Outcomes of Allogeneic Hematopoietic Cell Transplantation in T-cell Prolymphocytic Leukemia: A Contemporary Analysis from the Center for International Blood and Marrow Transplant Research

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Highlights

- Allogeneic HCT is effective in yielding durable remissions in patients with T-PLL
- Myeloablative conditioning, age greater than 60 and KPS <90 were all associated with reduced OS
- Reduced intensity conditioning and avoidance of in vivo T cell depletion correlated with better DFS and less TRM
- TBI was not found to any significant effect on OS, DFS or TRM

Outcomes of Allogeneic Hematopoietic Cell Transplantation in T-cell Prolymphocytic Leukemia: A Contemporary Analysis from the Center for International Blood and Marrow Transplant Research

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ABSTRACT

Background: T-cell prolymphocytic leukemia (T-PLL) is a rare, aggressive malignancy with limited treatment options and poor long-term survival. Previous studies of allogeneic hematopoietic cell transplantation (alloHCT) for T-PLL are limited by small numbers, and descriptions of patient and transplant characteristics and outcomes after alloHCT are sparse.

Objective: To describe outcomes of alloHCT in T-PLL and identify predictors of post-transplant relapse and survival.

Study Design: We conducted an analysis of data using the Center for International Blood and Marrow Transplant Research (CIBMTR) database on 266 patients with T-PLL who underwent alloHCT during 2008-2018.

Results: The 4-year rates of overall survival (OS), disease-free survival (DFS), relapse, and treatment-related mortality (TRM) were 30.0% (95% CI, 23.8-36.5%), 25.7% (95% CI, 20-32%), 41.9% (95% CI, 35.5-48.4%), and 32.4% (95% CI, 26.4-38.6%), respectively. In multivariable analyses, three variables were associated with inferior OS: myeloablative conditioning (MAC) (hazard ratio [HR] 2.18, p<0.0001); age older than 60 years (HR 1.61, p=0.0053); and suboptimal performance status defined by Karnofsky Performance Status (KPS) <90 (HR 1.53, p=0.0073). MAC also was associated with increased TRM (HR 3.31, p<0.0001), increased cumulative incidence of grade 2-4 acute graft-versus-host disease (GVHD) (HR 2.94, p=0.0011) and an inferior disease-free survival (HR 1.86, p=0.0004). Conditioning intensity was not associated with relapse; however stable disease/progression correlated with increased risk of relapse (HR 2.13, p=0.0072). Both in vivo T cell depletion (TCD) as part of conditioning and KPS <90 were

associated with worse TRM and inferior DFS. Total Body Irradiation was not found to have any significant effect on OS, DFS or TRM.

Conclusion: Our data showed that reduced-intensity conditioning *without* in vivo T-cell depletion (that is, without ATG or alemtuzumab) prior to alloHCT was associated with long-term disease-free survival in patients with T-PLL who were 60 or younger or who had KPS >90 or had chemo-sensitive disease.

INTRODUCTION

T-cell prolymphocytic leukemia (T-PLL) is a rare aggressive malignancy, representing approximately 2% of mature lymphocytic leukemias in adults[1,2]. Patients tend to be older, with a median age of 65 years at diagnosis. Typically, T-PLL presents with signs such as marked leukocytosis, hepatosplenomegaly, lymphadenopathy, and cutaneous lesions. Treatment options are generally limited, and outcomes are poor, with a reported median survival of 19 months[3]. Alemtuzumab, an anti-CD52 humanized monoclonal antibody, is often used in the front line in T-PLL. While complete remission (CR) rates with alemtuzumab are high (60-80%), most responses are brief, and the relapse rate remains high[4,5]. Survival of patients with relapsed T-PLL is dismal, as responses to second-line therapies are limited and generally short-lived [2,6].

Allogeneic hematopoietic cell transplantation (alloHCT) is a potential curative therapy for T-PLL and has been reported to yield durable remissions, notably in patients who are in complete remission prior to transplantation[7–12]. AlloHCT aided small subsets of patients with T-PLL, according to studies by the Center for International Blood and Marrow Transplant Research (CIBMTR) [10], European Society for Blood and Marrow Transplantation (EBMT) [7,13], the Francophone Society of Bone Marrow Transplantation and Cellular Therapy (SFGM-TC) [9], and the Japanese Society for Transplantation and Cellular Therapy (JSTCT) [14]. The benefits of alloHCT are limited by high rates of non-relapse mortality (NRM), ranging from 28-40%. In addition, there exists high risk of post-transplant relapse, many occurring within 2 years of alloHCT [10,15]. Because these studies were relatively small, researchers were unable to identify factors associated with sustained remission and improved overall survival (OS). Hence, using CIBMTR Research Database, the aim of this study is to evaluate the effectiveness of alloHCT in T-PLL and to identify predictors of post-transplant relapse and survival.

METHODS

Data sources

The CIBMTR is a nonprofit research collaboration of the National Marrow Donor Program (NMDP)/Be The Match and the Medical College of Wisconsin (MCW). More than 300 medical centers worldwide submit clinical data to the CIBMTR about HCT and other cellular therapies. Participating centers are required to report all transplantations consecutively. The CIBMTR ensures data quality through computerized checks for discrepancies, physicians' review of submitted data, and on-site audits of participating centers. The CIBMTR complies with federal regulations that protect human research participants. The Institutional Review Boards of MCW and NMDP approved this study.

Patient selection

Adults (aged 18 and older) who underwent first alloHCT for T-PLL during 2008-2018 were included in this analysis. Graft sources included peripheral blood stem cells (PBSC) and bone marrow. Eligible donors included human leukocyte antigen (HLA)-identical sibling donors or unrelated donors (URD) matched at the allele-level at HLA-A, -B, -C, and -DRB1, and alternative donor transplantation (haploidentical, mismatched unrelated donor). Cord blood and ex vivo T-cell depleted grafts were excluded, as were patients who received syngeneic transplants. AlloHCT recipients who received in vivo T-cell depletion (TCD) with anti-thymocyte globulin (ATG) or alemtuzumab were included.

Definitions and study endpoints

Disease response was defined based on National Cancer Institute-Sponsored Working Group guidelines for chronic lymphocytic leukemia. [16] The intensity of conditioning regimens was

defined using published consensus criteria.[17] The primary endpoint was OS. Death from any cause was considered an event, and surviving patients were censored at the time of last follow-up. Secondary endpoints included cumulative incidence of acute graft-versus-host disease (aGVHD), chronic graft-versus-host disease (cGVHD), treatment related mortality (TRM), progression/relapse, and disease-free survival (DFS). TRM was defined as death without preceding disease relapse/progression; relapse and progression were considered competing events. Progressive disease or recurrences of T-PLL were defined as progression after alloHCT or recurrence following CR; TRM was considered competing event. DFS was defined as survival following alloHCT without relapse or progression. Patients who survived without evidence of disease relapse or progression were censored at last follow-up. The causes of death were reported in accordance to the methodology described previously. [18]

Statistical analysis

Cumulative incidence of GVHD, relapse/progression, and TRM were calculated using the cumulative incidence estimator to accommodate for competing risks. Probabilities of OS and DFS were calculated using the Kaplan-Meier method for a univariable analysis. Multivariable regression analysis was performed using logistic regression for aGVHD, the proportional cause-specific hazards model for chronic GVHD, relapse, and TRM, and the Cox proportional hazards model for DFS and OS. The assumption of proportional hazards for each factor was tested for the proportional hazards and cause-specific hazards models, and a forward stepwise selection was used to select significant risk factors. In the final model, we retained factors with statistical significance of < 5%. We examined the interaction between the main effect and the other significant variables and found no center effect based on the score test of homogeneity[19]. The variables that were considered in the multivariable models included: recipient age, Karnofsky Performance Status (KPS), Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI), disease status at transplant, intensity of conditioning regimen, use of total body irradiation (TBI)

in conditioning, time from diagnosis to transplant, recipients' cytomegalovirus (CMV) serostatus, GVHD prophylaxis, donor type, graft source, use of ATG/alemtuzumab, and year of transplant. Adjusted probabilities [20,21] were calculated based on the final regression models for OS, DFS, relapse, and TRM.

