Supplementary Methods:

Patient eligibility and donor selection

Patients 18 – 74 years of age were eligible. The patient must have had a potentially suitable 8/8 or 7/8 HLA-matched unrelated donor available through the National Marrow Donor Program® (NMDP) bone marrow donor registry. Other eligibility criteria included performance status per ECOG and Karnofsky scales of ≤2 and ≥60%, respectively. Adequate organ function as defined by left ventricular ejection fraction > 45% by either MUGA or 2D echocardiogram, DLCO Adj > 50%, creatinine <1.5 mg/dl and creatinine clearance >50 ml/min/1.73 m^2, serum total bilirubin less than 2.5 mg/dl, and serum ALT and AST values less than or equal to 2.5 times the upper limit of normal, unless during induction phase and due to liver involvement by malignancy. Minimum absolute neutrophil count of 1,000 cells/μl and minimum platelet count (without transfusion) of 20,000/mm^3 unless thought to be due to bone marrow involvement by malignancy. Transplant recipients were excluded from study consideration in cases of active infection not responding to antimicrobial therapy, active CNS involvement by malignancy, progressive disease within 8 weeks of prior therapy or within 12 weeks after prior autologous stem cell transplantation, active or recent second malignancies unless they have undergone potentially curative therapy for that malignancy, HIV infection, chronic active hepatitis B, pregnancy or active lactation, and history of psychiatric disorder which may compromise compliance with transplant protocol, or which does not allow for appropriate informed consent.

Donor evaluation was in accordance with existing NMDP Standard Policies and Procedures. Volunteer unrelated donors had to be age 18 years or older, matched at a minimum of seven of eight loci (HLA-A, B, C, DRB1), by high resolution typing (>7/8 allele match) and have the ability to give informed consent.

Supportive Care/Infectious Prophylaxis

All recipients received prophylaxis against Pneumocystis jiroveci pneumonia (PJP), usually trimethoprim/sulfamethoxazole beginning with the first cycle of the induction therapy, continuing until transplantation, and resuming at the time of platelet recovery post-HSCT. PJP prophylaxis continued until immunosuppression was discontinued for at least 3 months. All recipients received fluconazole for prophylaxis against yeast infections and continued through transplantation until day +100 or as clinically indicated. During the peri-transplant period, recipients received prophylactic broad-spectrum antibiotics with IV ceftazidime from the onset of neutropenia (ANC <500/μl) or first fever (T >38.3°C) until neutropenia resolved. Recipients with neutropenia and fever that persisted longer than 4 days despite broad-spectrum antibiotics

received empiric antifungal therapy in accordance with standard practices. All recipients received valacyclovir for prophylaxis against herpes simplex virus (HSV) and Varicella zoster virus (VZV) infection/reactivation from the first day of pre-transplant induction chemotherapy, continuing through transplantation until immunosuppression is discontinued. Recipients with positive pre-transplant serology for Cytomegalovirus (CMV) and/or CMV-seropositive donors were monitored for CMV reactivation by clinical evaluation and weekly testing with peripheral CMV PCR assays as clinically appropriate. CMV reactivation or disease was treated with IV ganciclovir or foscarnet (Note: study was conducted prior to approval of letermovir for CMV prophylaxis). Weekly monitoring continued as feasible through 6 months post-transplant or longer for recipients on continued immunosuppression. All recipients underwent monitoring for reactivation of Epstein-Barr virus (EBV) by weekly quantitative PCR assays. Monitoring continued through day +180 post transplantation or longer for recipients deemed at continued high risk. Recipients who developed cGVHD received penicillin V for prophylaxis against bacterial infections. All recipients underwent standard infectious disease vaccinations schedule beginning 6 months after transplantation. Live vaccines were not given during the first 2 years after transplantation or in patients with ongoing chronic GVHD or immunosuppression.

All patients received ursodeoxycholic acid (ursodiol) for the prevention of hepatic complications after HSCT from day -6 until day +98 post-HSCT.

New onset of engraftment syndrome, acute or chronic GVHD were managed using systemic corticosteroids per standard practices. Patients with persistent or progressive malignancy post-HSCT, or mixed chimerism that does not improve after tapering or discontinuing immune suppression were eligible to receive donor lymphocytes infusion if available from their respective donor and no GVHD present. Recipients with mixed chimerism at day +28 underwent repeat chimerism assessment at day +42 (+/- 3 days) and every two weeks thereafter as deemed necessary. In addition to DLI, persistent or progressive disease was treated with any approved therapy at time thought to be in the best interest of the patient. Alternatively, such patients may be offered therapy on other NCI protocols.

Post-HSCT course/clinical follow up

After inpatient hospital discharge patients were seen in follow-up at the NIH Clinical Center at least twice weekly until day +100 or as medically indicated. Protocol-driven timepoints for data collection to evaluate GVHD, malignancy status, and late complications of HSCT were conducted at days +28 and +100; and at 6, 9, 12, 18, 24 months and then annually post-HSCT.

Study endpoints

Additional endpoints included rate of hematologic recovery, donor engraftment, day 100 treatment-related mortality (TRM), non-relapse (NRM) and relapse-related mortality, GRFS,[1] moderate-severe cGVHD-free survival (CFS), progression-free survival (PFS), OS, time to permanent discontinuation of systemic immunosuppressive therapy (IST) (defined as discontinuation of IST at any time and remaining off IST at time of data collection), rates of CMV reactivation, and overall toxicity profile of the two regimens determined by CTCAE v4.03.

Immunologic Correlates

Blood samples for immunologic correlates were collected for all patients up until time of relapse or death.

Flow cytometry: Serial assessment after transplant of the frequency and absolute numbers of CD3+, CD3+CD4+, and CD3+CD8+ (T), CD19+ (B) and CD3-CD56+ (NK) cells was performed by the NIH Clinical Center immunology laboratories. T-cell subsets, including Treg (estimated as CD25++CD127dim) CD4, non-Treg CD4, and CD8 T-cells, were characterized for recent thymic emigrants (CD45RA+CD31+), naïve (CD45RA+CCR7+), central memory (CD45RA-CCR7+), effector memory (CD45RA- CCR7-) and TEMRA (CD45RA+CCR7-) T-cell subsets. CD8 cells were also assessed for Tscm (CD8+CD45RA+CCR7dimCD95+). Data was collected on a Beckman Coulter Gallios and analyzed with FlowJo 9.9.6. Lymphocyte populations in AC versus TMS arms were compared by Mann-Whitney unpaired nonparametric tests.

Spectratyping: Global T-cell receptor Vβ repertoire diversity was assessed in the first 10 transplants in each arm. RNA from FACS-sorted CD4 and CD8 T-cells was isolated by chloroform extraction and isopropanol precipitation to generate cDNA.[2] A global repertoire skewing index (RSI) was calculated by summing the absolute disparity of the proportions of each spectratype peak from that peak in the normal standard for that Vβ family, and then averaging the divergence of all Vβ families.[3-4] RSI between arms were compared by Mann-Whitney unpaired nonparametric tests.

Repertoire diversity was assessed by semi-nested PCR using a panel of human Vβ sense and Cβ antisense oligoprimers, the second Cβ being fluorescently tagged. PCR products were assessed for DNA fragment length on an ABI 3130 capillary gel system. Genemapper (V3.7) software (PerkinElmer-Applied Biosystems) was used to identify each amplicon peak by PCR size and determine area under the peak. A normal control standard of repertoire diversity had

been calculated separately for CD4 and CD8 T cells by averaging the proportional areas of each spectratype peak in 20 Vb families from 20 normal donors.[3]

Recent studies of T-cell repopulation post-transplant have identified a subset of T-cells that had previously been included within the naive CCR7+CD45RA+ population.[5-8] These cells, termed T memory stem cells (Tscm) comprise a population with both the long-lived, self-replicating capacity of naive T-cells, and with the commitment and capacity to rapidly expand into memory and effector populations. These Tscm cells have been found to be expanded into readily identifiable subpopulations among naive cells, particularly in CD8 T-cells, after transplant (Figure 4A, 4D).[8] These Tscm have been distinguished by relatively dim expression of CCR7 and strong expression of the activation marker CD95. The identification of these cells in both AC and TMS patients was further substantiated by their expression of CD27 and CD28 (both absent in effectors), and their upregulation of both CD95 and a second activation marker, PD-1, which are not found in the CCR7++CD95- naive cells (data not shown).

Cytokine Measurement

Plasma samples at the timepoints of 3-, 6-, 9-, and 12- months post-transplantation were collected and analyzed. IFN- γ, IL-6, TNFα and CXCL-10 were assayed using V-PLEX from Meso-ScaleDiscovery (MSD). The BAFF, CXCL9, and ST2 high-sensitive assays were developed and customized for clinical testing using MSD electrochemiluminescence immunoassay technology with antibody pairs obtained from R&D Systems.

