Addition of Anti-thymocyte Globulin in Allogeneic Stem Cell Transplantation With Peripheral Stem Cells From Matched Unrelated Donors Improves Graft-Versus-Host Disease and Relapse Free Survival

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Abstract

In 2014 we introduced anti-thymocyte globulin (ATG) to the graft-versus-host disease (GvHD) prophylaxis regimen in allogeneic stem cell transplantation (Allo-HSCT) with peripheral stem cells (PBSC) from matched unrelated donors (MUD). We analysed the outcomes of 415 patients who went through MUD allo-HSCT and received PBSC with or without ATG. We report dramatic reduction of the incidence of chronic GvHD and our study illustrates the benefit of ATG in addition to standard GvHD prophylaxis.

Anti-thymocyte globulin (ATG) is commonly used to prevent graft-versus-host disease (GvHD) after allogeneic hematopoietic stem cell transplantation (allo-HSCT). To evaluate the impact of ATG as part of the GvHD prophylaxis in our institution, we report the outcome of 415 patients with matched unrelated donors (MUD) transplanted for hematological malignancies with or without ATG from 2005 to 2019 at Oslo University Hospital, Norway. The following groups were compared: (1) 154 patients transplanted with peripheral blood stem cells (PBSC) without ATG 2005-2014. (2) 137 patients transplanted with bone marrow stem cells (BMSC) 2005-2019. (3) 124 patients transplanted with PBSC and ATG (PBSC + ATG) 2014-2019. Three years survival was similar in the groups, 61% following allografting with PBSC, 54% with BMSC, and 59% with PBSC + ATG. Acute GvHD grade III-IV was 14%, 14%, and 7%; chronic GvHD was 81%, 32, and 26%; and extensive cGvHD 44%, 15%, and 6% in the corresponding groups. Both acute and chronic GvHD were significantly reduced in the PBSC + ATG-versus the PBSC group ($p < 0.05$ and $p < 0.001$ respectively).Transplant-related mortality (TRM) was 33%, 25%, and 17% ($p = 0.18$). Graft versus host disease and relapse free survival (GRFS) at 3 years was 43 %, 43%, and 64% in the groups. Adding ATG to the GvHD prophylaxis regimen of MUD allo-HSCT with PBSC resulted in a substantial reduction of both acute and chronic GvHD without compromising the disease control, reflected in a superior 3 years GRFS.

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Key Words: MUD, ATG, GvHD - prophylaxis, Allo-HSCT, GvHD

Introduction

Allo-HSCT has the potential to cure hematological malignancies. However, it is associated with severe morbidity and mortality.[1,2] Graft-versus-host disease (GvHD) and relapse are the major obstacles for cure and maintaining good quality of life after transplantation.[3-5] Individual thorough risk assessment before proceeding to transplant is required. An HLA-matched related donor (MRD) is still considered the best donor choice, although outcomes following transplants with matched unrelated donor (MUD) are approaching those of MRDs.[6-9]

The most frequently available source of allogeneic stem cells is currently PBSC from a MUD. Both PBSC compared to BMSC and MUD compared to MRD are associated with increased frequency and severity of GvHD.[10-12] Early studies suggested that adding ATG to GvHD prophylaxis was associated with delayed immune reconstitution and increased risk of viral infections, particularly cytomegalovirus (CMV) and Epstein-Barr virus (EBV) reactivation in addition to an increased risk of relapse.[10] However, addition of ATG to GvHD prophylaxis has been shown in several randomized

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prospective trials to significantly reduce cGvHD and to improve GvHD and relapse free survival (GRFS).[11-16] In the only double-blind trial in MUD/MAC, allo-HSCT ATG lowered moderate to severe cGvHD, but progression free survival (PFS) and overall survival (OS) also were lower, indicating that additional analyses are needed to understand the appropriate role for ATG in allo-HSCT.[19]

There is also evidence that addition of ATG may reduce cGvHD in the MRD setting.[14,17]

The standard backbone regimen to prevent GvHD is the combination of a calcineurin inhibitor and methotrexate.[18] Ex-vivo T-cell depletion, monoclonal antibodies, and in vivo T-cell depletion or post-transplant cyclophosphamide are supplementary alternatives [19-21].

The use of ATG has increased tremendously in the different transplant modalities[10,22-24] and is now part of the GvHD prophylaxis in most European transplant centers, both for PBSC- as well as BMSC/MUD transplants.

