG	2.47 (1.26-4.84)	0.008
LD-ATG	2.41 (1.07-5.42)	0.033
Age <45 years	0.52 (0.28-0.97)	0.971
MAC	0.94 (0.52-1.70)	0.852
DRI high/very high	1.81 (1.11-2.96)	0.017
HCT-CI score 0-2	0.60 (0.36-1.01)	0.052
Progression-free survival		
PTCY	1	NA
HD-ATG	2.44 (1.29-4.62)	0.006
LD-ATG	2.46 (1.13-5.34)	0.023
Age <45 years	0.61 (0.34-1.10)	0.102
MAC	0.92 (0.52-1.63)	0.784
DRI high/very high	1.86 (1.16-2.97)	0.010
HCT-CI score 0-2	0.62 (0.37-1.05)	0.074
GRFS		
PTCY	1	NA
HD-ATG	1.08 (0.92-1.63)	0.773
LD-ATG	1.06 (0.52-2.14)	0.878
Age <45 years	0.54 (0.32-0.93)	0.027
MAC	1.03 (0.61-1.74)	0.914
DRI high/very high	1.55 (1.00-2.38)	0.048
HCT-CI score 0-2	0.80 (0.45-1.32)	0.385
Non-relapse mortality		
PTCY	1	NA
HD-ATG	4.34 (1.52-12.4)	0.006
LD-ATG	4.28 (1.28-14.30)	0.018
Age <45y	0.43 (0.18-1.02)	0.056
MAC	0.88 (0.39-2.00)	0.766
DRI high/very high	1.15 (0.59-2.27)	0.680
HCT-CI score 0-2	0.82 (0.41-1.66)	0.578
Cumulative incidence of relapse		
PTCY	1	NA
HD-ATG	1.91 (0.86-4.28)	0.113
LD-ATG	1.81 (0.65-5.03)	0.253
Age <45 years	0.75 (0.34-1.65)	0.473
MAC	0.90 (0.42-1.93)	0.793
DRI high/very high	2.41 (1.28-4.54)	0.007
HCT-CI score 0-2	0.55 (0.27-1.12)	0.113

Hazard ratios comparing post-transplant cyclophosphamide (control group) *versus* low-dose antithymocyte globulin and *versus* high-dose antithymocyte globulin, age (<45 *vs*. >45 years), conditioning regimen (myeloablative *vs*. reduced intensity), Disease Risk Index (low/intermediate *vs*. high/very high), and Hematopoietic Cell Transplantation-specific Comorbidity Index score (0-2 *vs*. ≥3). Multivariate Cox proportional hazards regression analysis. Differences are considered statistically significant if P<0.05. HR: hazard ratio; 95 CI: 95% confidence interval; PTCY: post-transplant cyclophosphamide; NA: not applicable; HD-ATG: high-dose antithymocyte globulin; LD-ATG: low-dose antithymocyte globulin; MAC: myeloablative conditioning; DRI: Disease Risk Index; HCT-CI: Hematopoietic Cell Transplantation-specific Comorbidity Index; GRFS: severe graft-*versus*-host disease-free/relapse-free survival.

the impact of PTCY seems mainly linked to a reduction in NRM. However, limitations in this registry study should be considered, including the lack of information on ATG dosing and potential confounding biases related to registry-based data and the variability in practices across centers.