Statistical methods:

The trial was designed to estimate the rate of severe cGVHD in each of the two prophylaxis arms individually, with 44 randomized evaluable patients per arm in order to have a 90% confidence interval width of +/-10% for the proportion of patients with severe cGVHD, expected to be 20%. Time-to-event analyses all began at the date of transplant. The probability of survival (OS) or PFS as a function of time was determined until death or last follow-up for OS and until progression or death without progression as events for PFS, censoring at last follow-up. Both were estimated by the Kaplan-Meier method with the statistical significance of the difference of a pair of Kaplan-Meier curves determined by a log-rank test. All other time to event analyses were performed using cumulative incidence curves with competing risks as described by Gooley et. al,[9] with the significance of the difference among curves determined using Gray's method. Competing risks were identified separately for each endpoint. Specifically, analyses included cumulative incidence of progression competing with death, being taken off immunosuppression

competing with death or progression, relapse related mortality competing with NRM, TRM competing with progression, acute GVHD competing with death, progression, graft failure, and cGVHD, chronic GVHD competing with death, progression, and graft failure, and CMV reactivation competing with death.

Many factors were evaluated for their potential associations with survival, TRM, progression, any cGVHD, and severe cGVHD. For appropriate endpoints, these included age, sex, donor age, hematopoietic cell transplant-comorbidity index (HCT-CI) score,[10] HLA match, Karnofsky status, recipient CMV status, CMV match, CD34 cell dose, CD3 cell dose, number of prior treatments, prior transplant, disease status, Kahl relapse risk,[11] and chemosensitivity. Following univariate analyses based on log-rank test or Gray's test results as appropriate, those factors which were associated with p-values<0.10 were evaluated for their joint association with outcome using a Cox proportional hazards model. A sub-group analysis was conducted to investigate the association of baseline (defined as day -8, or day of first alemtuzumab infusion) absolute lymphocyte count (ALC) with clinical outcomes with use of alemtuzumab. Patients were grouped into 2 groups according to baseline ALC value with cut-off value of 2×10^9/L. The statistical significance of comparisons of continuous parameters between two groups were determined using a Wilcoxon rank sum test, while dichotomous parameters were compared between groups using Fisher's exact test. Comparisons of the distributions of grades of adverse events were made using a Cochran-Armitage test for trend. All p-values are two-tailed and reported without adjustment for multiple comparisons.

Cytokine levels at different time points were compared between two groups of interest using multiple Mann-Whitney-U tests and the false discovery rate (FDR) approach according to the two-stage linear step-up method.[12] For FDR, Q was defined as 5% and P-values of positive discoveries were displayed without adjustment. Cytokine levels at 3 and 6 months were used as continuous variables in univariate and multivariable Cox regression of OS. Scaled Schoenfeld residuals were inspected to confirm the proportional hazards assumption. Kaplan-Meier curves of cytokines that showed an association with OS in the univariate Cox regression were plotted using median and quartile cutoffs and compared by the log-rank test to explore binary versus continuous association with survival time. The Cox final model, adjusted for treatment arm, age ≥60, HCT-CI ≥2 and recipient CMV+ status, was built by including significant factors from the univariate analysis defined by p<0.05. GraphPad Prism 9.3.1.471 for Windows was used to perform statistics of cytokine analyses.

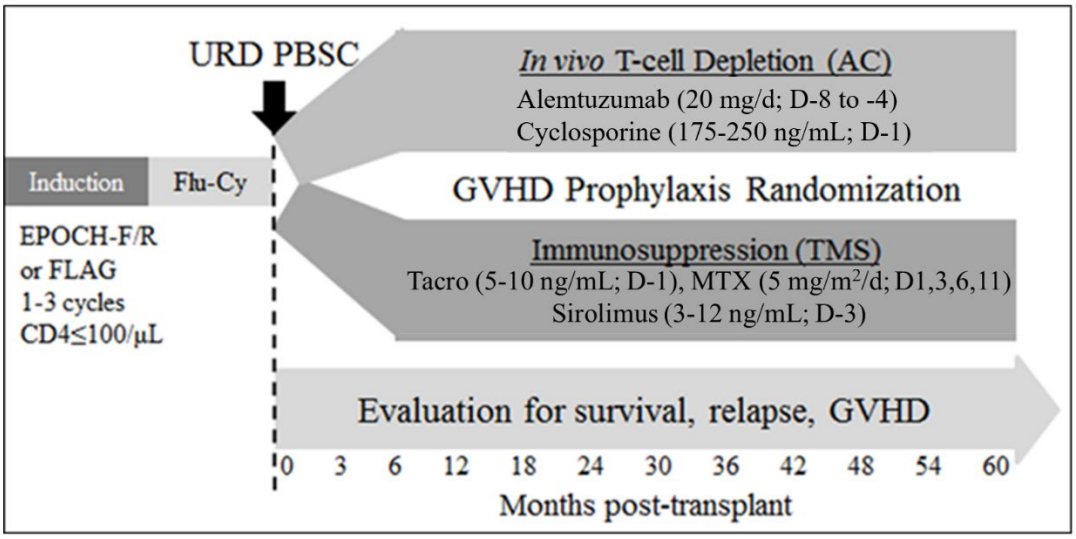
Data Sharing Statement: Please contact the corresponding author for any original data requests (Steven Z. Pavletic; pavletis@mail.nih.gov).

Supplementary Method References:

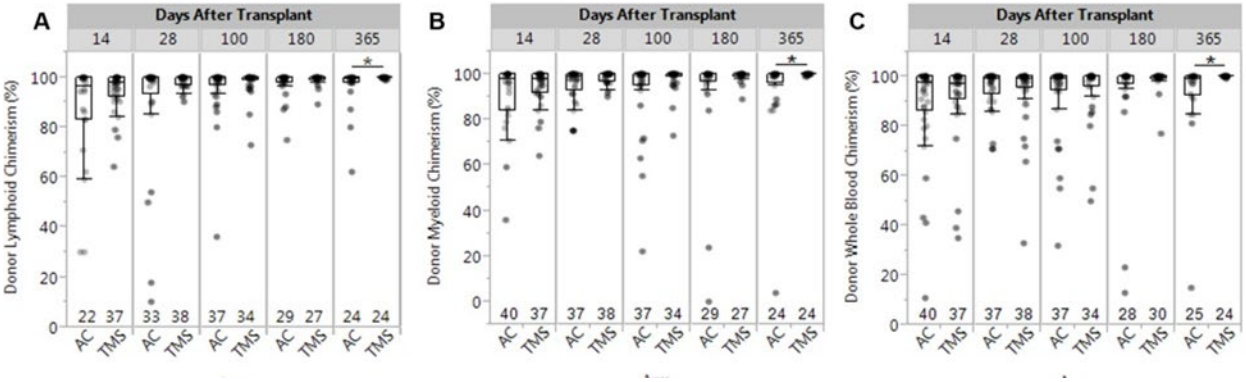
1. Holtan SG, DeFor TE, Lazaryan A, et al. Composite end point of graft-versus-host disease-free, relapse-free survival after allogeneic hematopoietic cell transplantation. *Blood.* 2015 Feb 19;125(8):1333-8.
2. Friedman TM, Varadi G, Hopely DD, et al. Nonmyeloablative conditioning allows for more rapid T-cell repertoire reconstitution following allogeneic matched unrelated bone marrow transplantation compared to myeloablative approaches. *Biol Blood Marrow Transplant.* 2001;7(12):656-64.
3. Memon SA, Sportès C, Flomerfelt FA, Gress RE, Hakim FT. Quantitative analysis of T cell receptor diversity in clinical samples of human peripheral blood. *J Immunol Methods*. 2012 Jan 31;375(1-2):84-92.
4. Sportès C, Hakim FT, Memon SA, et al. Administration of rhIL-7 in humans increases in vivo TCR repertoire diversity by preferential expansion of naive T cell subsets. *J Exp Med.* 2008 Jul 7;205(7):1701-14.
5. Cieri N, Oliveira G, Greco R, et al. Generation of human memory stem T cells after haploidentical T-replete hematopoietic stem cell transplantation. *Blood.* 2015 Apr 30;125(18):2865-74.
6. Dekker L, de Koning C, Lindemans C, Nierkens S. Reconstitution of T Cell Subsets Following Allogeneic Hematopoietic Cell Transplantation. *Cancers (Basel).* 2020 Jul 20;12(7):1974.
7. Jimbo K, Konuma T, Watanabe E, et al. T memory stem cells after allogeneic haematopoietic cell transplantation: unique long-term kinetics and influence of chronic graft-versus-host disease. *Br J Haematol.* 2019 Sep;186(6):866-878.
8. Soares MV, Azevedo RI, Ferreira IA, et al. Naive and Stem Cell Memory T Cell Subset Recovery Reveals Opposing Reconstitution Patterns in CD4 and CD8 T Cells in Chronic Graft vs. Host Disease. *Front Immunol.* 2019 Mar 6;10:334.
9. Gooley TA, Leisenring W, Crowley J, Storer BE. Estimation of failure probabilities in the presence of competing risks: new representations of old estimators. *Stat Med.* 1999 Mar 30;18(6):695-706.
10. Sorror ML, Maris MB, Storb R, et al. Hematopoietic cell transplantation (HCT)-specific comorbidity index: a new tool for risk assessment before allogeneic HCT. *Blood*. 2005 Oct 15;106(8):2912-9.
11. Kahl C, Storer BE, Sandmaier BM, et al. Relapse risk in patients with malignant diseases given allogeneic hematopoietic cell transplantation after nonmyeloablative conditioning. *Blood.* 2007 Oct 1;110(7):2744-8.
12. Benjamini Y, Krieger AM, Yekutieli D. Adaptive linear step-up procedures that control the false discovery rate. *Biometrika.* 2006 September;93;491–507.