ATG products differ in their manufacturing process, including the cell line used for immunization as well as the animals used for production. Anti-thymoglobulin is a polyclonal IgG immunoglobulin generated in rabbits by immunizing with either human thymocytes (Thymoglobulin: Sanofi, Paris, France) or with the Jurkat T-lymphoblastoid cell line (ATG-Fresenius, rebranded now as Grafalon, Neovii Biotech, GMBH, Gräfelfing, Germany). ATG binds directly to T-cell surface epitopes and induces complement-dependent cell lysis, thereby suppressing the recipients T-cell function. Due to its long half-life, ATG also interacts with the transplanted donor T-cells and evolving immune cells during engraftment. Its suppressive action on donor T-cells is the rationale for use as GvHD prophylaxis. ATG delays post-transplant lymphocyte recovery and increases the risk for infections, especially viral infections.[25,26]

In reduced intensity conditioning (RIC), the curative potential of the allo-HSCT is largely dependent on the donor T-cell graft-versus-leukemia (GVL) effect. Soiffer et al have shown an increased risk of relapse in RIC allo-HSCT with ATG, although in their study they used both horse ATG and high doses of rabbit ATG (7 mg/kg).[22] Both Baron et al and Devillier et al showed that low doses (< 6 mg/kg) of rabbit ATG (Thymoglobulin) are effective as GvHD prophylaxis without compromising disease control and outcomes in RIC.[23,24]

Several reviews and meta-analysis have confirmed the benefit of ATG in preventing GvHD.[27-29] However, the trials are very heterogeneous regarding conditioning regimens, patient characteristics, donor type, graft source, ATG brand, dosage, and timing of ATG administration, making interpretation and comparison challenging.[30]

In 2014 we added ATG to the GvHD prophylaxis regimen for patients undergoing allo-HSCT with PBSC from MUD in our institution. We have performed a retrospective analysis of the outcome in 415 patients who went through 10/10 MUD allo-HSCT with or without ATG for hematological malignancies at Oslo University Hospital. The aim of this retrospective analysis was to evaluate the results of adding ATG to the GvHD prophylaxis regimen in the MUD with PBSC.

Patients and Methods

Patients

We retrospectively collected data from 415 adult patients transplanted with 10/10 MUD for hematological malignancies (Table 1) between 2005 and 2019 at Oslo University Hospital, Norway.

The patients were categorized in three groups: (1) The PBSC group: 154 patients who received PBSC with no ATG between 2005 and 2014 prior to implementation of ATG as part of the GvHD prophylaxis. (2) The BMSC group: 137 patients receiving BMSC without ATG between 2005 and 2019. (3) The PBSC + ATG group: 124 patients receiving PBSC with ATG prophylaxis between 2014 and 2019. The patient characteristics are given in Table 1.

Conditioning and Stem Cell Source

Myeloablative conditioning (MAC, n = 233) consisted of busulfan 16 mg/kg in combination with cyclophosphamide 120 mg/kg, or fludarabin 150 mg/m², or TBI 13 Gy and cyclophosphamide 120 mg/kg. Reduced intensity conditioning (RIC, n = 182) consisted of fludarabin 150 mg/m² in combination with treosulfan 42 g/m², busulfan 8 mg/kg or cyclophosphamide 600 mg/m², or TBI 2 Gy. Eight patients received other MAC and RIC protocols. Prior to the introduction of ATG, we strived to use BMSC in MAC transplants because of the documented lower occurrence of cGvHD. Since the curative potential of RIC allo-HSCT is largely dependent on the donor T-cell graft-versus-leukemia (GVL) effect[31], we routinely use PBSC in the RIC setting.

Donors

For both donors and recipients, we performed high-resolution HLA matching for the HLA-A, -B, -C, -DRB1, and -DQB1 gene loci on two different time points for each recipient-donor pair. At least one typing was done in our hospital's HLA laboratory accredited by the European Federation of Immunogenetics. The other typing was performed either in our HLA laboratory or in a donor registry contract HLA laboratory. Due to changes in typing methods and technology from 2005 to 2018, combinations of various genotyping techniques (eg, sequence-specific oligonucleotide typing, sequence-specific primer typing, and sequence-based typing) were used to achieve high-resolution typing results.