Our former practice of administering HD-ATG was based on older studies,[9,10,29,30] in which ATG demonstrated a benefit. In recent years, various studies have evaluated lower doses of ATG but none of them was exclusively dedicated to MMUD alloHSCT. Reducing the dose of ATG was associated with a decrease in NRM, mainly due to a lower rate of infectious complications.[31-34] However, the optimal dose of ATG for MMUD alloHSCT remains unclear. Some studies have proposed adjusting ATG doses based on parameters such as serum ATG levels or lymphocyte counts.[35-37] These approaches are interesting because dose customization could limit severe immunosuppression and potentially reduce infectious mortality. However, studies specifically dedicated to MMUD transplants are needed to determine the optimal dose. In our study, low and high doses of ATG had similar outcomes

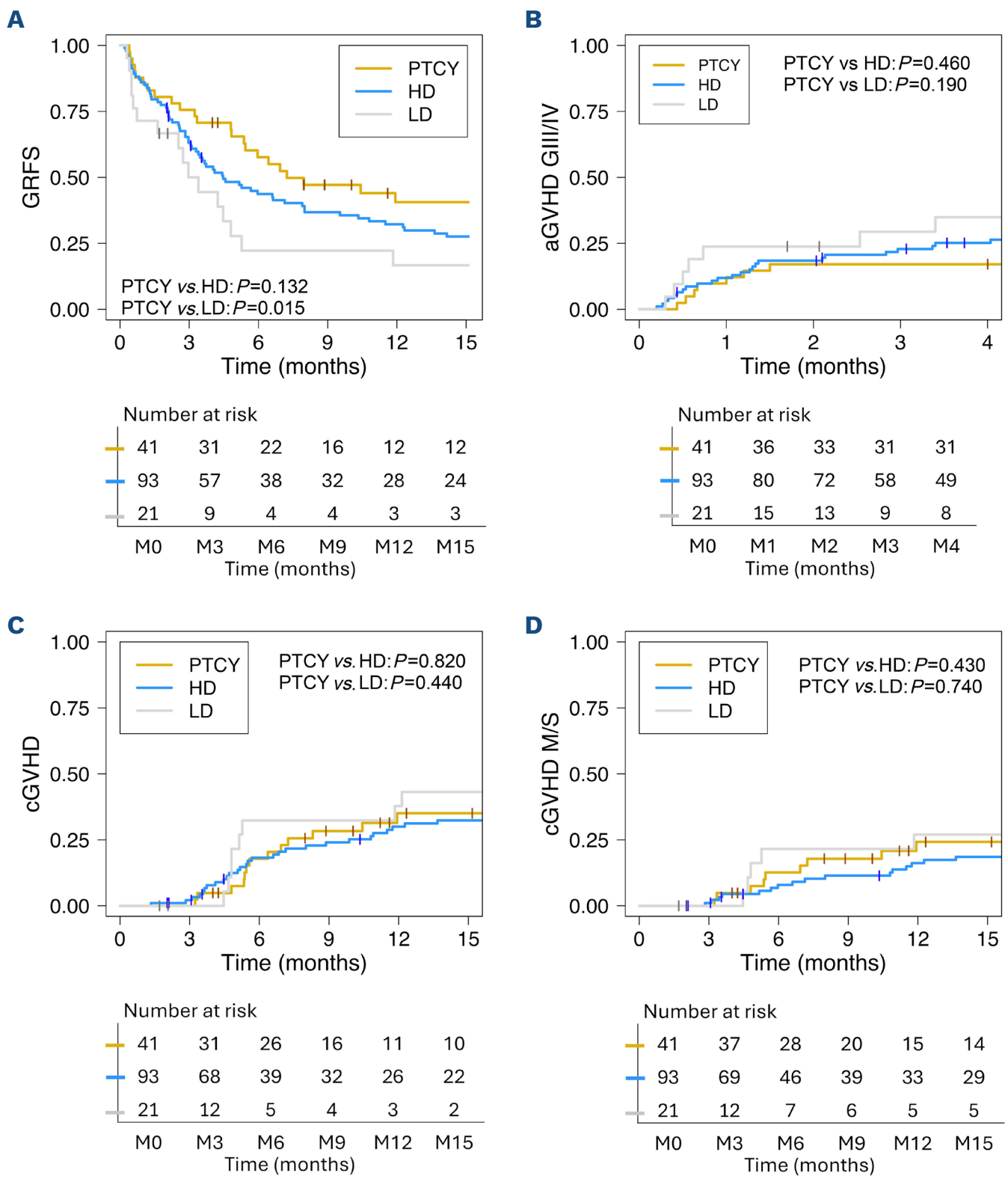

Figure 2. Graft-*versus*-host disease outcomes in the three groups. (A) Severe GvHD-free and relapse-free survival (GRFS). (B) Cumulative incidence of grade III-IV acute GvHD. (C) Cumulative incidence of all-grade chronic GvHD. (D) Cumulative incidence of moderate or severe chronic GvHD. Statistical analyses were performed at 1 year, except for the acute GvHD which was analyzed at day 100, using the Gray test with death and relapse as competing GvHD events. GRFS were analyzed at 1 year using a log-rank test. *P* values <0.05 are considered statistically significant. PTCY: post-transplant cyclophosphamide; HD: high-dose antithymocyte globulin; LD: low-dose antithymocyte globulin; aGvHD: acute graft-*versus*-host disease; cGvHD: chronic graft-*versus*-host disease; M/S: moderate or severe.