SUPPLEMENTARY FIGURES/TABLES

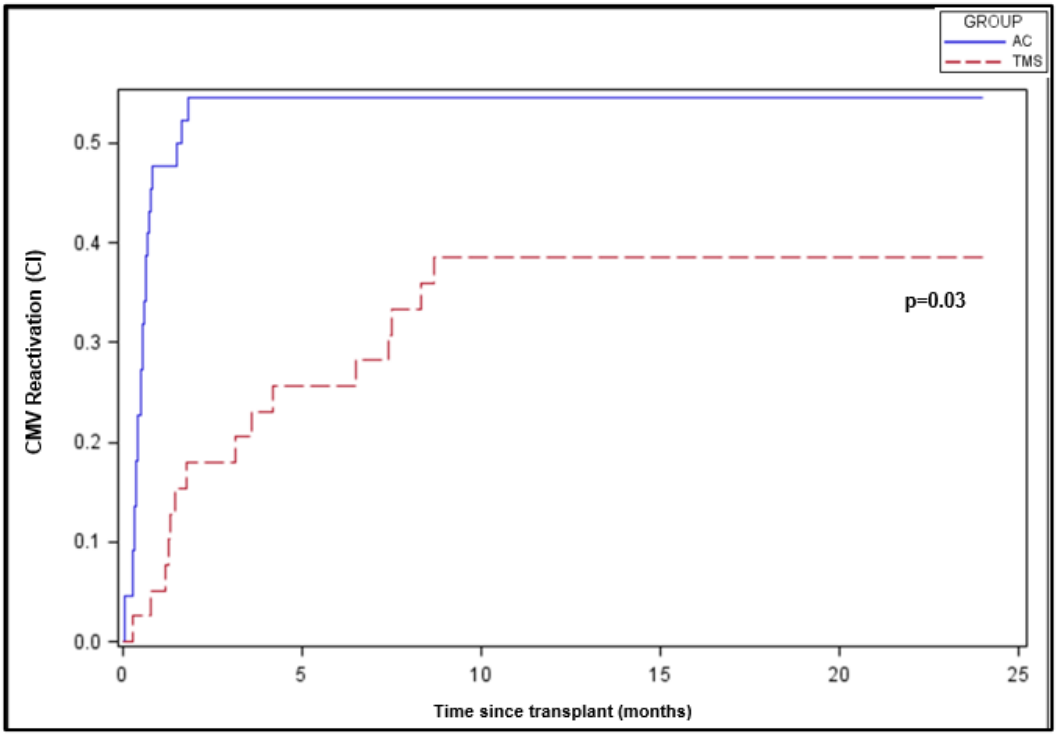
Supplementary Figure 1. Study schema



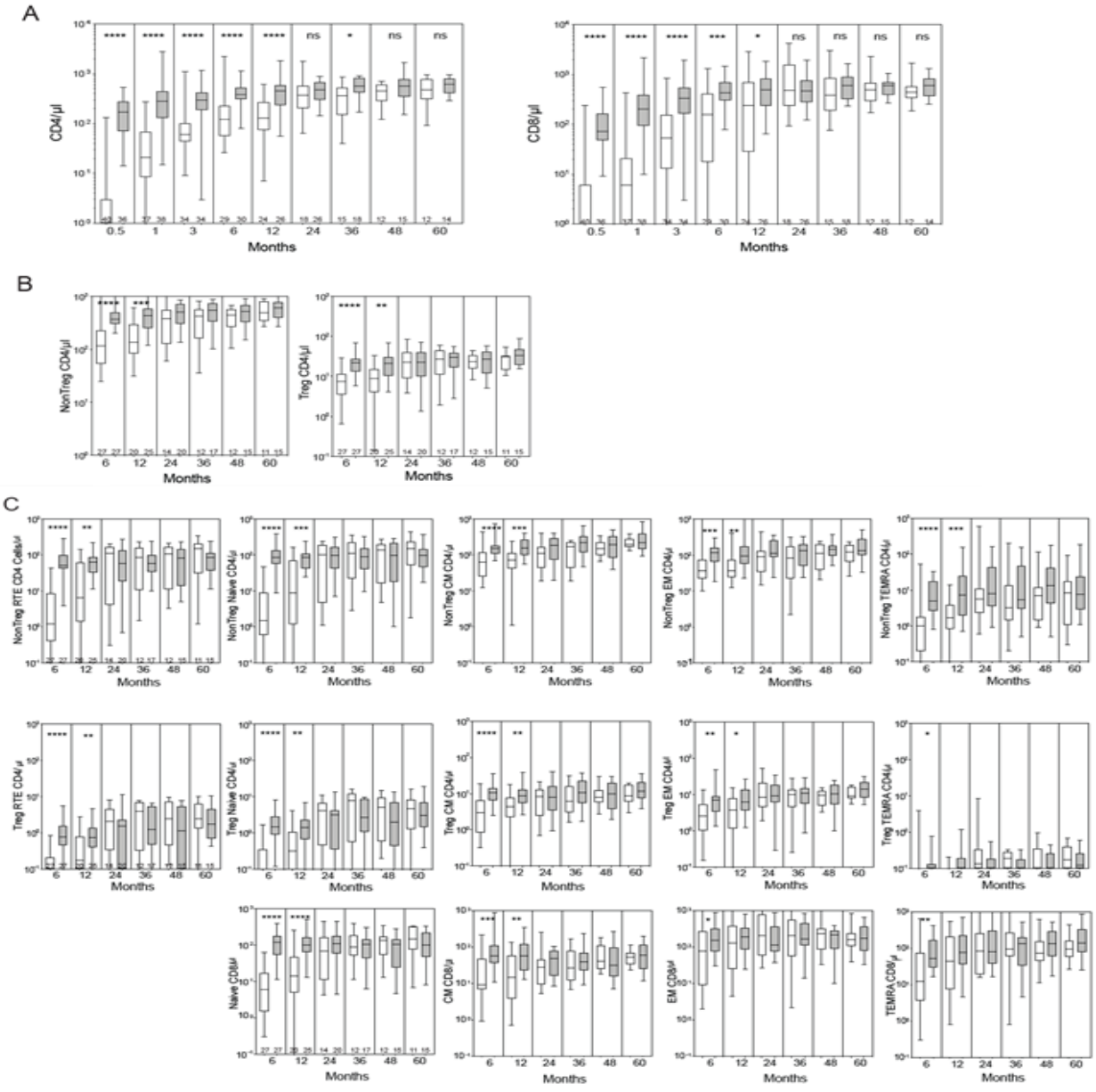
Supplementary Figure 2. Immune Reconstitution, Donor chimerism. A. Donor lymphoid, B. myeloid, C. whole blood chimerism per arm at Days +14, 28, 100, 180, 365 post-transplant.