GVHD Prophylaxis

GvHD prophylaxis consisted of cyclosporine (CsA) in combination with methotrexate (MTX) on day +1, +3, +6 (and +11) (n = 339), mycophenolate mofetil day 0 to +28 (n = 9), or sirolimus day -1 to +2 (n = 60). Seven patients received CsA alone.

We administered a low dose ATG (Thymoglobulin) of 2 mg/kg/day in 2 days (total dose 4 mg/kg) for PBSC 10/10 MUD.

Infection Prophylaxis

All patients received antifungal and herpes virus prophylaxis according to the European Conference on Infections in Leukemia (ECIL) guidelines in force at that time.[32] Patients at risk for EBV- or CMV reactivation were screened for viral replication according to institutional guidelines. Preemptive treatment was initiated according to the definitions given below.

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Table 1 Patient and Transplant Characteristics

	PBSC	PBSC + ATG	BMSC	p-value
n	154	124	137	
Age (median, Q1-Q3)	53 (42-60)	61 (51-65)	42 (29-51)	<0.001
Sex (M/F)	92/62	87/37	84/53	0.17
Diagnosis:				<0.001
AML/ALL	74	44	107	
CML	8	2	11	
Lymphoma/CLL	46	21	5	
MDS/MPN	25	56	14	
Stage:				0.02
CR1/CP1	41	42	75	
CR2-3/CP2-3	41	26	38	
Later	9	6	5	
Unknown	63	50	19	
Donor age:	30 (24-38)	25 (22-33)	29 (22-36)	<0.001
Sex mismatch:				
FtoM	25 (16%)	19 (15%)	22 (16%)	0.98
CD34 dose (median, Q1-Q3)	6.7 (5.2-8.4)	6.9 (5.7-8.7)	–	0.50
TNC (median, Q1-Q3)	–	–	2.7 (2.1-3.4)	
Conditioning:				
MAC/RIC	92/62	11/113	130/7	<0.001
TBI-based	3 (2%)	5 (4%)	17 (12%)	<0.001
GVHD prophylaxis:				<0.001
CsA+MTX	106	100	133	
CsA+MMF	4	4	1	
CsA+Sirolimus	39	20	1	
CsA alone	5	0	2	
CMV sero-status pre SCT:				
Match/Mismatch	90/59	76/46	82/48	0.89

M indicates male; F female; AML acute myeloid leukemia; ALL acute lymphoblastic leukemia; CLL chronic lymphocytic leukemia; MDS myelodysplastic syndrome; MPN myeloproliferative neoplasia; CR complete remission; CP chronic phase; FtoM female to male; SC stem cell; BMSC bone marrow stem cell; PBSC peripheral blood stem cell; TNC total nucleated cells; MAC myeloablative conditioning; RIC reduced intensity conditioning; TBI total body irradiation; CsA cyclosporine; MTX methotrexate; MMF mycophenolate mofetil.

Definitions

Engraftment was defined as absolute neutrophil count of at least 0.5×10^9/L for 3 days and platelet count at least 20×10^9/L for 5 days without transfusions. CMV reactivation was defined as quantitative value of CMV-DNA above 200 IU/ml and preemptive treatment with ganciclovir alternatively foscavir are standard of care. EBV reactivation was defined as quantitative value of EBV-DNA above 1000 IU/ml. According to our institutional guidelines, the threshold for EBV disease and preemptive EBV treatment with Rituximab 375 mg/m^b weekly up to 4 consecutive weeks was EBV DNA levels $\geq$ 20 000 IU/ml.

The procedures were performed in accordance with the Helsinki declaration, and the study was approved by The Regional Committee for Medical and Health Research Ethics South East Norway and the Data Protection Officer, Oslo University Hospital.

Statistics

The primary objective of the study was to analyze OS, GvHD, GRFS, RFS, TRM, infections, CMV, and EBV reactivations in the 3 patient cohorts.