RESULTS

Baseline characteristics

The study included 266 adults who received alloHCT for T-PLL. The median follow-up was 49 months (range 3.32-116.84). The baseline patient-, disease-, and transplantation-related characteristics are described in (Tables & Figures

Table 1, Supplementary Table 1). Participants' median age at the time of alloHCT was 59.1 years (range 25.0-76.3); 53% were male; and 58% had a KPS ≥90. The majority of alloHCT recipients were white (87%). Disease status at the time of HCT was CR, partial remission (PR) and chemo-refractory disease in 56%, 30% and 11%, respectively. Most patients received PBSC grafts (89%) and calcineurin-based GVHD prophylaxis (80%). Matched related donors (30%) and 8/8 matched unrelated donors (43%) were the most common types of donors. Reduced intensity and non-myeloablative conditioning (RIC/NMA) and myeloablative conditioning (MAC) were used in 70% and 30% of cases, respectively. Commonly utilized MAC regimens included cyclophosphamide-TBI (n=33) and busulfan-fludarabine (n=20) while commonly utilized RIC/NMA regimens included fludarabine-melphalan (n=55), fludarabine-busulfan (n=33), and fludarabine-TBI (n=32). A total of 49 patients (18%) received in vivo TCD with anti-thymocyte globulin (n=47) or alemtuzumab (n=2).

Overall survival and disease-free survival

The 4-year OS and DFS were 30.0% (95% CI, 23.8-36.5%) and 25.7% (95% CI, 20-32%), respectively (Supplementary Table 2). The 4-year OS based on donor for HLA matched sibling donor (MSD), 8/8 matched unrelated donor (MUD), haploidentical donor (haplo) and 7/8 mismatch unrelated donor (MMUD) was 40.1% (95% CI, 28.9-51.8%), 24.6% (95% CI, 16.2-34.2%), 33.9% (95% CI, 15-56%) and 26.8% (95% CI, 9.6-48.9%) respectively. The 4-year DFS based on donor for MSD, MUD, haplo and MMUD was 34.9% (95% CI, 24.4-46.3%), 19.6% (95% CI, 12-28.5%), 23.4% (95% CI, 8.2-43.3%), and 28.9% (95% CI, 10.4-52.1%) respectively (Supplementary Table 3).

On multivariate analyses, RIC/NMA conditioning regimen was significantly associated with longer DFS (hazard ratio [HR] 1.86; 95%CI, 1.32-2.61; p=0.0004) and OS (HR 2.18; 95% CI, 1.53-3.09; p<0.0001) when compared with MAC. (Figures 1, 2). Performance status (KPS <90%) was associated with both inferior DFS (HR 1.51; 95% CI, 1.12-2.05; p=0.0075) and OS (HR 1.53; 95% CI, 1.12-2.08; p=0.0073), as was recipient age >60 years, which was associated with inferior DFS (HR 1.41; 95% CI, 1.03-1.93; p=0.0337) and OS (HR 1.61; 95% CI, 1.15-2.24; p=0.0053). Use of in vivo TCD resulted in inferior DFS (HR 1.50; 95% CI, 1.05-2.15; p=0.0276), but had no significant effect on OS (Table 2). Time from diagnosis to transplant did not have any significant effect on DFS or OS.

TBI effect on OS and DFS was analyzed as part of conditioning intensity (Supplementary Table 7). When comparing MAC without TBI (MAC-Chemo) to MAC with TBI, TBI did not have any significant effect on OS (HR 0.83 (95% CI, 0.49-1.41; p=0.0073) or DFS (HR 1.01 (95% CI, 0.60-1.71; p=0.9628). Performing the same analysis with RIC comparing RIC with TBI to RIC without TBI (RIC-Chemo), TBI did not have any significant effect on OS (HR 1.22 (95% CI, 0.81-1.82; p=0.3437) or DFS (HR 1.17 (95% CI, 0.79-1.72; p=0.4390).

Treatment-related mortality

The 1-year and 4-year cumulative incidence of TRM were 21.5% (95% CI, 16.7-26.7), and 32.4% (95% CI, 26.4-38.6), respectively. The 4-year TRM based on donor for MSD, MUD, haplo and MMUD was 20.4% (95% CI, 11.8-30.7%), 36.6% (95% CI, 27.3-46.4%), 31.6% (95% CI, 15.5-50.3%), and 42.1% (95% CI, 23.2-62.4%) respectively (Supplementary Table 3).

On multivariate analysis, MAC resulted in increased cumulative incidence of TRM (HR 3.31; 95% CI 2.01-5.45; p<0.0001) when compared to RIC (Figure 3). Additionally, performance status (KPS < 90%) (HR 1.98; 95% CI, 1.25-3.14; p=0.0036) and use of in vivo TCD (HR 1.79; 95% CI, 1.07-2.98; p=0.0263) resulted in increased incidence of TRM (Table 2).

The effect of TBI on TRM was analyzed as part of conditioning intensity (Supplementary Table 7). When comparing MAC without TBI (MAC-Chemo) to MAC with TBI, TBI did not have any significant effect on TRM (HR 0.48 (95% CI, 0.22-1.05; p=0.0662). Comparing RIC with TBI to RIC without TBI (RIC-Chemo), TBI did not have any significant effect on TRM (HR 1.39 (95% CI, 0.74-2.64; p=0.3068).

Acute and chronic GVHD

The cumulative incidence of grades II-IV aGVHD at day 180 post alloHCT was 22.5% (95% CI, 16.8-28.9) while cumulative incidence of grades III-IV aGVHD at day 180 post alloHCT was 5.3% (95% CI, 2.8-8.6). (Supplementary Table 4). The cumulative incidence of grades II-IV aGVHD at day 180 based on donor for MSD, MUD, haplo and MMUD was 14.3% (95% CI, 6.4-24.7%), 25.7% (95% CI, 16.6-36%), 36.4% (95% CI, 17.5-57.8%) and 20% (95% CI, 5.6-40.4%) respectively (Supplementary Table 3). On multivariate analysis, MAC was predictive for increased risk of grades II-IV aGVHD (OR 2.94; 95% CI, 1.54-5.62; p=0.0011), while post-transplant cyclophosphamide (PTCy) predicted for reduced grades II-IV aGVHD (OR 0.26; 95% CI, 0.10-0.71; p=0.0082) (Table 2). In vivo TCD did not have a significant effect on aGVHD.

When comparing MAC with TBI to MAC without TBI as well as RIC with TBI to RIC without TBI, TBI did not have any significant effect on aGVHD (Supplemental Table 7).