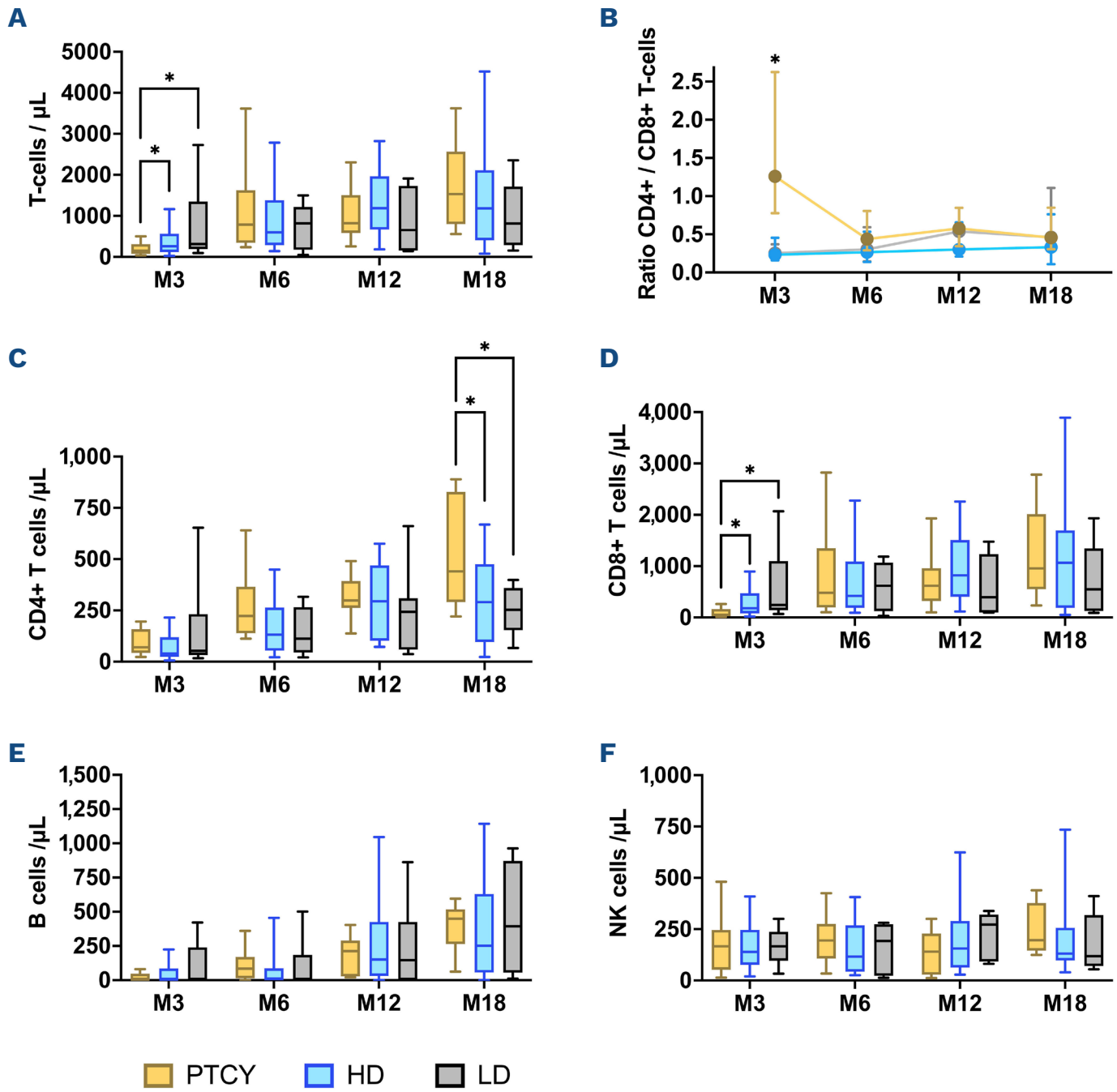

Figure 3. Evaluation of immune reconstitution after allogeneic hematopoietic stem cell transplantation. (A-F) Immune reconstitution over time is shown for T cells (A), the CD8/CD4 T-cell ratio (B), CD4⁺ T cells (C), CD8⁺ T cells (D), B cells (E), and NK cells (F). T cells were defined as CD45⁺CD3⁺ cells. CD4⁺ T cells were defined as CD45⁺CD3⁺CD4⁺CD8⁻ cells. CD8⁺ T cells were defined as CD45⁺CD3⁺CD4⁻CD8⁺ cells. B cells were defined as CD45⁺CD3⁻CD19⁺ cells. NK cells were defined as CD45⁺CD3⁻CD56⁺ cells. Analyses were performed using a two-way analysis of variance test. *P values <0.05 are considered statistically significant. M: months; NK: natural killer; PTCY: post-transplant cyclophosphamide; HD: high-dose antithymocyte globulin; LD: low-dose antithymocyte globulin.

Table 4. Immune reconstitution at 3 months after allogeneic hematopoietic stem cell transplantation.

Parameter, median (IQR)	PTCY N=34	HD-ATG N=62	LD-ATG N=13	*P*
N of T cells/µL	153.0 (75.5-311.3)	261.5 (117.8-565.0)	315.0 (192.0-1,349.0)	0.018
N of CD4⁺ T cells/µL	70.5 (43.0-158.5)	40.0 (23.5-118.8)	53.0 (32.0-231.5)	0.091
N of CD8⁺ T cells/µL	52.5 (24.3-164.5)	176.0 (79.5-468.5)	245.0 (143.5-1,098.0)	<0.001
CD4/CD8 ratio	1.26 (0.78-2.62)	0.23 (0.16-0.46)	0.25 (0.18-0.37)	<0.001
N of B cells/µL,	2.0 (0.0-47.8)	1.5 (0.0-85.5)	1 (0.0-239.5)	0.897
N of NK cells/µL	194.5 (109.5-273.5)	184.0 (121.0-292.0)	194.0 (135.3-251.8)	0.905

T cells were defined as CD45⁺CD3⁺ cells. CD4⁺ T cells were defined as CD45⁺CD3⁺CD4⁺CD8⁻ cells. CD8⁺ T cells were defined as CD45⁺CD3⁺CD4⁻CD8⁺ cells. B cells were defined as CD45⁺CD3⁻CD19⁺ cells. NK cells were defined as CD45⁺CD3⁻CD56⁺ cells. Analyses were performed using a Kruskal-Wallis test. *P* values <0.05 are considered statistically significant. IQR: interquartile range; PTCY: post-transplant cyclophosphamide; HD-ATG: high-dose antithymocyte globulin; LD-ATG: low-dose antithymocyte globulin; NK: natural killer.