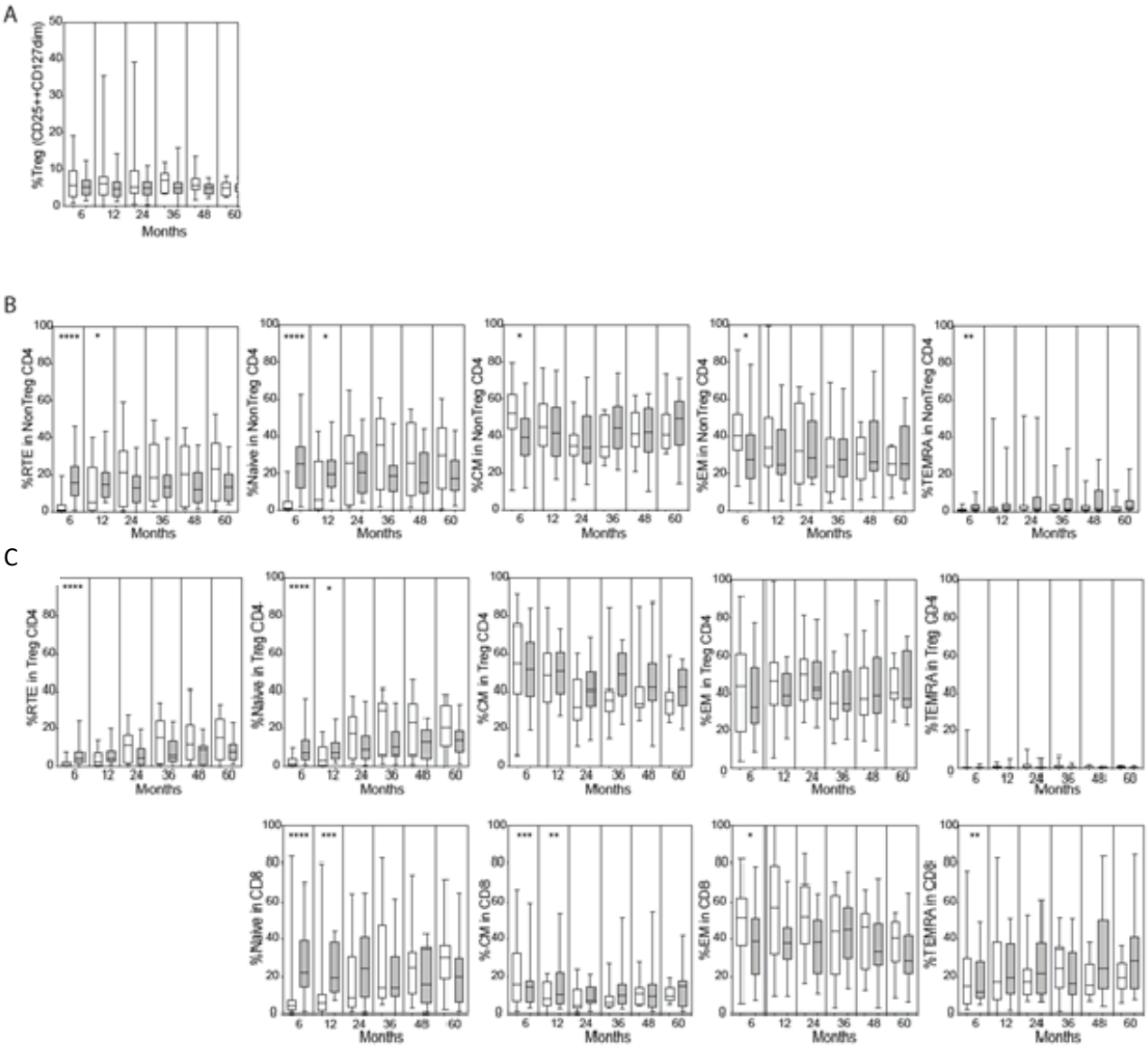
Supplementary Figure 3: Cumulative Incidence of CMV Reactivation (competing with death)



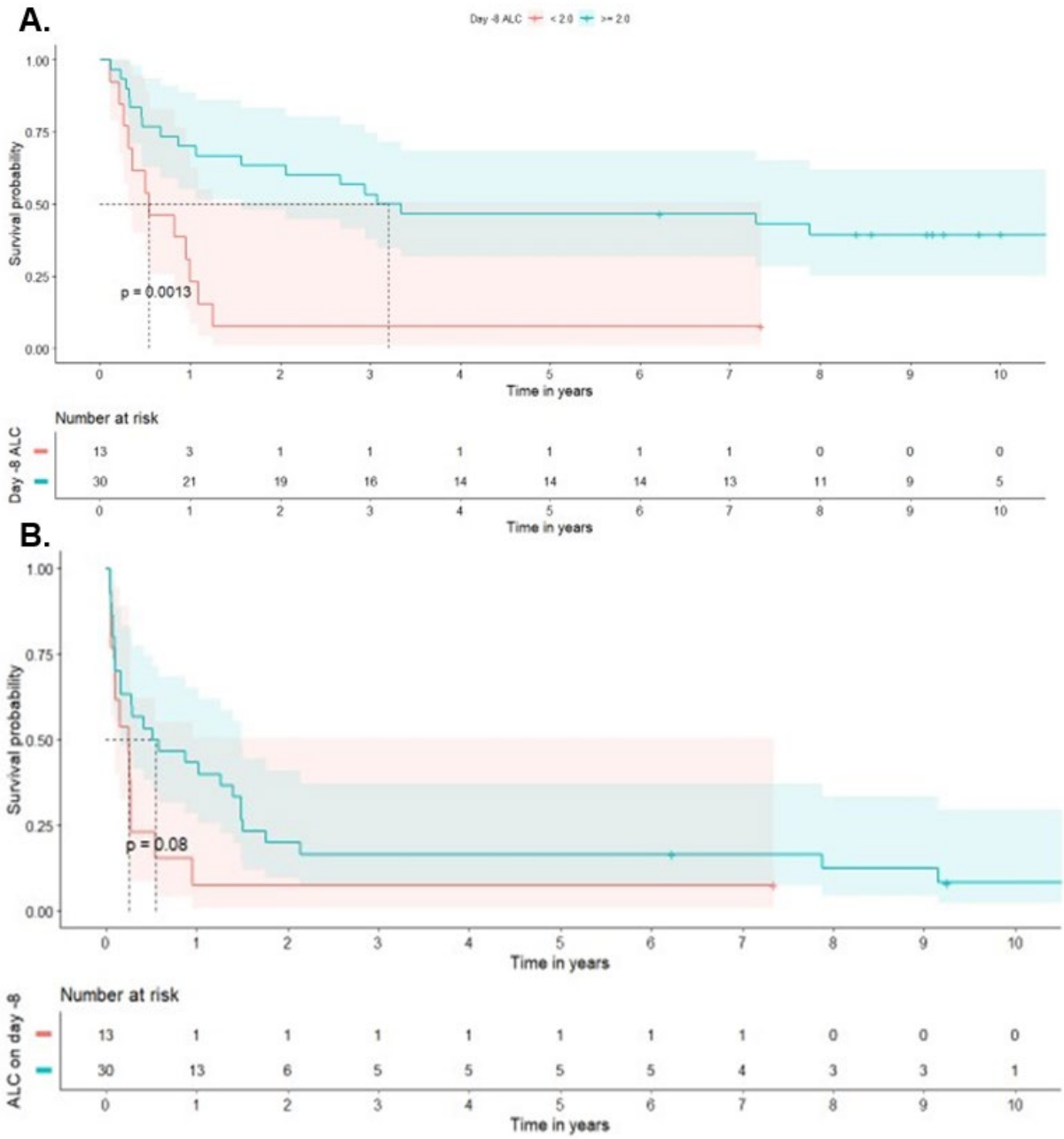
Supplementary Figure 5. Timecourse of T subset repopulation for the first 5 years in the AC and TMS arms. **A.** Timecourses of CD4 and CD8 T cell numbers/μl determined by NIH Clinical Laboratories. **B.** Timecourses of subsets of CD4 and CD8 T cells. CD4 cells were gated to distinguish Treg (CD127-CD25++) from nonTreg (conventional) CD4 T cells as in **Figure 4C.** **C.** The NonTreg and Treg CD4 and the CD8 cells were then gated to assess recent thymic emigrant (RTE) (CD45RA+CD34+), naive (CD45RA+CCR7+), central memory (CD45RA-CCR7+), effector memory (CD45RA-CCR7-) and TEMRA (CD45RA+CCR7-) subsets. T subset cells/μl were calculated from subset frequencies (see **Supplementary Figure 6**) and absolute number of CD4 and CD8 cells/μl. Box and whisker plots of AC (white box) and TMS (gray box) patients over a 5 year time course post transplant. Medians, quartiles and min/max values shown. Statistical significance as tested by Mann-Whitney unpaired non-parametric analysis: **** p <0.0001, *** p <0.001, ** p<0.01, * p<0.05. Number of patients assayed in each arm at each time point is shown below the white and gray boxes.