The analysis was performed on September 19, 2019. OS, RFS, and GRFS were calculated using the Kaplan-Meier method and compared with the log-rank test. For GRFS, relapse, death, severe acute GvHD (grades III-IV), and extensive chronic GvHD, whichever came first, were considered the events. Transplant-related mortality (TRM), GvHD, and relapse incidence (RI) were estimated using a nonparametric estimator of cumulative incidence curves taking competing events into consideration. Corrected multivariate risk factor analyses for TRM, RI, and GvHD were performed using the proportional subdistribution hazard regression model developed by Fine and Gray. Multivariate modeling for OS and RFS was carried out using Cox regression models (to estimate hazard ratios (HRs)). Corrections were made for the pretransplant factors that were different between the three groups (patient and donor age, diagnose, disease stage, RIC/MAC and GvHD prophylaxis). As the study covered a long period (2005 through 2019), we also included "year of HSCT" to correct for changes treatment performed during this time frame. All p-values were two-tailed. Categorical parameters were compared using the Chi-square test and continuous variables were compared using the Mann-Whitney test or the Kruskal-Wallis

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test. Analysis was performed using Statistica 13 software (StatSoft, Tulsa, OK) and the EZR statistical software.

Results

There was no significant difference in disease stage at transplantation, gender mismatch, stem cell dose, or CMV serological status pretransplant between the three groups. Patients in the PBSC + ATG group were significantly older, received grafts from younger donors, had the highest proportion of myelodysplastic syndrome, and a significantly higher number received RIC. The patient characteristics are given in Table 1.

Neutrophil Engraftment and Graft Failure

The median time to neutrophil engraftment was 13 days for the patients who received PBSC without ATG, interquartile range (IQR) 9 days to 18 days. Five patients in this group died before engraftment, and 1 experienced primary graft failure.

For patients who received BMSC, the median time to neutrophil engraftment was 21 days, IQR 18 days to 25 days. Three patients in this group died before engraftment, and 2 suffered primary graft failure. The median time to neutrophil engraftment for the PBSC + ATG patients was 15 days, IQR 14 days to 18 days. One patient in this group died before engraftment, and 2 had primary graft failure. Time to neutrophil engraftment was significantly longer in the BMSC group compared to both the PBSC ($p < 0.001$) and the PBSC + ATG group ($p < 0.001$). ATG delayed engraftment in patients receiving PBSC ($p = 0.01$).

Infections

Invasive fungal infections (IFI) were observed in 12% of patients in the PBSC group compared to 19% and 14% in the BMSC and PBSC + ATG groups ($p = 0.26$). CMV reactivation occurred in 44%, 32%, and 42% in the three groups, respectively ($p = 0.08$). The cumulative incidence of EBV reactivation was 71% following PBSC + ATG, which was significantly higher compared with the BMSC and PBSC at 9% and 11%, respectively ($p < 0.001$). In spite of the high EBV reactivation rate in the PBSC + ATG group, only 4 patients received rituximab for EBV reactivation preemptively whereas 2 patients received rituximab for post-transplant lymphoproliferative disease (PTLD). In one case, PTLD was diagnosed postmortem. For a number of patients in the non-ATG group (approximately 50%) and only 9% of the PBSC + ATG group, EBV-PCR was not measured due to institutional standard of care prior to implementation of ATG.

Acute and Chronic GvHD

The cumulative incidence of aGvHD grades II-IV in the PBSC group was 42%, 41% in the BMSC group, and 27% in the PBSC + ATG group ($p = 0.007$) (Figure 1A).

The cumulative incidence of severe acute GvHD grades III-IV in the PBSC, BMSC, and PBSC + ATG group were 14%, 14%, and 7%, respectively (Figure 1B). The PBSC + ATG group had significantly less severe aGvHD compared both to the BMSC group ($p < 0.05$) and PBSC group ($p = 0.045$).

The cumulative incidence of cGvHD was significantly higher in the PBSC group (81%) compared to the BMSC group (32%, $p < 0.001$) and the PBSC + ATG group (26%, $p < 0.001$) (Figure 1C). The incidence of extensive cGvHD was also significantly higher in the PBSC group (44%) compared to the other two groups (15% and 6%, respectively, $p = 0.03$).

Table 2 Causes of Death

CoD	BMSC	PBSC	PBSC + ATG
Relapse	31 (23%)	16 (10%)	16 (13%)
Infection	8 (6%)	19 (12%)	4 (3%)
GVHD	4 (3%)	18 (12%)	6 (5%)
MOF	14 (10%)	11 (7%)	6 (5%)
Other	8 (6%)	12 (8%)	3 (3%)

CoD causes of death; MOF multiple organ failure

Treatment Related Mortality (TRM)

There was no difference between the PBSC + ATG group and the BMSC group regarding 3-year treatment-related mortality (17% vs 25%, $p = 0.18$). On the contrary, the 3-year TRM was significantly lower in the PBSC + ATG group than in the PBSC group, 17% and 33% respectively ($p = 0.024$) (Figure 2A). The TRM > 3 years in the PBSC group is caused by infections ($n = 5$), secondary malignancies ($n = 3$), suicide ($n = 1$), and "other" ($n = 3$). Among these 12 late TRM, 10 suffered from extensive cGvHD, which predispose to the before-mentioned causes of death.