and were both associated with lower OS and higher NRM than PTCY, suggesting that even the use of HD-ATG is not associated with better outcomes in the context of MMUD.
In this study, the PTCY group had lower rates of CMV and EBV infections compared to the ATG groups. These differences may be attributed to the impact of GvHD prophylaxis on immune reconstitution. Consistent with findings from previous studies,[38-40] PTCY was associated with preferential recovery of naïve and memory CD4$^+$ T cells, with slower CD8$^+$ T-cell reconstitution. The enhanced reconstitution of these CD4$^+$ T-cell subsets has been identified as a protective factor against infections, particularly CMV and EBV reactivations, potentially explaining their reduced incidence in the PTCY group.[41,42] Although some studies[38,39] have reported slower NK-cell reconstitution following alloHSCT with PTCY prophylaxis, no significant differences in NK-cell recovery were observed between the three groups in this study. Finally, Jimenez *et al.*[40] reported a delay in B-cell recovery in their ATG group, not found in our study. However, the higher rate of EBV reactivation, associated with frequent use of preemptive rituximab treatment in ATG groups, could induce a delay in B-cell recovery.
This study has certain limitations that may affect the robustness of its conclusions.
The size of the PTCY group (N=41) may impact the statistical power of our results. Moreover, despite standardized medical practices in accordance with JACIE guidelines,[43] and similar monitoring of viral infections such as EBV and CMV, supportive care strategies have evolved over time within the department and could have disproportionately benefited the more recently transplanted PTCY group. For example, the introduction of novel therapies, such as letermovir for CMV infection prophylaxis,[44] may have contributed to the observed reduction in CMV infection rates, potentially playing a role in the reduced NRM observed in this group. Similarly, advancements in the management of steroid-refractory GVHD, such as the use of ruxolitinib,[45,46] may have improved GvHD-related mortality outcomes in this group, even though consistent evidence of a direct survival benefit is lacking in the current literature.[21,45,46] Additionally, differences in immunosuppressive drugs prophylaxis between groups could also have an impact on clinical outcomes. Methotrexate was mainly used in the HD group with a myeloablative conditioning regimen, whereas mycophenolate mofetil was predominantly used in the other groups. While a meta-analysis[47] suggests that the combination of cyclosporine A and methotrexate may be associated with a lower incidence of grade 3-4 GvHD, no significant impact on NRM has been demonstrated, thereby limiting its potential influence on the clinical outcomes in this study.
To conclude, compared to high or low doses of ATG, the use of PTCY as GvHD prophylaxis was associated with higher OS and PFS, primarily driven by reduced NRM. These results, contributing to the increasing retrospective evidence, further support the potential of PTCY as a new standard for GvHD prophylaxis in MMUD alloHSCT. An ongoing randomized clinical trial (NCT05153226) will provide additional evidence to define the best prophylaxis strategy.

Disclosures

DM has received research funding from Sanofi and Novartis and consulting fees from CSL Behring, Incyte, Jazz Pharmaceuticals, Novartis, Sanofi and Mallinckrodt. None of the other authors has any conflicts of interest to disclose.

Contributions

JB and DM designed the study. JB, DM, MR, AX, FSdF, FC, GS and RPdL provided patients' data. JB collected data. JB, EK and DM analyzed data and interpreted results. JB and EK prepared figures. JB and DM wrote the original version of the manuscript. All authors contributed to reviewing and editing the manuscript and approved the final version.

Data-sharing statement

The datasets used in the current study are available from the corresponding author upon reasonable request.