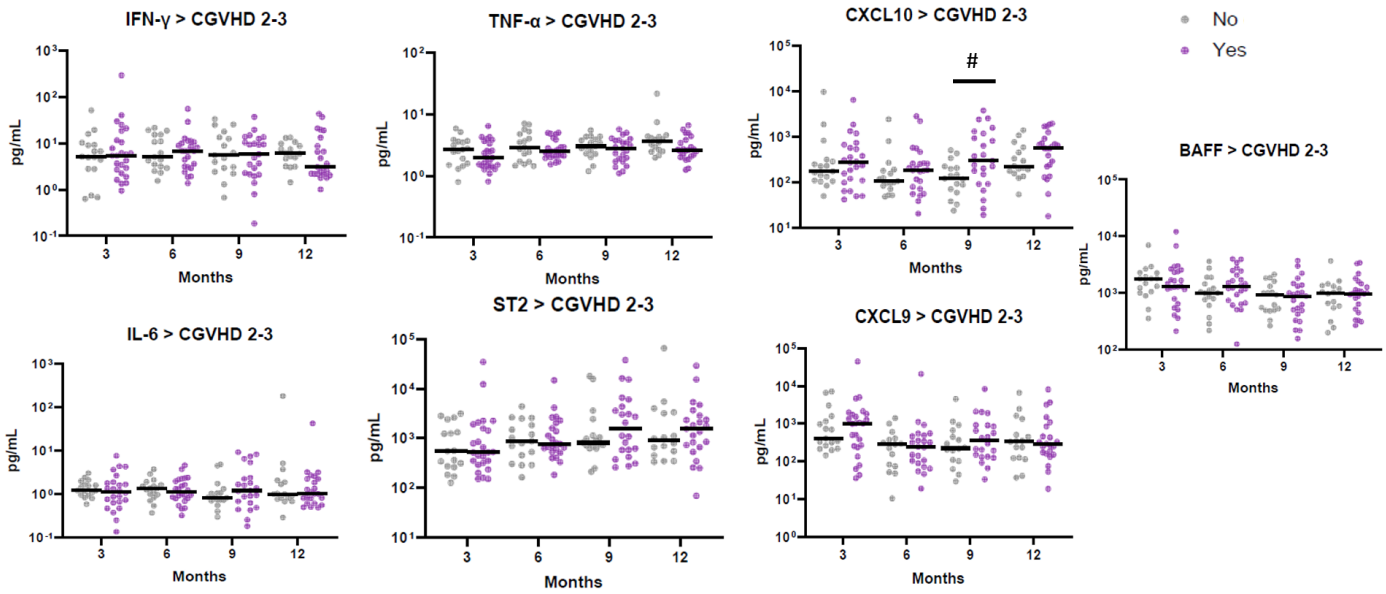
Supplementary Figure 6. Timecourse of T subset repopulation for the first 5 years in the AC and TMS arms. Timecourses of the percentages of subsets of CD4 and CD8 T cells. CD4 cells were gated to distinguish **A**. Treg (CD127-CD25++) from **B.** nonTreg (conventional) CD4 T cells as in Figure 4C. The NonTreg (**B.**) and Treg (**C.**) CD4 and the CD8 cells were then gated to assess recent thymic emigrant (RTE) (CD45RA+CD34+), naive (CD45RA+CCR7+), central memory (CD45RA-CCR7+), effector memory (CD45RA-CCR7-) and TEMRA (CD45RA+CCR7-) subsets. Box and whisker plots of AC (white box) and TMS (gray box) patients over a 5 year time course post transplant. Medians, quartiles and min/max values shown. Statistical significance as tested by Mann-Whitney unpaired non-parametric analysis: **** p <0.0001, *** p <0.001, ** p<0.01, * p<0.05.



Supplementary Figure 8. OS (A) and GRFS (B) by Day-8 ALC on Day 1 for patients on AC arm. Red vs green lines represent low vs high baseline ALC groups.



Supplementary Figure 8. Cytokine levels at 3-, 6-, 9- and 12- months among patients who developed moderate-to-severe chronic GVHD (purple circles) and those who did not (gray circles). Patients were included in this analysis if they were alive for 365 days posttransplant and did not develop relapse or progression prior to chronic GVHD diagnosis. #: p-value <0.05, q-value >0.05.



Supplementary Table 1. Acute GVHD maximum grade by arm and organ involvement with staging.

	AC, n=44	TMS, n=39
Maximum Grade Acute GVHD, n (%)		
1	6 (14)	5 (13)
2	9 (20)	10 (26)
3	11 (25)	9 (23)
4	4 (9)	2 (5)
Total	30 (68)	26 (67)
Acute GVHD Stage Organ Involvement, n (%)		
Skin		
1	4 (10)	4 (10)
2	10 (24)	2 (5)
3	2 (5)	2 (5)
4	0 (0)	0 (0)
GI		
1	8 (19)	8 (21)
2	6 (14)	5 (13)
3	6 (14)	3 (8)
4	1 (2)	2 (5)
Liver		
1	1 (2)	1 (2)
2	0 (0)	0 (0)
3	1 (2)	1 (2)
4	3 (7)	1 (2)

Supplementary Table 2. Chronic GVHD characteristics and specific organ involvement.

	AC, n=44	TMS, n=39
Maximum Chronic GVHD Global Severity Score, n (%)		
Mild	5 (11)	1 (3)
Moderate	4 (9)	9 (23)
Severe	3 (7)	14 (36)
Total	12 (27)	24 (62)
Onset of cGVHD, n (%)		
De Novo	2 (5)	8 (21)
Quiescent	5 (11)	12 (31)
Progressive	5 (11)	4 (10)
Type of cGVHD, n (%)		
Classic	6 (14)	15 (38)
Overlap	6 (14)	10 (26)
cGVHD Organ Involvement, n (%)		
Skin		
1	4 (10)	5 (13)
2	2 (5)	4 (10)
3	3 (7)	12 (31)
Mouth		
1	2 (5)	7 (18)
2	1 (2)	7 (18)
3	0 (0)	3 (8)
Eyes		
1	2 (5)	8 (21)
2	1 (2)	5 (13)
3	0 (0)	1 (3)
GI		
1	1 (2)	0 (0)
2	0 (0)	4 (10)
3	0 (0)	2 (5)
Liver		
1	0 (0)	5 (13)
2	1 (2)	4 (10)
3	0 (0)	1 (3)
Lungs		
1	2 (5)	3 (8)
2	0 (0)	1 (3)
3	0 (0)	0 (0)
Joints/Fascia		
1	0 (0)	2 (5)
2	0 (0)	1 (3)
3	0 (0)	0 (0)
Genital Tract (females only)	n=15	n=15
1	1 (7)	2 (13)
2	0 (0)	1 (7)
3	0 (0)	1 (7)

Supplementary Table 3: Adverse Events (Grade 3-4) through 100 days post-HSCT.

Grade 3-4 Adverse Events through Day +100, n (%)			
Adverse Event Category	AC N=44	TMS N=39	p-value
Allergy/immunology			
No	44 (100)	37 (95)	0.22
Yes	0 (0)	2 (5)	
Allergic reaction/hypersensitivity	0 (0)	2 (5)	
Cardiac arrhythmia			
No	41 (93)	37 (95)	1.00
Yes	3 (7)	2 (5)	
Atrial fibrillation	0 (0)	1 (3)	
Prolonged QTc interval	1 (2)	0 (0)	
Sinus tachycardia	1 (2)	0 (0)	
Ventricular tachycardia	1 (2)	1 (3)	
Cardiac general			
No	44 (100)	39 (100)	-
Yes	0 (0)	0 (0)	
Coagulation			
No	38 (86)	37 (95)	0.27
Yes	6 (14)	2 (5)	
Prolonged partial thromboplastin time	4 (9)	2 (5)	
Thrombotic microangiopathy	2 (5)	0 (0)	
Constitutional symptoms			
No	38 (86)	37 (95)	0.27
Yes	6 (14)	2 (5)	
Fatigue	3 (7)	0 (0)	
Fever	3 (7)	2 (5)	
Dermatology/skin			
No	39 (89)	37 (95)	0.44
Yes	5 (11)	2 (5)	
Dry skin	1 (2)	0 (0)	
Rash/desquamation	3 (7)	1 (3)	
Skin breakdown/decubitus ulcer	0 (0)	1 (3)	
Ulceration	1 (2)	0 (0)	
Endocrine			
No	43 (98)	38 (97)	1.00
Yes	1 (2)	1 (3)	
Glucose intolerance	1 (2)	1 (3)	
Gastrointestinal			
No	33 (75)	30 (77)	1.00
Yes	11 (25)	9 (23)	

Anorexia	1 (2)	0 (0)	
Diarrhea	8 (18)	7 (18)	
Dysphagia	1 (2)	0 (0)	
Fistula	0 (0)	1 (3)	
Nausea	2 (5)	3 (7)	
Obstruction	0 (0)	1 (3)	
Perforation	0 (0)	1 (3)	
Other	0 (0)	1 (3)	
Hemorrhage/bleeding			
No	41 (93)	37 (95)	1.00
Yes	3 (7)	2 (5)	
Anus	0 (0)	1 (3)	
Bladder	0 (0)	1 (3)	
Lower GI	1 (2)	1 (3)	
Pulmonary	1 (2)	0 (0)	
Upper GI	1 (2)	0 (0)	
Urinary	1 (2)	0 (0)	
Hepatobiliary/pancreas			
No	43 (98)	39 (100)	1.00
Yes	1 (2)	0 (0)	
Liver dysfunction/failure	1 (2)	0 (0)	
Infection			
Any			
No	9 (20)	18 (46)	**0.019**
Yes	35 (80)	21 (54)	
Bacterial			
No	18 (41)	29 (74)	**0.0037**
Yes	26 (59)	10 (26)	
Bacteremia	7 (16)	6 (15)	
Catheter-related	7 (16)	3 (7)	
C. diff colitis	1 (2)	2 (5)	
Lung	2 (5)	1 (3)	
Urinary tract	2 (5)	1 (3)	
Viral			
No	29 (66)	30 (77)	0.33
Yes	15 (34)	9 (23)	
Adenovirus	2 (5)	0 (0)	
BK virus	2 (5)	3 (7)	
CMV reactivation	18 (41)	4 (10)	
EBV	2 (5)	1 (3)	
HHV6	1 (2)	3 (7)	
HSV	1 (2)	0 (0)	
Influenza	1 (2)	1 (3)	