The cumulative incidences of chronic GVHD (cGVHD) at 1 year and 2 years post-transplant were 38.8% (95% CI, 32.9-44.9) and 45.5% (95% CI, 39.2-51.8), respectively. Among those with cGVHD at 1 year, 71% had extensive cGVHD and 29% with limited cGVHD, while at 2 years, cGVHD was extensive in 72% and limited in 28% of recipients with cGVHD. The cumulative incidence of cGVHD at 2 years post-transplant based on donor for MSD, MUD, haplo and MMUD was 47.5% (95% CI, 35.8-59.3%), 47.6% (95% CI, 37.9-57.4%), 33.9% (95% CI, 16.6-53.9%) and 49.1% (95% CI, 31.5-66.8%) respectively (Supplementary Table 3).

Age, conditioning intensity and in vivo TCD had no significant effect on chronic GVHD. PTCy-based GVHD prophylaxis was associated with less chronic GVHD when compared to calcineurin based GVHD prophylaxis (Table 2). We also observed alloHCT performed before 2011 was associated with increased incidence of cGVHD than those performed after 2011. (Supplementary Table 6).

Relapse

The cumulative incidence of relapse/progression at 1 year and 4 years was 27.6% (95% CI, 22.3-33.2%) and 41.9% (95% CI, 35.5-48.4%). Based on the multivariate analyses (Table 2), age and conditioning intensity were not associated with rate of relapse. Stable or progressive disease at time of alloHCT was associated with increased incidence of relapse (HR 2.13; 95%CI 1.23-3.71; p=0.0072) when compared to CR. However, the depth of response at HCT (PR vs CR), in vivo TCD and TBI-based conditioning were not associated with the incidence of relapse.

Causes of death

The most common cause of death was relapse of the primary disease (52%), followed by infection (15%) and GVHD (13%). (Supplementary Table 5).

DISCUSSION

Using the CIBMTR database, we showed that long-term disease-free survival can be achieved in patients with T-PLL. We observed that RIC/NMA conditioning regimens are associated with reduced TRM and improved DFS and OS. Our analysis also found that the use of in vivo TCD strategies (ATG and/or alemtuzumab) resulted in an increased TRM and inferior DFS. Disease relapse continues to pose a challenge, with a 4-year relapse incidence of 41%. Patients with chemo-sensitive disease prior to transplant had a reduced incidence of relapse.

Data from this analysis are consistent with previous registry studies from the SFGM and the JSHCT (Table 3). The SFGM study retrospectively reported 3-year OS and DFS estimates at 36% and 26% in 27 patients with median follow-up of 33 months, while the JSHCT reported 3-year OS and PFS of 39.8% and 33.5% respectively in 20 patients with median follow-up of 51 months [9,14]. The EBMT study, a prospective observational study amongst recipients age 65 and younger with median follow-up of 50 months, reported 4-year OS and PFS of 42% and 30%, respectively[13]. However, in the EBMT series, the oldest patient was 59 years, whereas in this current CIBMTR study, 42% of patients were older than 60 years, which more closely reflects the median age of T-PLL diagnosis in the US.

The intensity of conditioning regimens across these three studies was comparable. RIC/NMA regimens were utilized in 70% patients in the current study, compared to 60% in SFGM, 50% in JSHCT and 65% in EBMT. RIC/NMA conditioning in younger patients was associated with reduced TRM and improved DFS and OS compared to younger patients receiving MAC conditioning. The survival benefit offered with RIC/NMA conditioning may be explained by graft-

versus-leukemia (GVL) effect. A study by Sellner and colleagues evaluated a longitudinal quantitative minimal residual disease using clone-specific T-cell receptor (TCR)-based real-time quantitative polymerase chain reaction (PCR): They demonstrated minimal residual disease responses post-alloHCT were associated with a shift from a clonal, T-PLL-driven profile to a polyclonal signature, effectively validating GVL effect in T-PLL[22]. In our analysis, a surrogate marker of GVL, which is the impact of in vivo TCD on relapse, was not evident. The use of in vivo TCD was associated with inferior DFS due to increased risk of TRM.

High incidences of TRM have been reported in prior studies of alloHCT for T-PLL. The 4-year TRM of 32.4% is similar to reports by the EBMT (4-year NRM 32%) and SFGM (3-year TRM 31%). Predictably, we observed reduced TRM and reduced incidence of aGVHD with the use of RIC/NMA conditioning regimens. We observed that in vivo TCD was linked to increased TRM. In the current study, 18% of patients received in vivo TCD, mostly with ATG, compared to the EBMT study, in which 51% received TCD. AlloHCT with TCD has been associated with delayed immune reconstitution and increased risk of infection[23–25]. Infection was reported as the second most common cause of death. Ongoing T-cell depletion caused by pre-transplant alemtuzumab therapy might influence TRM. Additionally, one could hypothesize that ongoing T cell depletion from pre-transplant alemtuzumab therapy, in addition to the use of RIC/NMA conditioning regimens and PTCy GVHD prophylaxis, could explain the low incidence of aGVHD and severe aGVHD observed. However, we could not answer this question conclusively in this analysis, because data for time from last alemtuzumab dose to transplant nor T cell reconstitution data were available.

Outcomes were by donor type were also reviewed (supplementary table 3). Although small in numbers, it is worth mentioning that we observed both haploidentical and mismatch unrelated transplants as feasible and effective in patients with T-PLL. Haploidentical transplants in particular we found to have less cGVHD and TRM w/ comparable 4 year relapse, DFS and OS when comparing to MUD and MMUD transplants. It is important to note that donor type was not

found to be significant on multivariate analyses and these findings are on univariate analysis only, so it is difficult to draw significant conclusions regarding choice of ideal donor. However, with increased utilization of haploidentical transplantation [26] and feasibility and effectiveness of PTCy in allo-HCT with MMUD [27], allo-HCT should be considered for patients with T-PLL even in the absence of a HLA matched donor.

Controlling disease and preventing relapse remain difficult in patients after alloHCT. Achieving complete remission prior to alloHCT was associated with less relapse, but only when compared to stable or progressive disease and not when compared to partial remission, suggesting that chemoresponsive disease prior to alloHCT is more significant than the depth of remission. Additionally, in this analysis, we investigated the role of total body irradiation. A prospective study by the EBMT identified TBI dose of 6 Gy or more as predictive of a reduced relapse risk in a univariable analysis[13]. We looked specifically whether adding TBI to both MAC and RIC would affect OS, DFS or TRM. When comparing MAC with TBI to MAC without TBI as well as RIC with TBI to RIC without TBI, we did not appreciate any significant effect on OS, DFS and TRM. Our analysis showed differences in survival outcomes with respect to pre-transplant conditioning were more attributed to comparing conditioning intensity (MAC vs RIC) rather than use of TBI

We found that relapse rates increased over time. Incidence of relapse increased, from 27.6% at 1 year, to 41.9% at 4 years. Unfortunately, there is no standard minimal residual disease test for T-PLL, and such a test potentially could help forecast early relapse. Late relapse may reflect waning GVL effect over time. Post-transplant immune modulation strategies may help prevent late relapse. Venetoclax [28], histone deacetylase (HDAC) inhibitors [29], *p53* reactivators [30,31], and Janus kinase/signal transducers and activators of transcription (JAK/STAT) inhibitors [32–35] have previously demonstrated some pre-clinical and/or clinical activity in T-PLL, and warrant further investigation for post-transplant maintenance.