References

1. Anasetti C, Beatty PG, Storb R, et al. Effect of HLA incompatibility on graft-versus-host disease, relapse, and survival after marrow transplantation for patients with leukemia or lymphoma. Hum Immunol. 1990;29(2):79-91.
2. Loiseau P, Busson M, Balere M-L, et al. HLA association with hematopoietic stem cell transplantation outcome: the number of mismatches at HLA-A, -B, -C, -DRB1, or -DQB1 is strongly associated with overall survival. Biol Blood Marrow Transplant. 2007;13(8):965-974.
3. Fürst D, Müller C, Vucinic V, et al. High-resolution HLA matching in hematopoietic stem cell transplantation: a retrospective collaborative analysis. Blood. 2013;122(18):3220-3229.
4. Verneris MR, Lee SJ, Ahn KW, et al. HLA mismatch is associated with worse outcomes after unrelated donor reduced-intensity conditioning hematopoietic cell transplantation: an analysis from the Center for International Blood and Marrow Transplant Research. Biol Blood Marrow Transplant. 2015;21(10):1783-1789.
5. Aversa F, Terenzi A, Tabilio A, et al. Full haplotype-mismatched hematopoietic stem-cell transplantation: a phase II study in patients with acute leukemia at high risk of relapse. J Clin Oncol. 2005;23(15):3447-3454.
6. Kröger N, Zabelina T, Binder T, et al. HLA-mismatched unrelated donors as an alternative graft source for allogeneic stem cell transplantation after antithymocyte globulin-containing conditioning regimen. Biol Blood Marrow Transplant. 2009;15(4):454-462.