RSV	1 (2)	0 (0)	
Other*			
No	33 (75)	26 (67)	0.47
Yes	11 (25)	13 (33)	
Febrile Neutropenia (NOS)	8 (18)	5 (13)	
Fungal	2 (5)	1 (3)	
Parasitic	1 (2)	0 (0)	
Lymphatics			
No	43 (98)	39 (100)	1.00
Yes	1 (2)	0 (0)	
Edema	1 (2)	0 (0)	
Metabolic/laboratory			
No	16 (36)	12 (31)	0.65
Yes	28 (64)	27 (69)	
Acidosis	1 (2)	0 (0)	
Alkaline phosphatase	2 (5)	2 (5)	
ALT, SGPT	6 (14)	11 (28)	
AST SGOT	6 (14)	14 (36)	
Creatinine	4 (9)	4 (10)	
GGT	1 (2)	0 (0)	
Hyperbilirubinemia	6 (14)	2 (5)	
Hypercalcemia	1 (2)	0 (0)	
Hyperkalemia	3 (7)	2 (5)	
Hypermagnesemia	10 (23)	13 (33)	
Hyperuricemia	5 (11)	1 (3)	
Hypoalbuminemia	5 (11)	4 (10)	
Hypocalcemia	2 (5)	0 (0)	
Hypokalemia	9 (20)	2 (5)	
Hypomagnesemia	9 (20)	2 (5)	
Hyponatremia	5 (11)	5 (13)	
Hypophosphatemia	9 (20)	14 (36)	
Other - Steroid-induced hyperglycemia	0 (0)	1 (3)	
Musculoskeletal/soft tissue			
No	42 (5)	38 (97)	1.00
Yes	2 (5)	1 (3)	
Arthritis	0 (0)	1 (3)	
Muscle weakness (not due to neuropathy)	1 (2)	0 (0)	
Myositis	1 (2)	0 (0)	
Neurology			
No	35 (80)	36 (92)	0.12
Yes	9 (20)	3 (8)	
Ataxia	1 (2)	0 (0)	
Cognitive disturbance	1 (2)	0 (0)	

Confusion	1 (2)	1 (3)	
Dizziness	1 (2)	0 (0)	
Encephalopathy	2 (5)	1 (3)	
Mood alteration - anxiety	0 (0)	1 (3)	
Neurology - other	1 (2)	0 (0)	
Neuropathy - motor	1 (2)	0 (0)	
Neuropathy - sensory	1 (2)	0 (0)	
Seizure	2 (5)	0 (0)	
Somnolence/depressed levels	1 (2)	0 (0)	
Syncope	1 (2)	0 (0)	
Ocular/visual			
No	44 (100)	39 (100)	-
Yes	0 (0)	0 (0)	
Pain			
No	42 (95)	35 (90)	0.41
Yes	2 (5)	4 (10)	
Abdomen	0 (0)	1 (3)	
Anus	0 (0)	1 (3)	
Back	1 (2)	0 (0)	
Joint	1 (2)	0 (0)	
Muscle weakness (not due to neuropathy)	0 (0)	1 (3)	
Throat/pharynx/larynx	0 (0)	1 (3)	
Pulmonary/upper respiratory			
No	34 (77)	33 (85)	0.42
Yes	10 (23)	6 (15)	
ARDS	2 (5)	0 (0)	
DLCO	1 (2)	0 (0)	
Dyspnea	1 (2)	2 (5)	
Hypoxia	7 (16)	6 (15)	
Pleural effusion	2 (5)	0 (0)	
Pneumonitis/pulmonary	2 (5)	0 (0)	
Other - infiltrates, fungal pneumonia	1 (2)	0 (0)	
Renal/genitourinary			
No	36 (82)	28 (72)	0.31
Yes	8 (18)	11 (28)	
Cystitis	0 (0)	1 (3)	
Obstruction	1 (2)	0 (0)	
Other - acute kidney injury	1 (2)	1 (3)	
Other - dysuria	0 (0)	2 (5)	
Renal failure	6 (14)	8 (20)	
Secondary malignancy			
No	42 (95)	39 (100)	0.50
Yes	2 (5)	0 (0)	

PTLD	2 (5)	0 (0)	
Vascular			
No	42 (95)	36 (92)	0.66
Yes	2 (5)	3 (8)	
Thrombosis/embolism (vascular access-related)	1 (2)	1 (3)	
Thrombosis/thrombus/embolism	1 (2)	2 (5)	

Supplementary Table 4: Factors associated with cumulative incidence of severe chronic GVHD competing with death or progression in univariate analysis.

Description	Category	Cumulative Incidence at 1 Year (95% CI)	Cumulative Incidence at 2 Years (95% CI)	Cumulative Incidence at 5 Years (95% CI)	p-value
Treatment Arm	AC	0	0.045 (0.008-0.139)	0.045 (0.008-0.139)	**0.0002**
	TMS	0.103 (0.032-0.223)	0.256 (0.131-0.403)	0.285 (0.230-0.537)	
Age	20-35	0.095 (0.014-0.273)	0.238 (0.079-0.445)	0.286 (0.105-0.499)	0.93
	35-50	0.050 (0.003-0.219)	0.050 (0.003-0.219)	0.100 (0.014-0.287)	
	50-60	0.100 (0.016-0.279)	0.250 (0.086-0.457)	0.350 (0.147-0.562)	
	60+	0	0.045 (0.003-0.199)	0.091 (0.013-0.267)	
HCT-CI	1-3	0.063 (0.020-0.143)	0.190 (0.104-0.297)	0.254 (0.153-0.368)	0.059
	4+	0	0	0.050 (0.002-0.224)	
AC Arm	1-3	0	0.067 (0.011-0.197)	0.067 (0.011-0.197)	0.34
	4+	0	0	0	
TMS Arm	1-3	0.121 (0.037-0.259)	0.303 (0.154-0.466)	0.424 (0.249-0.589)	0.32
	4+	0	0	NR	
Karnofsky Performance Status	60-90	0.057 (0.018-0.130)	0.086 (0.034-0.167)	0.157 (0.082-0.254)	**0.015**
	100	0	0.462 (0.173-0.711)	0.462 (0.173-0.711)	
AC Arm	60-90	0	0	0	**0.0026**
	100	0	0.250 (0.027-0.587)	0.250 (0.027-0.587)	
TMS Arm	60-90	0.118 (0.036-0.253)	0.176 (0.069-0.324)	0.324 (0.171-0.487)	**0.034**
	100	0	0.800 (0.047-0.984)	0.800 (0.047-0.984)	
CD34+ Cell Dose	2-7	0.075 (0.019-0.185)	0.250 (0.127-0.393)	0.325 (0.184-0.474)	**0.039**
	7+	0.024 (0.002-0.111)	0.048 (0.008-0.145)	0.095 (0.028-0.212)	
AC Arm	2-7	0	0.071 (0.004-0.291)	0.071 (0.004-0.291)	0.86
	7+	0	0.034 (0.002-0.157)	0.034 (0.002-0.157)	
TMS Arm	2-7	0.115 (0.028-0.273)	0.346 (0.168-0.532)	0.462 (0.257-0.644)	0.16
	7+	0.077 (0.003-0.317)	0.077 (0.003-0.317)	0.231 (0.045-0.500)	

Parameters not associated with overall survival were sex (p=0.64), donor age group (4 groups; global p=0.65), prior transplant (none vs. any; p=0.82), disease status at transplant (no disease vs. active disease or minimal residual disease; p=0.71), chemosensitivity (sensitive vs. resistant; p=0.80), CMV match (mismatch vs. match; p=0.37), donor-recipient sex match (female donor, male recipient vs. other; p=0.77), Kahl relapse risk (low vs. intermediate/standard vs. high; global p=0.26 // low vs. intermediate/standard/high; p=0.85 // low/intermediate/standard vs. high; p=0.15), HLA Match (match vs. mismatch; 0.39), recipient CMV status (negative vs. positive; p=0.39), and CD3+ cell dose (quartiles; p=0.42).
Abbreviations: NR – not reached

Supplementary Table 5: Factors associated with cumulative incidence of severe chronic GVHD in multivariable analysis. Model resulted from backward selection from factors identified in univariate analysis; no other factors included in final model.

Parameter	HR (95% CI)	p-value
Treatment Arm		
AC	1.00 (reference)	**0.0079**
TMS	7.42 (1.69-32.50)	

Supplementary Table 6: Factors associated with cumulative incidence of treatment-related mortality (TRM) competing with relapse in univariate analysis.