This study has limitations inherent to a retrospective registry study. As this data was obtained from a transplant registry, we could not compare outcomes with patients who did not undergo alloHCT. Another limitation was the lack of pertinent pre-transplant information, such as cytogenetics, mutation data and details of therapies prior to alloHCT. Details of pre-HCT induction therapy were not available for most of our study participants, so we did not include this information in our analyses. The lack of consensus disease response criteria is a notable limitation. The CIBMTR registry defined T-PLL response criteria based on international consensus response criteria for chronic lymphocytic leukemia[16]. Only recently in 2019 were consensus T-PLL response guidelines were published[12]. Given that patients included in this analysis date back to 2008, utilizing the updated criteria was not feasible. Finally, detailed data were not available regarding the timing and severity of infections, as well as immune reconstitution.

CONCLUSION

In summary, alloHCT results in durable remissions and disease control in some patients with T-PLL. Relapse continues to remain a barrier to long-term survival. Reduced-intensity conditioning and avoidance of in vivo TCD are associated with improved outcomes. Molecular monitoring of patients for recurrence after transplant could be undertaken to identify early relapses for treatment and potentially donor lymphocyte therapy. Other novel approaches combined with alloHCT warrant investigation to further improve outcomes of alloHCT in T-PLL.

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DATA USE STATEMENT

CIBMTR supports accessibility of research in accord with the National Institutes of Health (NIH) Data Sharing Policy and the National Cancer Institute (NCI) Cancer Moonshot Public Access and Data Sharing Policy. The CIBMTR only releases de-identified datasets that comply with all relevant global regulations regarding privacy and confidentiality.

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TABLES & FIGURES

Table 1 Baseline characteristics of patients who had first alloHCT for T-PLL, 2000-2018

Characteristic	No. (%)
No. patients	266
No. centers	87
Sex	
Male	140 (53)
Female	126 (47)
Age, y	
Median age (range), y	59.1 (25.01-76.26)
18-29	1 (0)
30-39	7 (3)
40-49	38 (14)
50-59	98 (37)
60-69	101 (38)
≥ 70	21 (8)
Karnofsky Performance Status score	
90-100	153 (58)
< 90	101 (38)
Not reported	12 (4)
HCT-CI	
0	73 (27)
1-2	84 (31)
3-4	77 (25)
≥ 5	28 (11)
Not reported	4 (6)
Remission status at HCT	
Complete remission	149 (56)
Partial response	80 (30)
No response/ stable/ progression	31(11)
Not reported	6 (2)
Graft source	
Bone marrow	30 (11)
Peripheral blood	236 (89)
Time from diagnosis to HCT	
Median (range)	7.85 (2.07-81.74)
< 6 months	82 (31)
6-11 months	103 (39)
≥ 12 months	81 (30)
Donor type	
HLA-identical sibling	80 (30)
Haploidentical	30 (11)
URD 8/8	115 (43)
URD 7/8	33 (12)
Other related	8 (3)

Characteristic	No. (%)
Conditioning regimen intensity [a]	
Myeloablative with TBI	**44 (17)**
Myeloablative without TBI	**34 (13)**
Reduced-intensity with TBI	**75 (28)**
Reduced-intensity without TBI	**113 (42)**
GVHD prophylaxis	
CNI + MMF ± others (except PTCy)	68 (26)
CNI + MTX ± others (except MMF, PTCy)	123 (46)
CNI + others (except MMF, MTX, PTCy)	20 (8)
Other prophylaxis [b]	55 (21)
In vivo T cell depletion (ATG/alemtuzumab) [c]	
Yes	**49 (18)**
No	**217 (82)**
Median follow-up (range), months	49 (3.32-116.84)

Abbreviations: alloHCT, allogeneic hematopoietic cell transplantation; ATG, anti-thymocyte globulin; CNI, calcineurin inhibitor; GVHD, graft-versus-host disease; HCT, hematopoietic cell transplantation; HCT-CI, Hematopoietic Cell Transplantation Comorbidity Index; HLA, human leukocyte antigen; MMF, mycophenolate mofetil; MTX, methotrexate; PTCy, post-transplant cyclophosphamide; TBI, total body irradiation; T-PLL, T-cell prolymphocytic leukemia; URD, unrelated donor.

[a] Refer to Supplementary Table 1 for full conditioning list

[b] Other: CNI alone (12), CNI + PTCy + MMF (32), PTCy-MMF (1), sirolimus + PTCy (2), MTX alone (3), sirolimus-MMF-PTCy (1), monoclonal antibody + MMF (3), PTCy alone (1)

[c] ATG n=47, alemtuzumab n=2

Table 2 Multivariable regression analysis

Factors	N	OR/HR (95% CI)	P-value	Overall P-value
Overall survival				
Conditioning regimen				
RIC/NMA	188	1.00 (Reference)		< 0.0001
MAC	78	2.18 (1.53- 3.09)	< 0.0001	
Age				
≤ 60	142	1.00 (Reference)		0.0053
> 60	122	1.61 (1.15- 2.24)	0.0053	
KPS				
≥ 90%	153	1.00 (Reference)		0.0272
< 90%	101	1.53 (1.12- 2.08)	0.0073	
Not reported	12	1.23 (0.60- 2.54)	0.573	
Disease-free survival				
Conditioning regimen				
RIC/NMA	77	1.00 (Reference)		0.0004
MAC	187	1.86 (1.32-2.61)	0.0004	
Age				
≤ 60	142	1.00 (Reference)		0.0337
> 60	122	1.41 (1.03- 1.93)	0.0337	
KPS				
≥ 90%	152	1.00 (Reference)		0.0075
< 90%	101	1.51 (1.12- 2.05)	0.0075	
Not reported	11	1.13 (0.53-2.44)	0.7507	
In vivo T-cell depletion				
No	215	1.00 (Reference)		0.0253
Yes	49	1.50 (1.05-2.13)	0.0253	
Treatment-related mortality				
Conditioning regimen				
RIC/NMA	187	1.00 (Reference)		< 0.0001
MAC	77	3.31 (2.01-5.45)	< 0.0001	
Age				
≤ 60	142	1.0 (Reference)		0.0108
> 60	122	1.87 (1.16- 3.04)	0.0108	
KPS				
≥ 90%	152	1.00 (Reference)		0.0142
< 90%	101	1.98 (1.25- 3.14)	0.0036	
Not reported	11	1.18 (0.36-3.83)	0.7811	
In vivo T-cell depletion				
No	215	1.00 (Reference)		0.0263
Yes	49	1.79 (1.07-2.98)	0.0263	
Acute GVHD				
Conditioning regimen				
RIC/NMA	172	1.00 (Reference)		0.0011
MAC	75	2.94 (1.54- 5.62)	0.0011	
GVHD prophylaxis				
CNI + MMF	65	1.00 (Reference)		0.0093
CNI + MTX	114	0.56 (0.28-1.14)	0.1077	
CNI + others (except MMF, MTX, PTCy)	18	0.36 (0.11-1.17)	0.0902	
PTCy ± others	33	0.26 (0.10-0.71)	0.0082	
Other prophylaxis	17	2.17 (0.71- 6.60)	0.174	