7. Bacigalupo A. ATG in allogeneic stem cell transplantation: standard of care in 2017? Point. Blood Adv. 2017;1(9):569-572.
8. Penack O, Marchetti M, Ruutu T, et al. Prophylaxis and management of graft versus host disease after stem-cell transplantation for haematological malignancies: updated consensus recommendations of the European Society for Blood and Marrow Transplantation. Lancet Haematol. 2020;7(2):e157-e167.
9. Socié G, Schmoor C, Bethge WA, et al. Chronic graft-versus-host disease: long-term results from a randomized trial on graft-versus-host disease prophylaxis with or without anti-T-cell globulin ATG-Fresenius. Blood. 2011;117(23):6375-6382.
10. Finke J, Bethge WA, Schmoor C, et al. Standard graft-versus-host disease prophylaxis with or without anti-T-cell globulin in haematopoietic cell transplantation from matched unrelated donors: a randomised, open-label, multicentre phase 3 trial. Lancet Oncol. 2009;10(9):855-864.
11. Luznik L, O'Donnell PV, Symons HJ, et al. HLA-haploidentical bone marrow transplantation for hematologic malignancies using nonmyeloablative conditioning and high-dose, posttransplantation cyclophosphamide. Biol Blood Marrow Transplant. 2008;14(6):641-650.
12. Raiola AM, Dominietto A, Ghiso A, et al. Unmanipulated haploidentical bone marrow transplantation and posttransplantation cyclophosphamide for hematologic malignancies after myeloablative conditioning. Biol Blood Marrow Transplant. 2013;19(1):117-122.
13. Bolaños-Meade J, Hamadani M, Wu J, et al. Post-transplantation cyclophosphamide-based graft-versus-host disease prophylaxis. N Engl J Med. 2023;388(25):2338-2348.
14. Battipaglia G, Labopin M, Kröger N, et al. Posttransplant cyclophosphamide vs antithymocyte globulin in HLA-mismatched unrelated donor transplantation. Blood. 2019;134(11):892-899.
15. Nykolyszyn C, Granata A, Pagliardini T, et al. Posttransplantation cyclophosphamide vs. antithymocyte globulin as GVHD prophylaxis for mismatched unrelated hematopoietic stem cell transplantation. Bone Marrow Transplant. 2020;55(2):349-355.
16. Soltermann Y, Heim D, Medinger M, et al. Reduced dose of post-transplantation cyclophosphamide compared to ATG for graft-versus-host disease prophylaxis in recipients of mismatched unrelated donor hematopoietic cell transplantation: a single-center study. Ann Hematol. 2019;98(6):1485-1493.
17. Mehta RS, Saliba RM, Chen J, et al. Post-transplantation cyclophosphamide versus conventional graft-versus-host disease prophylaxis in mismatched unrelated donor haematopoietic cell transplantation. Br J Haematol. 2016;173(3):444-455.
18. Bailén R, Kwon M, Pascual-Cascón MJ, et al. Post-transplant cyclophosphamide for GVHD prophylaxis compared to ATG-based prophylaxis in unrelated donor transplantation. Ann Hematol. 2021;100(2):541-553.
19. Modi D, Kondrat K, Kim S, et al. Post-transplant cyclophosphamide versus thymoglobulin in HLA-mismatched unrelated donor transplant for acute myelogenous leukemia and myelodysplastic syndrome. Transplant Cell Ther. 2021;27(9):760-767.
20. Paviglianiti A, Ngoya M, Peña M, et al. Graft-versus-host-disease prophylaxis with ATG or PTCY in patients with lymphoproliferative disorders undergoing reduced intensity conditioning regimen HCT from one antigen mismatched unrelated donor. Bone Marrow Transplant. 2024;59(5):597-603.