GvHD and Relapse-free Survival (GRFS)

Three years after transplantation, the rate of GRFS was 43% for both the PBSC group and the BMSC group but 64% in the PBSC + ATG group, $p = 0.005$. The addition of ATG to PBSC increased GRFS significantly (Figure 2B).

Relapse

The cumulative incidence of relapse 3 years after transplantation was 11% in the PBSC, 24% in the BMSC, and 19% in the PBSC + ATG group (Figure 2C). The relapse difference between PBSC and BMSC was significant only in univariant analysis ($p < 0.01$), and there was no relapse difference in PBSC + ATG vs BMSC ($p = 0.14$) (Figure 2C).

Survival

Three years after transplantation, the probability of survival was 61% in the PBSC group, 54% in the BMSC group, and 59% in the PBSC + ATG group (Figure 2D). There was no significant difference either in RFS or OS in the PBSC + ATG group compared to the two other groups. Causes of death are presented in Table 2. The main causes of death both in the BMSC and the PBSC + ATG groups are relapses. There is, however, no difference in relapse rates in the PBSC and the PBSC + ATG groups (Table 2).

Multivariate Analysis

In the corrected multivariate analysis, we found that the addition of ATG to PBSC resulted in less chronic GvHD compared to PBSC without ATG (Table 3). GRFS was significantly better in the PBSC + ATG group compared to the BMSC (Table 3). There

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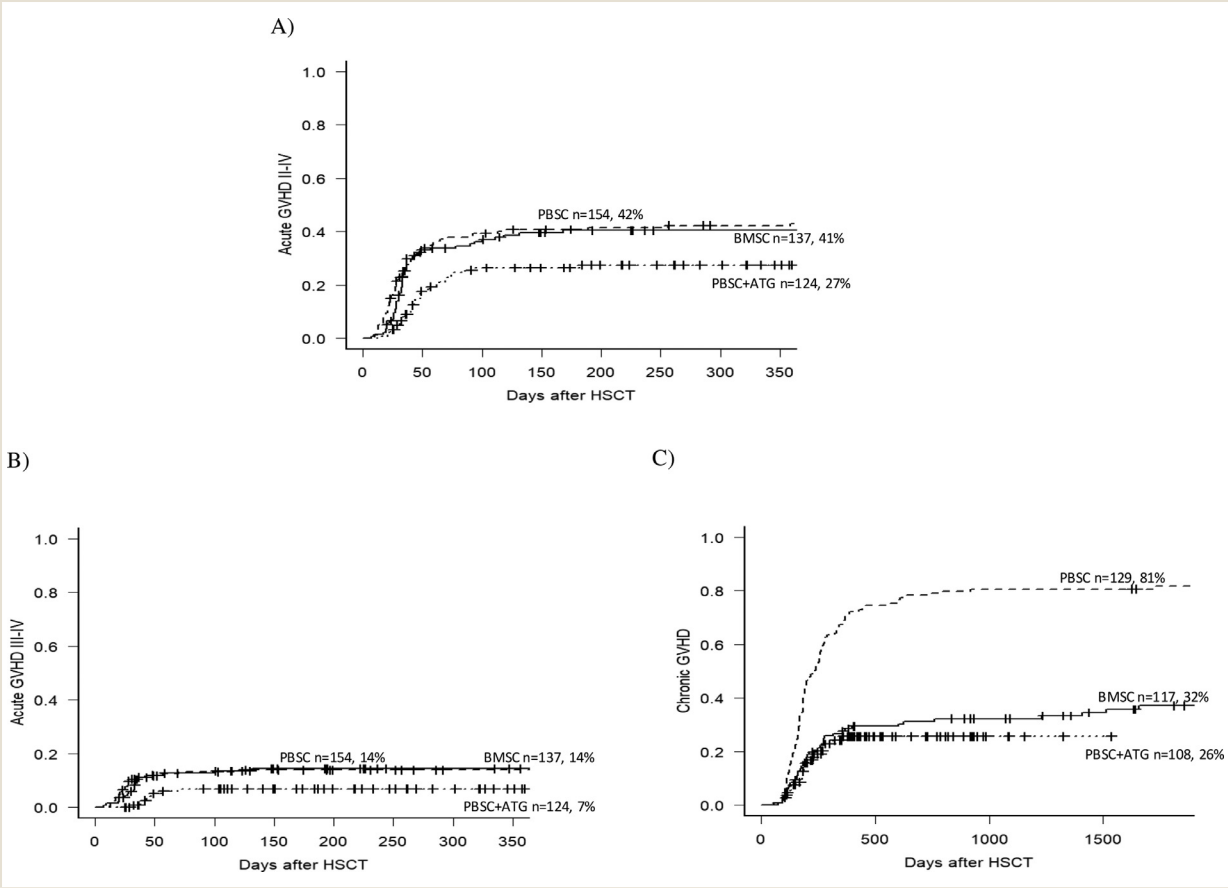
Figure 1 Cumulative incidence of (A) acute GvHD II-IV, (B) acute GvHD III-IV, and (C) chronic GvHD after MUD HSCT in patients receiving PBSC, BMSC, or PBSC + ATG.