Factors	N	OR/HR (95% CI)	P-value	Overall P-value
Chronic GVHD				
GVHD prophylaxis				
CNI + MMF ± others (except PTCy)	67	1.00 (Reference)		0.0015
CNI + MTX ± others (except MMF, PTCy)	121	1.06 (0.68- 1.65)	0.8045	
CNI + others (except MMF, MTX, PTCy)	20	2.35 (1.31- 4.20)	0.0041	
PTCy ± others	37	0.44 (0.19- 1.05)	0.0645	
Other prophylaxis	17	0.65 (0.25- 1.66)	0.3677	
Year of transplant				
2008-2011	50	1.00 (Reference)		0.0216
2012-2015	110	0.62 (0.39-0.97)	0.0382	
2016-2018	102	0.48 (0.28-0.82)	0.0069	
Relapse				
Disease status at HCT				
CR	149	1.00 (Reference)		0.0486
PR	80	1.40 (0.91-2.17)	0.1257	
No response/ SD/ PD	31	2.13 (1.23-3.71)	0.0072	
Not reported	6	0.94 (0.23- 3.87)	0.932	

Abbreviations: CNI, calcineurin inhibitor; CR, complete remission; GVHD, graft-versus-host disease; HCT, hematopoietic cell transplantation; HR, hazard ratio; KPS, Karnofsky Performance Status; MAC, myeloablative conditioning; MMF, mycophenolate mofetil; MTX, methotrexate; OR, odds ratio; PD, progressive disease; PR, partial remission; PTCy, post-transplant cyclophosphamide; RIC/NMA, reduced-intensity conditioning/nonmyeloablative conditioning; SD, stable disease;

Table 3 Selected studies of alloHCT in T-PLL

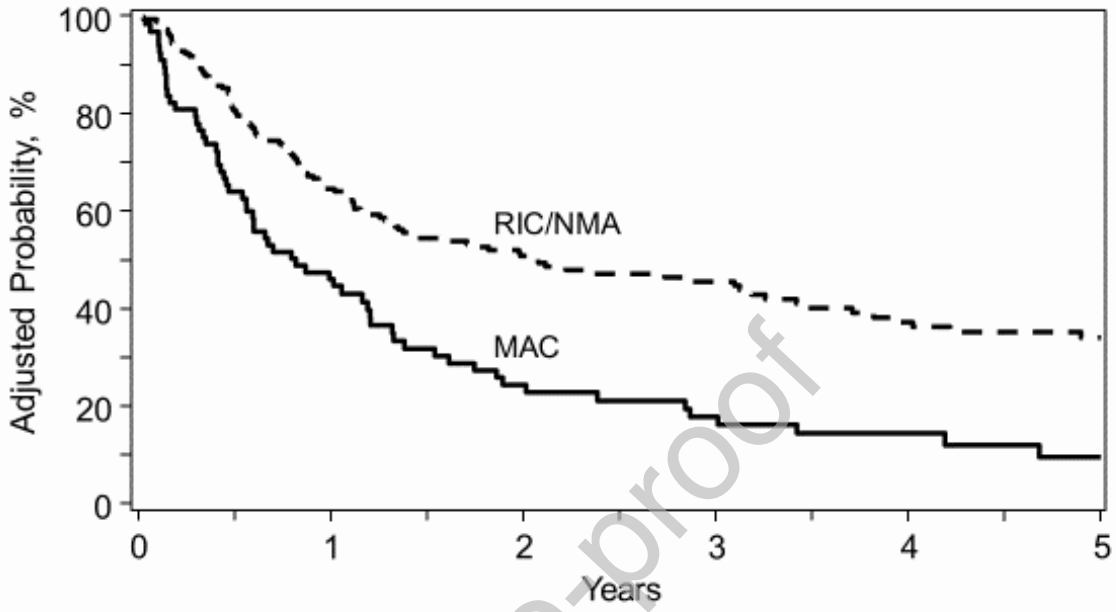
Publication	Study	No. patients	Remission status at alloHCT (N)	Donor type	Regimen intensity (N)	Outcomes
Wiktor-Jedrzejczak et al. [13]	EBMT	37 [a]	CR=22 PR=10 Other=5	MRD=15 MUD=22	MAC=13 RIC=24	4 year OS: 42% 4 year NRM: 32% 4 year relapse: 38%
Kalaycio et al.[10]	CIBMTR	47* (21 T-PLL) [b]	CR=16 PR=8 Other=21	MRD=11 MUD=19 Other: 13	MAC=19 NMA=14	1 year OS: 48% 1 year NRM: 28% 1 year relapse: 28%
Guillaume et al. [9]	SFGM-TC	27	CR=14 PR=10 Other=3	MRD=10 MUD=17	MAC=10 NMA=17	3 year OS: 36% 3 year NRM: 31% 3 year relapse: 47%
Dholaria et al. [8]	Moffitt Cancer Center	11	CR=9 PR=1 Other=1	MRD =5 MUD=3 Other=3	MAC=8 RIC=3	4 year OS: 56% 4 year NRM: 34% 4 year relapse: 21%
Yamasaki et al. [14]	JSHCT	20	CR=6 PR=1 Other=13	MRD =5 MUD=6 Haplo=2 MMUD=7 UCB: 2	MAC=10 RIC=10	3 year OS: 39.8% 1 year NRM: 20.9% 3 year relapse: 69.6%
Murthy et al (current study)	CIBMTR	266	CR=149 PR=80 Other=37	MRD =80 MUD=115 Haplo=30 MMUD=33 Other=8	MAC=78 RIC=188	4 year OS: 30% 4 year TRM: 32.4% 4 year relapse: 41.9%

Abbreviations: B-PLL, B cell prolymphocytic leukemia; CIBMTR, Center for International Blood and Marrow Transplant Research; CR, complete remission; EBMT, European Society for Blood and Marrow Transplantation; haplo, haploidentical donor; HCT, hematopoietic cell transplantation; JSHCT, Japan Society for Hematopoietic Cell Transplantation (now known as the Japanese Society for Transplantation and Cellular Therapy; MRD, matched related donor; MMUD, mismatched unrelated donor; MUD, matched unrelated donor; NRM, nonrelapse mortality; OS, overall survival; PR, partial response; SFGM-TC, Francophone Society of Bone Marrow Transplantation and Cellular Therapy; T-PLL, T-cell prolymphocytic leukemia; UCB, umbilical cord blood.

[a] Data available for 36 patients

[b] B-PLL and T-PLL

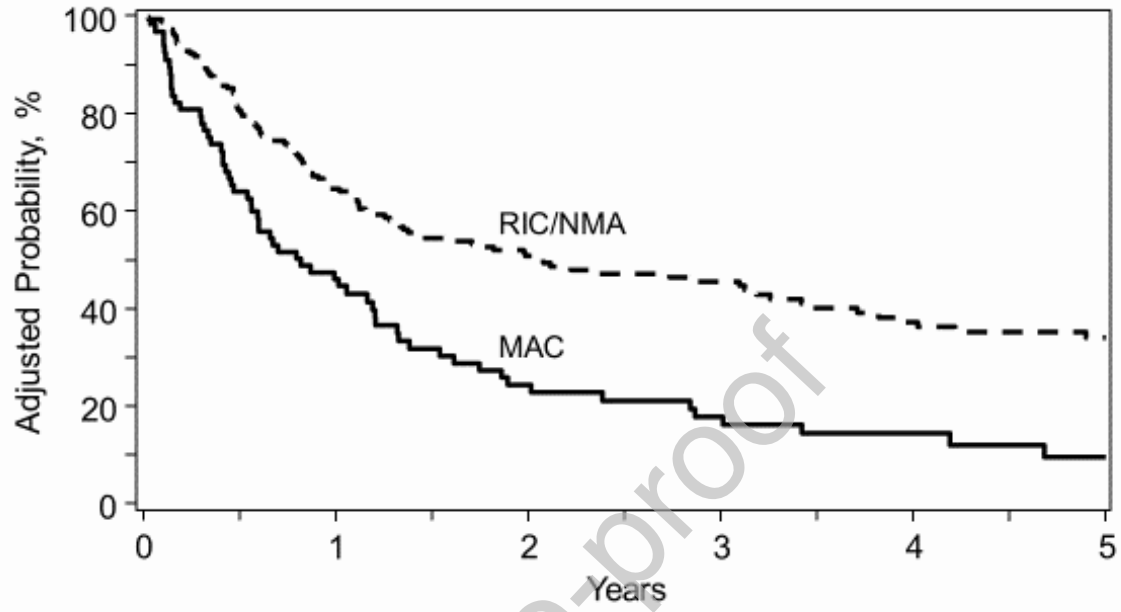
Figure 1 Adjusted overall survival by conditioning intensity (P<0.0001)