21. Penack O, Marchetti M, Aljurf M, et al. Prophylaxis and management of graft-versus-host disease after stem-cell transplantation for haematological malignancies: updated consensus recommendations of the European Society for Blood and Marrow Transplantation. Lancet Haematol. 2024;11(2):e147-e159.
22. Penack O, Abouqateb M, Peczynski C, et al. PTCy versus ATG as graft-versus-host disease prophylaxis in mismatched unrelated stem cell transplantation. Blood Cancer J. 2024;14(1):45.
23. Baron F, Mohty M, Blaise D, et al. Anti-thymocyte globulin as graft-versus-host disease prevention in the setting of allogeneic peripheral blood stem cell transplantation: a review from the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation. Haematologica. 2017;102(2):224-234.
24. Jethava YS, Sica S, Savani B, et al. Conditioning regimens for allogeneic hematopoietic stem cell transplants in acute myeloid leukemia. Bone Marrow Transplant. 2017;52(11):1504-1511.
25. Harris AC, Young R, Devine S, et al. International, multicenter standardization of acute graft-versus-host disease clinical data collection: a report from the Mount Sinai Acute GVHD International Consortium. Biol Blood Marrow Transplant. 2016;22(1):4-10.
26. Jagasia MH, Greinix HT, Arora M, et al. National Institutes of Health consensus development project on criteria for clinical trials in chronic graft-versus-host disease: I. The 2014 Diagnosis and Staging Working Group Report. Biol Blood Marrow Transplant. 2015;21(3):389-401.e1.
27. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. J Am Stat Assoc. 1999;94(446):496-509.
28. R Core Team (2025). R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna, Austria. https://www.R-project.org/
29. Bacigalupo A, Lamparelli T, Bruzzi P, et al. Antithymocyte globulin for graft-versus-host disease prophylaxis in transplants from unrelated donors: 2 randomized studies from Gruppo Italiano Trapianti Midollo Osseo (GITMO). Blood. 2001;98(10):2942-2947.
30. Bacigalupo A, Lamparelli T, Barisione G, et al. Thymoglobulin prevents chronic graft-versus-host disease, chronic lung dysfunction, and late transplant-related mortality: long-term follow-up of a randomized trial in patients undergoing unrelated donor transplantation. Biol Blood Marrow Transplant J Am Soc Blood Marrow Transplant. 2006;12(5):560-565.
31. Butera S, Cerrano M, Brunello L, et al. Impact of anti-thymocyte globulin dose for graft-versus-host disease prophylaxis in allogeneic hematopoietic cell transplantation from matched unrelated donors: a multicenter experience. Ann Hematol. 2021;100(7):1837-1847.
32. Devillier R, Labopin M, Chevallier P, et al. Impact of antithymocyte globulin doses in reduced intensity conditioning before allogeneic transplantation from matched sibling donor for patients with acute myeloid leukemia: a report from the Acute Leukemia Working Party of European Group of Bone Marrow Transplantation. Bone Marrow Transplant. 2018;53(4):431-437.
33. Binkert L, Medinger M, Halter JP, et al. Lower dose anti-thymocyte globulin for GvHD prophylaxis results in improved survival after allogeneic stem cell transplantation. Bone Marrow Transplant. 2015;50(10):1331-1336.
34. Ayuk F, Diyachenko G, Zabelina T, et al. Comparison of two doses of antithymocyte globulin in patients undergoing