Description	Category	Cumulative Incidence at 1 Year (95% CI)	Cumulative Incidence at 2 Years (95% CI)	Cumulative Incidence at 5 Years (95% CI)	p-value
Treatment Arm	AC	0.205 (0.100-0.336)	0.273 (0.150-0.411)	0.295 (0.167-0.435)	0.33
	TMS	0.205 (0.095-0.345)	0.205 (0.095-0.345)	0.385 (0.232-0.535)	
Age	20-59	0.148 (0.072-0.249)	0.180 (0.095-0.287)	0.262 (0.158-0.378)	**0.031**
	60+	0.364 (0.169-0.563)	0.409 (0.202-0.607)	0.545 (0.306-0.733)	
AC Arm	20-59	0.176 (0.070-0.323)	0.235 (0.108-0.391)	0.265 (0.128-0.423)	0.45
	60+	0.300 (0.061-0.595)	0.400 (0.107-0.687)	0.400 (0.107-0.687)	
TMS Arm	20-59	0.111 (0.027-0.263)	0.111 (0.027-0.263)	0.259 (0.111-0.436)	**0.017**
	60+	0.417 (0.138-0.679)	0.417 (0.138-0.679)	0.667 (0.293-0.879)	
HCT-CI	0-1	0.080 (0.013-0.230)	0.080 (0.013-0.230)	0.120 (0.029-0.282)	**0.0027**
	2+	0.259 (0.153-0.377)	0.310 (0.196-0.432)	0.431 (0.300-0.555)	
AC Arm	0-1	0.143 (0.020-0.379)	0.143 (0.02-0.379)	0.143 (0.020-0.379)	0.12
	2+	0.233 (0.100-0.399)	0.333 (0.170-0.506)	0.367 (0.195-0.540)	
TMS Arm	0-1	0	0	0.091 (0.004-0.350)	**0.011**
	2+	0.286 (0.132-0.460)	0.286 (0.132-0.460)	0.500 (0.299-0.672)	
Recipient CMV Status	Negative	0.083 (0.021-0.203)	0.139 (0.049-0.273)	0.222 (0.102-0.371)	**0.031**
	Positive	0.298 (0.174-0.432)	0.319 (0.191-0.455)	0.426 (0.280-0.564)	
AC Arm	Negative	0.059 (0.003-0.245)	0.176 (0.039-0.396)	0.176 (0.039-0.396)	0.11
	Positive	0.296 (0.136-0.476)	0.333 (0.162-0.515)	0.370 (0.189-0.553)	
TMS Arm	Negative	0.105 (0.016-0.291)	0.105 (0.016-0.291)	0.263 (0.091-0.475)	0.12
	Positive	0.300 (0.118-0.505)	0.300 (0.118-0.508)	0.500 (0.259-0.701)	
CD34+ Cell Dose (*10^6 cells)	2.0-7.0	0.213 (0.120-0.324)	0.262 (0.159-0.378)	0.395 (0.232-0.535)	0.066
	>7.0	0.190 (0.055-0.387)	0.190 (0.055-0.387)	0.190 (0.055-0.387)	
AC Arm	2.0-7.0	0.172 (0.061-0.331)	0.276 (0.127-0.445)	0.310 (0.151-0.485)	0.80
	>7.0	0.286 (0.077-0.542)	0.286 (0.077-0.542)	0.286 (0.077-0.542)	
TMS Arm	2.0-7.0	0.250 (0.116-0.410)	0.250 (0.116-0.410)	0.369 (0.287-0.632)	**0.025**
	>7.0	0	0	0	

Parameters not associated with treatment-related mortality were sex (p=0.64), donor age (4 groups; global p=0.99), number of prior treatment regimens (0-2 vs. 3+; p=0.87), prior transplants (none vs. any; p=0.47), disease status at transplant (no disease vs. active disease or minimal residual disease; p=0.78), chemosensitivity (sensitive vs. resistant; p=0.59), CMV match (mismatch vs. match; p=0.14), donor-recipient sex match (female donor, male recipient vs. other; p=0.83), Kahl relapse risk (low vs. intermediate/standard vs. high; global p=0.36), CD3+ cell dose (quartiles; p=0.31), and Karnofsky performance status at transplant (90-100 vs. 60-80; p=0.19). Abbreviations: NR – not reached

Supplementary Table 7: Factors associated with TRM in multivariable analysis. Model resulted from backward selection from factors identified in univariate analysis.

Parameter	HR (95% CI)	p-value
Treatment Arm		
AC	1.00 (reference)	0.64
TMS	0.84 (0.39-1.77)	
Age at Transplant		
20-59	1.00 (reference)	**0.0089**
60+	2.81 (1.30-6.11)	
Recipient CMV Status		
Negative	1.00 (reference)	**0.0042**
Positive	3.16 (1.44-6.93)	
HCT-CI Score		
0-1	1.00 (reference)	**0.0010**
2+	7.73 (2.29-26.08)	

Supplementary Table 8: Factors associated with overall survival (OS) in univariate analysis.

Description	Category	Median OS (years) (95% CI)	1-Year Probability (95% CI)	2-Year Probability (95% CI)	5-Year Probability (95% CI)	p-value
Treatment Arm	AC	1.4 (0.7-7.3)	0.568 (0.410-0.699)	0.477 (0.325-0.615)	0.364 (0.226-0.503)	0.30
	TMS	3.6 (2.2-NE)	0.718 (0.549-0.833)	0.718 (0.549-0.833)	0.462 (0.302-0.607)	
Age	20-59	4.3 (2.1-NE)	0.689 (0.556-0.789)	0.639 (0.506-0.746)	0.492 (0.362-0.609)	**0.021**
	60+	1.0 (0.4-3.1)	0.500 (0.282-0.684)	0.455 (0.244-0.643)	0.182 (0.057-0.363)	
AC Arm	20-59	1.4 (0.5-NE)	0.559 (0.378-0.706)	0.471 (0.298-0.625)	0.412 (0.248-0.569)	0.63
	60+	1.6 (0.2-3.3)	0.600 (0.253-0.827)	0.500 (0.184-0.753)	0.200 (0.031-0.475)	
TMS Arm	20-59	9.1 (3.4-NE)	0.852 (0.652-0.942)	0.852 (0.652-0.942)	0.593 (0.386-0.750)	**0.0039**
	60+	0.8 (0.1-3.6)	0.417 (0.152-0.665)	0.417 (0.152-0.665)	0.167 (0.027-0.413)	
HCT-CI	0-1	NR	0.800 (0.584-0.911)	0.760 (0.542-0.884)	0.600 (0.384-0.761)	**0.011**
	2+	2.4 (0.7-3.5)	0.569 (0.432-0.684)	0.517 (0.382-0.676)	0.328 (0.212-0.448)	
AC Arm	0-1	2.7 (0.8-NE)	0.643 (0.343-0.833)	0.571 (0.284-0.780)	0.429 (0.177-0.660)	0.27
	2+	1.1 (0.5-7.3)	0.533 (0.343-0.691)	0.433 (0.256-0.599)	0.333 (0.175-0.500)	
TMS Arm	0-1	NR	1	1	0.818 (0.447-0.951)	**0.0065**
	2+	3.3 (0.6-4.3)	0.607 (0.404-0.760)	0.607 (0.404-0.760)	0.321 (0.161-0.493)	
HLA Match	7/8	0.7 (0.3-7.3)	0.412 (0.186-0.626)	0.412 (0.186-0.626)	0.294 (0.107-0.511)	0.091
	8/8	3.4 (2.1-9.1)	0.697 (0.571-0.793)	0.636 (0.508-0.739)	0.439 (0.318-0.554)	
AC Arm	7/8	0.5 (0.3-NE)	0.333 (0.078-0.623)	0.333 (0.078-0.623)	0.333 (0.078-0.623)	0.29
	8/8	2.1 (1.0-7.9)	0.629 (0.448-0.765)	0.514 (0.340-0.664)	0.371 (0.216-0.527)	
TMS Arm	7/8	1.8 (0.0-NE)	0.500 (0.152-0.775)	0.500 (0.152-0.775)	0.250 (0.037-0.558	0.13
	8/8	5.8 (2.6-NE)	0.774 (0.584-0.885)	0.774 (0.584-0.885)	0.516 (0.330-0.674)	
Karnofsky Performance Status	60-80	1.0 (0.3-3.5)	0.438 (0.198-0.656)	0.375 (0.154-0.598)	0.188 (0.046-0.402)	0.055
	90-100	3.4 (2.1-9.1)	0.687 (0.561-0.783)	0.642 (0.515-0.744)	0.463 (0.341-0.576)	
AC Arm	60-80	1.0 (0.2-2.1)	0.364 (0.112-0.627)	0.273 (0.065-0.539)	0.182 (0.029-0.442)	0.12
	90-100	2.9 (0.8-NE)	0.636 (0.449-0.775)	0.545 (0.363-0.696)	0.424 (0.256-0.583)	
TMS Arm	60-80	3.5 (0.2-NE)	0.600 (0.126-0.882)	0.600 (0.126-0.882)	0.200 (0.01-0.582)	0.39
	90-100	5.0 (2.2-NE)	0.735 (0.553-0.853)	0.735 (0.553-0.853)	0.500 (0.324-0.653)	
Recipient CMV Status	Negative	6.5 (2.1-NE)	0.778 (0.604-0.882)	0.694 (0.517-0.818)	0.528 (0.355-0.674)	**0.024**
	Positive	2.6 (0.5-3.5)	0.532 (0.381-0.662)	0.511 (0.361-0.642)	0.319 (0.193-0.453)	
AC Arm	Negative	2.1 (0.5-NE)	0.706 (0.431-0.866)	0.529 (0.276-0.730)	0.412 (0.186-0.626)	0.46
	Positive	1.0 (0.3-7.9)	0.481 (0.287-0.652)	0.444 (0.256-0.617)	0.333 (0.168-0.509)	
TMS Arm	Negative	NR	0.842 (0.587-0.946)	0.842 (0.587-0.946)	0.632 (0.379-0.804)	**0.016**
	Positive	2.9 (0.4-6.8)	0.600 (0.357-0.776)	0.600 (0.357-0.776)	0.300 (0.123-0.501)	
Number of Prior Treatment Regimens	0-2	7.9 (1.1-NE)	0.718 (0.549-0.833)	0.641 (0.470-0.769)	0.538 (0.372-0.679)	0.059
	3+	2.7 (0.7-3.5)	0.568 (0.410-0.699)	0.545 (0.388-0.678)	0.295 (0.170-0.432)	
AC Arm	0-2	7.9 (0.5-NE)	0.733 (0.436-0.891)	0.533 (0.263-0.744)	0.533 (0.263-0.744)	0.13
	3+	1.0 (0.5-3.1)	0.486 (0.295-0.648)	0.448 (0.265-0.616)	0.276 (0.131-0.443)	
TMS Arm	0-2	7.5 (0.7-NE)	0.708 (0.484-0.849)	0.708 (0.484-0.849)	0.542 (0.327-0.714)	0.40
	3+	3.5 (0.5-6.8)	0.733 (0.436-0.891)	0.733 (0.436-0.891)	0.333 (0.122-0.564)	