N at Risk	0	1	2	3	4	5
MAC	188	114	75	54	35	28
RIC/NMA	78	38	18	12	7	4

MAC, myeloablative conditioning; RIC/NMA, reduced-intensity conditioning/nonmyeloablative conditioning.

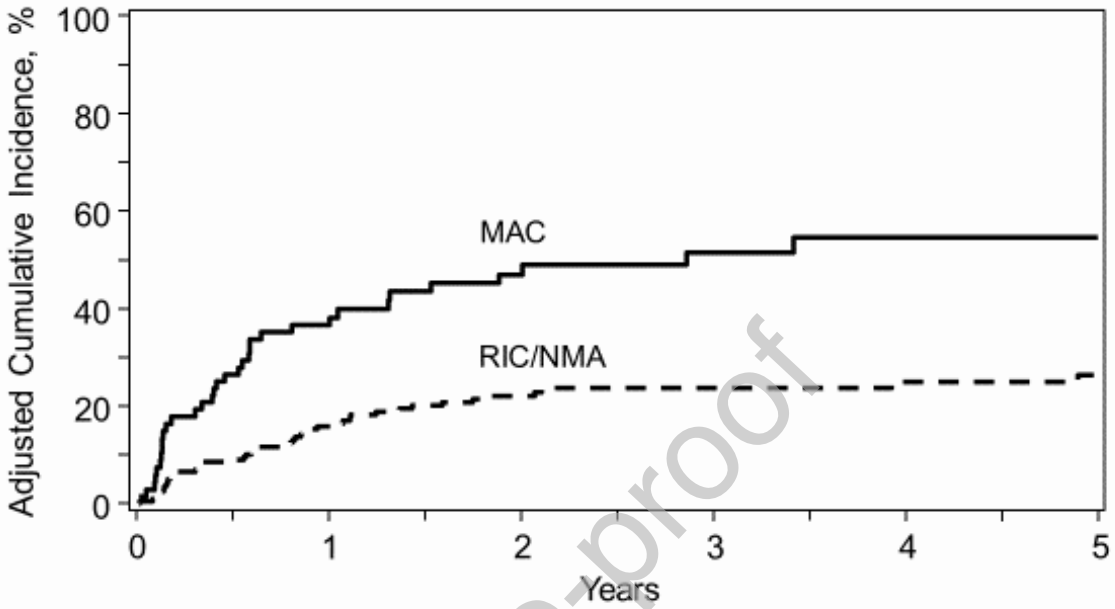
Figure 2 Adjusted disease-free survival, by conditioning intensity (P= 0.0004)



N at Risk	0	1	2	3	4	5
MAC	188	114	75	54	35	28
RIC/NMA	78	38	18	12	7	4

MAC, myeloablative conditioning; RIC/NMA, reduced-intensity conditioning/nonmyeloablative conditioning.

Figure 3 Adjusted treatment-related mortality, by conditioning intensity (P<0.0001)



N at Risk	0	1	2	3	4	5
MAC	186	100	62	40	27	23
RIC/NMA	77	33	14	10	6	5

MAC, myeloablative conditioning; RIC/NMA, reduced-intensity conditioning/nonmyeloablative conditioning.

SUPPLEMENTARY MATERIAL

The material accompanies “Outcomes of Allogeneic Hematopoietic Cell Transplantation in T-cell Prolymphocytic Leukemia: a contemporary analysis from the Center for International Blood and Marrow Transplant Research,” by Hemant S. Murthy et al, Transplantation and Cellular Therapy, December 2021

Supplementary Content:

Supplementary Table 1: Full Conditioning Regimen List (n= 266)

	No. (%)
Myeloablative with TBI	
TBI/Cy	33 (12)
TBI/Cy/Thiotepa	1 (0)
TBI/Cy/etoposide	1 (0)
TBI/Mel	1 (0)
TBI/Flu	7 (3)
TBI only	1 (0)
Myeloablative without TBI	
Bu/Cy	4 (2)
Flu/Bu	20 (8)
Flu/Mel	1 (0)
Bu/Pentostatin	1 (0)
Bu/Gemcitabine	4 (2)
Bu/Thiotepa/ Clofarabine	4 (2)
RIC/NMA with TBI	
TBI/Cy/Flu	28 (11)
TBI/Mel	7 (3)
TBI/Flu	31 (12)
TBI/Pentostatin	8 (3)
TBI only	1 (0)
RIC/NMA without TBI	
Flu/Bu	33 (12)
Flu/Mel	55 (21)
Flu/Cy/Rituximab	1 (0)
Cy/Flu	12 (5)
BEAM	8 (3)
TLI	4 (2)

Abbreviations: Bu, busulfan; BEAM, carmustine, etoposide, cytarabine, melphalan; Cy, cyclophosphamide; Flu, fludarabine; Mel, melphalan; RIC/NMA, reduced-intensity conditioning/nonmyeloablative conditioning; TBI, total body irradiation; TLI, total lymphoid irradiation

Supplementary Table 2: Univariate analysis

Outcomes	**(N=266)**	**Prob (95% CI)**
Non-relapse mortality	263	
1-year		21.5 (16.7-26.7)%
2-year		28.6 (23.1-34.4)%
3-year		30.8 (25.1-36.8)%
4-year		32.4 (26.4-38.6)%
Relapse	263	
1-year		27.6 (22.3-33.2)%
2-year		35.9 (30.1-42)%
3-year		40.4 (34.2-46.8)%
4-year		41.9 (35.5-48.4)%
Progression-free survival	263	
1-year		51 (44.9-57)%
2-year		35.5 (29.6-41.6)%
3-year		28.8 (23-34.9)%
4-year		25.7 (20-32)%
Overall survival	266	
1-year		59.3 (53.3-65.2)%
2-year		43.2 (37-49.4)%
3-year		37.2 (31.1-43.6)%
4-year		30 (23.8-36.5)%