matched unrelated donor allogeneic stem cell transplantation. Biol Blood Marrow Transplant. 2008;14(8):913-919.
35. Jamani K, Dabas R, Kangarloo SB, et al. Rabbit antithymocyte globulin serum levels: factors impacting the levels and clinical outcomes impacted by the levels. Biol Blood Marrow Transplant. 2019;25(4):639-647.
36. Admiraal R, Nierkens S, de Witte MA, et al. Association between anti-thymocyte globulin exposure and survival outcomes in adult unrelated haemopoietic cell transplantation: a retrospective, pharmacodynamic cohort analysis. Lancet Haematol. 2017;4(4):e183-e191.
37. Kennedy VE, Chen H, Savani BN, et al. Optimizing antithymocyte globulin dosing for unrelated donor allogeneic hematopoietic cell transplantation based on recipient absolute lymphocyte count. Biol Blood Marrow Transplant. 2018;24(1):150-155.
38. Retière C, Willem C, Guillaume T, et al. Impact on early outcomes and immune reconstitution of high-dose post-transplant cyclophosphamide vs anti-thymocyte globulin after reduced intensity conditioning peripheral blood stem cell allogeneic transplantation. Oncotarget. 2018;9(14):11451-11464.
39. Massoud R, Gagelmann N, Fritzsche-Friedland U, et al. Comparison of immune reconstitution between anti-T-lymphocyte globulin and posttransplant cyclophosphamide as acute graft-versus-host disease prophylaxis in allogeneic myeloablative peripheral blood stem cell transplantation. Haematologica. 2022;107(4):857-867.
40. Jimenez Jimenez A, Komanduri K, Brown S, et al. Improved GRFS after posttransplant cyclophosphamide-based vs ATG-based HLA-mismatched unrelated donor transplant. Blood Adv. 2022;6(15):4491-4500.
41. Servais S, Lengline E, Porcher R, et al. Long-term immune reconstitution and infection burden after mismatched hematopoietic stem cell transplantation. Biol Blood Marrow Transplant. 2014;20(4):507-517.
42. Troullioud Lucas AG, Lindemans CA, Bhoopalan SV, et al. Early immune reconstitution as predictor for outcomes after allogeneic hematopoietic cell transplant; a tri-institutional analysis. Cytotherapy. 2023;25(9):977-985.
43. JACIE Standards. EBMT. https://www.ebmt.org/accreditation/jacie-standards Accessed November 3, 2024.
44. Marty FM, Ljungman P, Chemaly RF, et al. Letermovir prophylaxis for cytomegalovirus in hematopoietic-cell transplantation. N Engl J Med. 2017;377(25):2433-2444.
45. Zeiser R, von Bubnoff N, Butler J, et al. Ruxolitinib for glucocorticoid-refractory acute graft-versus-host disease. N Engl J Med. 2020;382(19):1800-1810.
46. Zeiser R, Polverelli N, Ram R, et al. Ruxolitinib for glucocorticoid-refractory chronic graft-versus-host disease. N Engl J Med. 2021;385(3):228-238.
47. Ram R, Yeshurun M, Vidal L, Shpilberg O, Gafter-Gvili A. Mycophenolate mofetil vs. methotrexate for the prevention of graft-versus-host-disease – systematic review and meta-analysis. Leuk Res. 2014;38(3):352-360.