was a trend for less acute GvHD II-IV and better GRFS in the PBSC + ATG group compared to the PBSC group. Chronic GvHD tended to be higher in the BMSC group compared to the PBSC + ATG group.

Discussion

GvHD and relapse are the major obstacles encountered after allo-HSCT. The standard regimen for prevention of GvHD is the combination of a calcineurin inhibitor and methotrexate. Due to an unacceptable high incidence of cGvHD in patients transplanted up to 2014 with PBSC from MUD in our institution, we implemented ATG as part of the GvHD prophylaxis regimen in the MUD PBSC setting from February 2014.

The incidence of cGvHD was dramatically reduced from 81% to 26% in patients receiving MUD PBSC after the introduction of ATG in the GvHD prophylaxis regimen without increasing the incidence of relapse or leading to more graft failure. This is in harmony with published data.[12,14,23,25,33,34] In fact, in our material there is a trend toward lower incidence of cGvHD in the PBSC + ATG group compared with the BMSC group. The incidence of acute GvHD was also significantly reduced by adding ATG. This is also in accordance with previous studies[29,35-37]; as a matter of fact, the incidence of severe aGvHD in the PBSC + ATG group is lower than in the BMSC group. We raise the question as to the outcome when ATG is added to the GvHD prophylaxis regimen in patients allografted with BMSC. The available studies show conflicting results. Bacigalupo et al showed significant reduction in both severe aGvHD and cGvHD among MUD BMSC patients who received ATG 7.5-10 mg/kg.[11] On the other hand, Ravinet et al reported no significant impact of ATG in MUD BMSC. In this study, various total doses of ATG were used at the discretion of the attending physician (range <5 to ≥10 mg/kg, only 10 patients received ATG less than 5 mg/kg).[38] In both studies, Thymoglobulin was used, as in our study.

In the multivariate analysis corrected for patient and donor age, diagnosis, disease stage, conditioning regimen, and GvHD prophylaxis, the addition of ATG to MUD allo-HSCT with PBSC did not increase relapse rate. Our registry data did not include sufficient data to define the disease risk index in all patients. We acknowledge that the disease risk index would have allowed better comparability between groups and with published data.

Cumulative incidence (CI) of TRM for all three groups appears to not reach a plateau, most evident for the PBSC group (Figure 2A). This may be explained by the observation that the majority of