Supplementary Table 3: Univariate Analysis Stratified by Donor

	HLA-id sib (N = 80)		Haplo (N = 30)		URD 8/8 (N = 115)		URD 7/8 (N = 33)	
Outcomes	**N**	**Prob (95% CI)**	**N**	**Prob (95% CI)**	**N**	**Prob (95% CI)**	**N**	**Prob (95% CI)**
Acute 2-4 GVHD	56		22		78		20	
100-day		12.5 (5.2-22.5)%		31.8 (14-52.9)%		24.4 (15.5-34.6)%		20 (5.6-40.4)%
6 months		14.3 (6.4-24.7)%		36.4 (17.5-57.8)%		25.7 (16.6-36)%		20 (5.6-40.4)%
1-year		17.9 (9-29)%		36.4 (17.5-57.8)%		28.4 (18.9-39)%		20 (5.6-40.4)%
Acute 3-4 GVHD	70		26		96		26	
100-day		4.3 (0.8-10.3)%		0%		6.3 (2.3-12)%		7.7 (0.7-21.1)%
6 months		5.7 (1.5-12.4)%		0%		6.3 (2.3-12)%		7.7 (0.7-21.1)%
1-year		8.6 (3.2-16.4)%		0%		7.4 (3-13.5)%		7.7 (0.7-21.1)%
Chronic GVHD	79		29		111		33	
1-year		40.3 (29.5-51.6)%		24.4 (10.4-41.9)%		39.4 (30.4-48.8)%		49.1 (31.5-66.8)%
2-year		47.5 (35.8-59.3)%		33.9 (16.6-53.9)%		47.6 (37.9-57.4)%		49.1 (31.5-66.8)%
3-year		50.2 (37.9-62.4)%		33.9 (16.6-53.9)%		47.6 (37.9-57.4)%		54.5 (32.3-75.9)%
4-year		50.2 (37.9-62.4)%		33.9 (16.6-53.9)%		47.6 (37.9-57.4)%		54.5 (32.3-75.9)%
Treatment related mortality	80		30		114		31	
1-year		11.3 (5.3-19.1)%		27.2 (12.6-44.9)%		23 (15.7-31.2)%		32.3 (16.9-49.9)%
2-year		18.2 (10.4-27.7)%		31.6 (15.5-50.3)%		31.6 (23-40.8)%		35.7 (19.6-53.7)%
3-year		18.2 (10.4-27.7)%		31.6 (15.5-50.3)%		35.1 (26.1-44.6)%		42.1 (23.2-62.4)%
4-year		20.4 (11.8-30.7)%		31.6 (15.5-50.3)%		36.6 (27.3-46.4)%		42.1 (23.2-62.4)%
Relapse	80		30		114		31	
1-year		37.7 (27.3-48.7)%		20.2 (7.7-36.6)%		25.7 (18-34.2)%		19.4 (7.4-35.2)%
2-year		44.7 (33.7-55.9)%		33.3 (16.4-52.9)%		36.2 (27.2-45.6)%		19.4 (7.4-35.2)%
3-year		44.7 (33.7-55.9)%		45 (24.4-66.6)%		42.3 (32.7-52.2)%		19.4 (7.4-35.2)%
4-year		44.7 (33.7-55.9)%		45 (24.4-66.6)%		43.8 (34-53.9)%		29 (9.5-53.8)%
Disease free survival	80		30		114		31	
1-year		51 (40.1-61.9)%		52.6 (34.8-70.1)%		51.3 (42.1-60.5)%		48.4 (31.3-65.7)%
2-year		37.1 (26.6-48.2)%		35.1 (18.2-54.2)%		32.3 (23.6-41.6)%		44.9 (28-62.5)%
3-year		37.1 (26.6-48.2)%		23.4 (8.2-43.3)%		22.6 (14.7-31.6)%		38.5 (20.8-58)%
4-year		34.9 (24.4-46.3)%		23.4 (8.2-43.3)%		19.6 (12-28.5)%		28.9 (10.4-52.1)%
Overall survival	80		30		115		33	
1-year		61.1 (50.1-71.4)%		59.4 (41.4-76.1)%		60.2 (51.1-69)%		54.5 (37.6-70.9)%
2-year		47.3 (36.2-58.4)%		42.4 (24.5-61.4)%		40.9 (31.6-50.6)%		41.7 (25.5-58.9)%
3-year		45.6 (34.6-56.9)%		33.9 (15-56)%		32.7 (23.7-42.4)%		35.8 (19-54.5)%
4-year		40.1 (28.9-51.8)%		33.9 (15-56)%		24.6 (16.2-34.2)%		26.8 (9.6-48.9)%

Supplementary Table 4: Cumulative incidence of graft failure and GVHD

	(N=266)	**Prob (95% CI)**
Graft failure	265	
100-day		1.1 (0.1-3.2)%
Acute 2-4 GVHD	182	
100-day		20.3 (14.8-26.5)%
6-month		22.5 (16.8-28.9)%
1-year		24.8 (18.8-31.3)%
Acute 3-4 GVHD	226	
100-day		4.9 (2.4-8.1)%
6-month		5.3 (2.8-8.6)%
1-year		6.7 (3.8-10.3)%
Chronic GVHD	260	
1-year		38.8 (32.9-44.9)%
2-year		45.5 (39.2-51.8)%
3-year		47.2 (40.6-53.7)%
4-year		47.2 (40.6-53.7)%

Abbreviations: GVHD, graft-versus-host disease

Supplementary Table 5: Causes of death

	No. (%)
Deaths, no. (%)	175 (66)
Cause of death,no. (%)	
Primary disease	91 (52)
GVHD	22 (13)
Infection	27 (15)
IPn/ARDS	2 (1)
Organ failure	5 (3)
Organ toxicity	1 (0)
Secondary malignancy	4 (2)
Vascular	20 (11)
Unknown	3 (1)

Abbreviations: GVHD, graft-versus-host disease; IPn/ARDS, interstitial pneumonitis/acute respiratory distress syndrome

Supplementary Table 6: Full multivariate analysis

	No.	OR	95% CI lower limit	95% CI upper limit	P-value	Overall P-value
Acute GVHD II-IV						
Conditioning regimen intensity						
RIC/NMA	172	1.00	Reference			0.0011
MAC	75	2.94	1.54	5.62	0.0011	
GVHD prophylaxis						
CNI + MMF ± others (except PTCY)	65	1.00	Reference			0.0093
CNI + MTX ± others (except MMF, PTCY)	114	0.56	0.28	1.14	0.1077	
CNI + others (except MMF, MTX, PTCY)	18	0.36	0.11	1.17	0.0902	
PTCy ± others	33	0.26	0.10	0.71	0.0082	
Other prophylaxis	17	2.17	0.71	6.60	0.174	
Contrast						
CNI + MTX ± others (except MMF, PTCY) vs. CNI + others (except MMF, MTX, PTCY)		1.55	0.50	4.84	0.4499	
CNI + MTX ± others (except MMF, PTCY) vs. PTCy ± others		2.14	0.83	5.54	0.1176	
CNI + MTX ± others (except MMF, PTCY) vs. others		0.26	0.08	0.80	0.0184	
CNI + others (except MMF, MTX, PTCY) vs. PTCy ± others		1.38	0.36	5.36	0.6422	
CNI + others (except MMF, MTX, PTCY) vs. others		0.17	0.04	0.72	0.0166	
PTCy ± others vs. other prophylaxis		0.12	0.03	0.45	0.0017	
Acute GVHD III-IV						
Conditioning regimen intensity						
RIC/NMA	172	1	Reference			0.0253
MAC	75	2.3	1.1	4.9	0.0253	

	No.	OR	95% CI lower limit	95% CI upper limit	P-value	Overall P-value
Chronic GVHD						
GVHD prophylaxis						
CNI + MMF ± others (except PTCY)	67	1	Reference			0.0015
CNI + MTX ± others (except MMF, PTCY)	121	1.06	0.68	1.65	0.8045	
CNI + others (except MMF, MTX, PTCY)	20	2.35	1.31	4.20	0.0041	
PTCy ± others	37	0.44	0.19	1.05	0.0645	
Other prophylaxis	17	0.65	0.25	1.66	0.3677	
Year of transplant						
2008-2011	50	1	Reference			0.0216
2012-2015	110	0.62	0.39	0.97	0.0382	
2016-2018	102	0.48	0.28	0.82	0.0069	
Contrast						
CNI + MTX ± others (except MMF, PTCY) vs. CNI + others (except MMF, MTX, PTCY)		0.451	0.262	0.775	0.0039	
CNI + MTX ± others (except MMF, PTCY) vs. PTCy ± others		2.383	1.050	5.412	0.0379	
CNI + MTX ± others (except MMF, PTCY) vs. other prophylaxis		1.631	0.649	4.100	0.2986	
CNI + others (except MMF, MTX, PTCY) vs. PTCy ± others		5.290	2.164	12.936	0.0003	
CNI + others (except MMF, MTX, PTCY) vs. others		3.619	1.339	9.784	0.0112	
PTCy ± others vs. others		0.684	0.213	2.197	0.5236	
2012-2015 vs. 2016-2018		1.291	0.816	2.042	0.2759	
Relapse						
Disease status at HCT						
CR	149	1	Reference			0.0486
PR	80	1.40	0.91	2.17	0.1257	
No response/stable disease/progression	31	2.13	1.23	3.71	0.0072	
Not reported	6	0.94	0.23	3.87	0.932	
Contrast						
PR vs. no response/stable disease/progression		0.66	0.37	1.18	0.157	
PR vs. not reported		1.49	0.36	6.22	0.5818	
No response/stable disease/progression vs. not reported		2.27	0.52	9.85	0.2737	

	No.	OR	95% CI lower limit	95% CI upper limit	P-value	Overall P-value
Treatment-related mortality						
Conditioning regimen intensity						
RIC/NMA	187	1	Reference			< .0001
MAC	77	3.31	2.01	5.45	< .0001	
Age						
≤ 60	142	1	Reference			0.0108
> 60	122	1.87	1.16	3.04	0.0108	
KPS						
≥ 90%	152	1	Reference			0.0142
< 90%	101	1.98	1.25	3.14	0.0036	
Not reported	11	1.18	0.36	3.83	0.7811	
ATG/Campath use						
No	215	1	Reference			0.0263
Yes	49	1.79	1.07	2.98	0.0263	
Contrast						
< 90% vs. Not reported		1.677	0.512	5.488	0.3931	
Disease-free survival						
Conditioning regimen intensity						
RIC/NMA	187	1	Reference			0.0004
MAC	77	1.86	1.32	2.61	0.0004	
Age						
≤ 60	142	1	Reference			0.0337
> 60	122	1.41	1.03	1.93	0.0337	
KPS						
≥ 90%	152	1	Reference			0.028
< 90%	101	1.51	1.12	2.05	0.0075	
Not reported	11	1.13	0.53	2.44	0.7507	
ATG/Campath use						
No	215	1	Reference			0.0253
Yes	49	1.50	1.05	2.13	0.0253	
Contrast						
< 90% vs. not reported		1.34	0.61	2.92	0.4655	

	No.	OR	95% CI lower limit	95% CI upper limit	P-value	Overall P-value
Overall Survival						
Conditioning regimen intensity						
RIC/NMA	78	1	Reference			< .0001
MAC	188	2.18	1.53	3.09	< .0001	
Age						
≤ 60	142	1	Reference			0.0053
> 60	122	1.61	1.15	2.24	0.0053	
KPS						
≥ 90%	153	1	Reference			0.0272
< 90%	101	1.53	1.12	2.08	0.0073	
Not reported	12	1.23	0.60	2.54	0.573	
Contrast						
< 90% vs. not reported		1.241	0.594	2.593	0.5666	

Abbreviations: ATG, anti-thymocyte globulin; CNI, calcineurin inhibitor; CR, complete remission; GVHD, graft-versus-host disease; HCT, hematopoietic cell transplantation; KPS, Karnofsky Performance Status score; MAC, myeloablative conditioning; MMF, mycophenolate mofetil; MTX, methotrexate; NMA, nonmyeloablative conditioning; OR, odds ratio; PR, partial response; PTCy, post-transplant cyclophosphamide; RIC, reduced-intensity conditioning.

Supplementary Table 7: Full multivariate analysis (Conditioning intensity +/- Total Body Irradiation)

Factors	N	OR/HR (95% CI)	P-value	Overall P-value
Overall survival				
Conditioning regimen intensity				
MAC-TBI	43	1.00 (Reference)		0.0001
MAC-Chemo	34	0.83 (0.49-1.41)	0.4974	
RIC/NMA-TBI	74	0.46 (0.28-0.76)	0.0022	
RIC/NMA-Chemo	113	0.38 (0.24-0.61)	<.0001	
Contrast				
Mac-Chemo vs. RIC/NMA-TBI		1.80 (1.07-3.03)	0.0269	
Mac-Chemo vs. RIC/NMA-Chemo		2.19 (1.36-3.51)	0.0012	
RIC/NMA-TBI vs. RIC/NMA-Chemo		1.22 (0.81-1.82)	0.3437	
Disease-free survival				
Conditioning regimen intensity				
MAC-TBI	43	1.00 (Reference)		0.022
MAC-Chemo	34	1.01 (0.60-1.71)	0.9628	
RIC/NMA-TBI	74	0.68 (0.44-1.05)	0.0844	
RIC/NMA-Chemo	113	0.58 (0.38-0.89)	0.0117	
Contrast				
Mac-Chemo vs. RIC/NMA-TBI		1.49 (0.91-2.45)	0.1138	
Mac-Chemo vs. RIC/NMA-Chemo		1.74 (1.10-2.75)	0.0186	
RIC/NMA-TBI vs. RIC/NMA-Chemo		1.17 (0.79-1.72)	0.439	
Treatment-related mortality				
Conditioning regimen intensity				
MAC-TBI	43	1.00 (Reference)		<.0001
MAC-Chemo	34	0.48 (0.22-1.05)	0.0662	
RIC/NMA-TBI	74	0.24 (0.12-0.49)	<.0001	
RIC/NMA-Chemo	113	0.17 (0.09-0.34)	<.0001	

Contrast				
Mac-Chemo vs. RIC/NMA-TBI		1.99 (0.88-4.48)	0.0972	
Mac-Chemo vs. RIC/NMA-Chemo		2.77 (1.32-5.85)	0.0073	
RIC/NMA-TBI vs. RIC/NMA-Chemo		1.39 (0.74-2.64)	0.3068	
Acute GVHD				
Conditioning regimen intensity				
MAC-TBI	42	1.00 (Reference)		0.0205
MAC-Chemo	34	1.30 (0.52-3.24)	0.5747	
RIC/NMA-TBI	71	0.41 (0.19-0.90)	0.0257	
RIC/NMA-Chemo	108	0.56 (0.27-1.14)	0.1102	
Contrast				
Mac-Chemo vs. RIC/NMA-TBI		3.18 (1.36-7.43)	0.0075	
Mac-Chemo vs. RIC/NMA-Chemo		2.33 (1.06-5.12)	0.0345	
RIC/NMA-TBI vs. RIC/NMA-Chemo		0.73 (0.39-1.39)	0.3398	

Abbreviations: GVHD, graft-versus-host disease; MAC, myeloablative conditioning; NMA, nonmyeloablative conditioning; OR, odds ratio; RIC, reduced-intensity conditioning; TBI, total body irradiation