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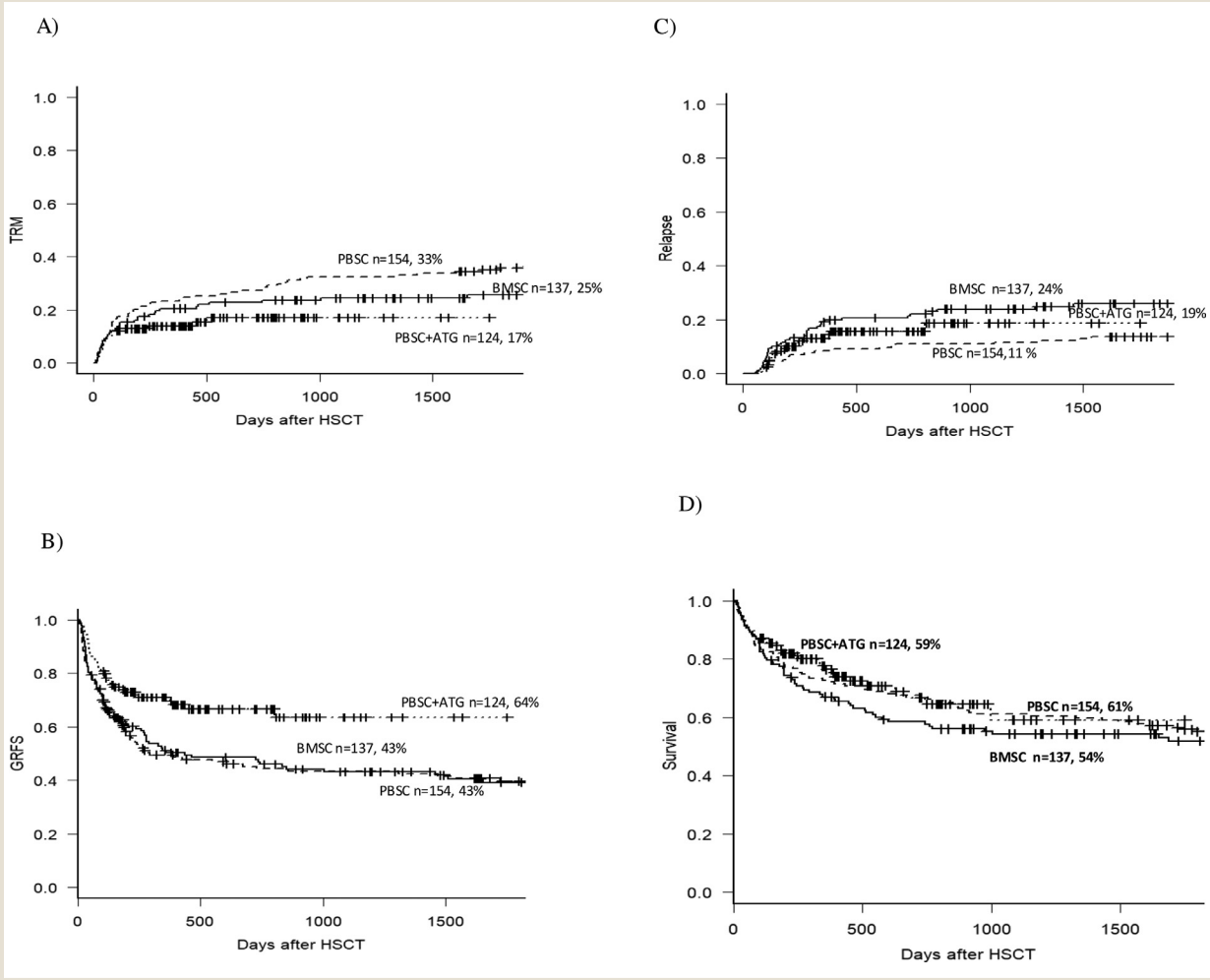
Figure 2 (A) Cumulative incidence of Transplant-related mortality (TRM), (B) probability of GRFS, and (C) cumulative incidence of relapse and (D) probability of survival (OS), after MUD HSCT in patients receiving PBSC, BMSC, or PBSC + ATG.



patients in the PBSC group developed extensive cGvHD, making them more prone to infections and death.

GRFS is an increasingly recognized outcome measure after allo-HSCT.[39] GRFS is defined as lack of severe aGvHD grade III-IV, cGvHD that necessitates systemic treatment, relapse, and death.[39-41] Our findings demonstrate that ATG increases GRFS by reducing severe acute and chronic GvHD which most likely increases quality of life (QoL). Severe aGVHD and cGVHD have a detrimental impact on QoL and patient suffering.[42]

EBV reactivation and EBV-related post-transplant lymphoproliferative disease (PTLD) have been shown to be associated with T-cell depletion using ATG formulations[43,44] and pretransplant EBV sero-status. As expected, the occurrence of EBV reactivation was significantly higher in the PBSC + ATG group compared to the BMSC and PBSC groups. We now perform weekly monitoring with quantitative EBV-PCR in blood until 4 months after allo-HSCT for all patients who receive ATG. After the implementation of weekly monitoring and preemptive treatment with rituximab, we have encountered only one patient with verified PLTD among the PBSC + ATG group.

Supportive care before, during, and after HSCT has improved in recent years[45] and could have had an impact on the study, but in the multivariate analysis we included "year of HSCT" to correct for treatment changes performed during this time frame. The retrospective nature of our data is a limitation. Our study population is heterogeneous in terms of disease type, disease stage, and conditioning regimen. Comparing our study with data from available clinical trials using ATG as part of the GvHD prophylaxis is challenging due to differences among studies in terms of ATG dosing, timing, length of administration, type of preparation, and transplant characteristics including disease group, donor type, graft source, and conditioning regimen.[23,27,28] Nonetheless, our data support previous reports that a dramatic reduction in cGvHD may be accomplished by ATG.

Our study shows that the addition of low-dose (4 mg/kg) ATG in allo-HSCT decreases the incidence of GvHD and notably increases

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Table 3 Multivariate Analysis for Various Outcome Variables Corrected for Differences Between the Groups. Corrected for (Patient and Donor Age, Diagnosis, Disease Stage, RIC/MAC and GvHD Prophylaxis), and Year of HSCT

	HR, 95% CI, p-value
Mortality	
BMSC	0.96, 0.37-2.48, 0.93
PBSC	0.90, 0.38-2.13, 0.80
PBSC + ATG	Ref
TRM	
BMSC	0.96, 0.37-2.48, 0.92
PBSC	0.90, 0.38-2.13, 0.80
PBSC + ATG	Ref
Relapse	
BMSC	2.11, 0.81-5.49, 0.13
PBSC	1.13, 0.44-2.93, 0.80
PBSC + ATG	Ref
Acute GVHD II-IV	
BMSC	1.65, 0.81-3.35, 0.17
PBSC	1.81, 0.92-3.57, 0.08
PBSC + ATG	Ref
Acute GVHD III-IV	
BMSC	1.81, 0.47-6.95, 0.39
PBSC	1.84, 0.51-6.66, 0.35
PBSC + ATG	Ref
Chronic GVHD	
BMSC	1.87, 0.90-3.87, 0.09
PBSC	5.49, 2.82-10.7, <0.001
PBSC + ATG	Ref
GRFS	
BMSC	2.00, 1.05-3.79, 0.03
PBSC	1.67, 0.92-3.05, 0.09
PBSC + ATG	Ref

HR hazard ratio; CI confidence interval.

GRFS, thus illustrating the benefit of ATG in addition to standard GvHD prophylaxis in allo-HSCT.

Clinical Practice Points

- Allogeneic stem cell transplantation (allo-HSCT) is associated with severe morbidity and mortality. Graft-versus-host disease (GvHD) and relapse are major obstacles for cure and maintaining good quality of life after transplantation.
- Anti-thymocyte globulin (ATG) is commonly used to prevent GvHD after allo-HSCT. In 2014 we added ATG to the GvHD prophylaxis regimen for patients undergoing allo-HSCT with peripheral stem cells (PBSC) from matched unrelated donor (MUD) at our institution. We administered a low dose ATG (Thymoglobulin) of 2 mg/kg/day in 2 days (total dose 4 mg/kg) for PBSC 10/10 MUD.
- We compare the outcome of 415 adult patients with haematological malignancies undergoing allo-HSCT with MUD and PBSC with or without ATG.
- There was no significant difference in disease stage at transplantation, gender mismatch, stem cell dose, or CMV serological status pretransplant between the patients who received and those who did not receive ATG. Patients who received ATG were significantly older, received grafts from younger donors, and had the highest proportion of myelodysplastic syndrome, and a significantly higher number received reduced intensity conditioning (RIC) regimen.
- The incidence of chronic GvHD was dramatically reduced in patients receiving MUD PBSC with low-dose ATG in the GvHD prophylaxis regimen without increasing the incidence of relapse or leading to more graft failure.
- Our data support previous reports that the addition of ATG to the standard GvHD prophylaxis decreases the incidence of both acute and chronic GvHD and increases the GvHD-free, relapse-free survival significantly.

Declaration of Competing Interests

None.

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