Parameters not associated with overall survival were sex (p=0.75), donor age group (4 groups; global p=0.12), prior transplant (none vs. any; p=0.38), disease status at transplant (no disease vs. active disease or minimal residual disease; p=0.30), chemosensitivity (sensitive vs. resistant; p=0.19), CMV match (mismatch vs. match; p=0.79), donor-recipient sex match (female donor, male recipient vs. other; p=0.68), Kahl relapse risk (low vs. intermediate/standard vs. high; global p=0.51 // low/intermediate/standard vs. high; p=0.35), CD34+ cell dose (quartiles; p=0.96), and CD3+ cell dose (quartiles; p=0.70).
Abbreviations: NE – not estimable, NR – not reached

Supplementary Table 9: Factors associated with OS in multivariable analysis. Model resulted from backward selection from factors identified in univariate analysis.

Parameter	HR (95% CI)	p-value
Treatment Arm		
AC	1.00 (reference)	0.35
TMS	0.77 (0.45-1.33)	
Age at Transplant		
20-59	1.00 (reference)	**0.0062**
60+	2.27 (1.26-4.07)	
HCT-CI		
0-1	1.00 (reference)	**0.0038**
2+	2.71 (1.38-5.34)	
Recipient CMV Status		
Negative	1.00 (reference)	**0.013**
Positive	2.06 (1.17-3.63)	

Supplementary Table 10: Factors associated with GVHD-free, relapse-free survival (GRFS) in univariate analysis.

Description	Category	Median GRFS (years) (95% CI)	1-Year GRFS Probability (95% CI)	2-Year GRFS Probability (95% CI)	5-Year GRFS Probability (95% CI)	p-value
Treatment Arm	AC	0.29 (0.16-0.95)	0.341 (0.207-0.480)	0.182 (0.085-0.307)	0.136 (0.055-25.4)	0.71
	TMS	0.61 (0.40-1.00)	0.308 (0.173-0.454)	0.179 (0.079-0.313)	0.076 (0.020-0.187)	
HCT-CI	0-1	1.26 (0.69-2.06)	0.520 (0.312-0.692)	0.320 (0.152-0.502)	0.200 (0.073-0.372)	**0.0045**
	2+	0.31 (0.27-0.54)	0.241 (0.141-0.357)	0.121 (0.053-0.218)	0.069 (0.022-0.153)	
AC Arm	0-1	1.33 (0.26-9.16)	0.571 (0.284-0.780)	0.286 (0.088-0.524)	0.286 (0.088-0.524)	0.022
	2+	0.21 (0.10-0.51)	0.233 (0.103-0.394)	0.133 (0.042-0.278)	0.067 (0.012-0.192)	
TMS Arm	0-1	1.00 (0.50-3.02)	0.455 (0.167-0.707)	0.364 (0.112-0.627)	0.091 (0.005-0.333)	0.13
	2+	0.54 (0.30-0.92)	0.250 (0.111-0.418)	0.107 (0.027-0.251)	0.071 (0.013-0.204)	
HLA Match	7/8	0.28 (0.09-0.64)	0.118 (0.020-0.312)	0.059 (0.004-0.235)	0.059 (0.004-0.235)	0.059
	8/8	0.59 (0.40-1.00)	0.348 (0.237-0.463)	0.212 (0.123-0.317)	0.121 (0.057-0.212)	
AC Arm	7/8	0.16 (0.05-0.29)	0.110 (0.006-0.388)	NR	NR	**0.043**
	8/8	0.54 (0.16-1.26)	0.400 (0.240-0.555)	0.229 (0.108-0.376)	0.171 (0.070-0.311)	
TMS Arm	7/8	0.59 (0.07-1.00)	0.125 (0.007-0.423)	0.125 (0.007-0.423)	0.125 (0.007-0.423)	0.66
	8/8	0.61 (0.40-1.00)	0.290 (0.145-0.453)	0.194 (0.079-0.383)	0.067 (0.011-0.189)	
Kahl Relapse Risk	Low	1.00 (0.32-1.49)	0.481 (0.287-0.652)	0.259 (0.115-0.431)	0.185 (0.067-0.348)	**0.024**
	Intermediate/ Standard or High	0.41 (0.26-0.54)	0.250 (0.146-0.368)	0.143 (0.067-0.247)	0.071 (0.023-0.158)	
AC Arm	Low	0.95 (0.28-1.49)	0.462 (0.192-0.696)	0.154 (0.025-0.388)	0.154 (0.025-0.388)	0.29
	Intermediate/ Standard or High	0.26 (0.10-0.51)	0.290 (0.145-0.453)	0.194 (0.079-0.346)	0.129 (0.041-0.270)	
TMS Arm	Low	1.00 (0.31-3.07)	0.500 (0.229-0.722)	0.357 (0.130-0.594)	0.214 (0.052-0.448)	**0.019**
	Intermediate/ Standard or High	0.53 (0.35-0.92)	0.200 (0.073-0.372)	0.080 (0.014-0.235)	NR	
Disease Status at Transplant	No Disease	0.98 (0.40-1.49)	0.448 (0.265-0.616)	0.241 (0.107-0.405)	0.138 (0.043-0.286)	0.056
	Active/Minimal Residual Disease	0.35 (0.16-0.58)	0.235 (0.130-0.358)	0.137 (0.060-0.246)	0.098 (0.036-0.197)	
AC Arm	No Disease	0.91 (0.26-1.51)	0.438 (0.198-0.655)	0.188 (0.046-0.402)	0.188 (0.046-0.402)	0.15
	Active/Minimal Residual Disease	0.21 (0.10-0.54)	0.269 (0.119-0.445)	0.154 (0.048-0.315)	0.115 (0.029-0.267)	
TMS Arm	No Disease	1.00 (0.40-2.06)	0.462 (0.192-0.696)	0.308 (0.095-0.554)	0.077 (0.005-0.292)	0.16
	Active/Minimal Residual Disease	0.50 (0.31-0.70)	0.200 (0.073-0.372)	0.120 (0.030-0.277)	0.080 (0.014-0.225)	
Disease Chemosensitivity	Chemosensitive	0.87 (0.50-1.00)	0.388 (0.253-0.520)	0.224 (0.120-0.348)	0.143 (0.063-0.255)	**0.023**
	Chemoresistant	0.28 (0.10-0.58)	0.200 (0.081-0.356)	0.100 (0.025-0.236)	0.067 (0.012-0.192)	
AC Arm	Chemosensitive	0.51 (0.11-1.49)	0.407 (0.225-0.582)	0.185 (0.067-0.348)	0.185 (0.067-0.348)	0.21
	Chemoresistant	0.27 (0.08-0.58)	0.214 (0.052-0.448)	0.143 (0.023-0.366)	0.071 (0.005-0.275)	
TMS Arm	Chemosensitive	0.95 (0.50-1.39)	0.364 (0.174-0.557)	0.273 (0.111-0.464)	0.091 (0.016-0.251)	**0.044**
	Chemoresistant	0.33 (0.09-0.61)	0.188 (0.046-0.402)	0.063 (0.004-0.247)	0.063 (0.004-0.247)	

Parameters not associated with overall survival were sex (p=0.57), recipient age at transplant (20-59 vs. 60+; p=0.76), donor age group (4 groups; global p=0.35), prior transplant (none vs. any; p=0.57), number of prior treatment regimens (0-2 vs. 3+; p=0.31), CMV match (mismatch vs. match; p=0.11), recipient CMV Status (negative vs. positive; p=0.17), donor-recipient sex match (female donor, male recipient vs. other; p=0.26), Karnofsky performance status (60-80 vs. 90-100; p=0.35), CD34+ cell dose (quartiles; p=0.64), and CD3+ cell dose (quartiles; p=0.35).
Abbreviations: NR – not reached

Supplementary Table 11: Factors associated with GRFS in multivariable analysis. Model resulted from backward selection from factors identified in univariate analysis.

Parameter	HR (95% CI)	p-value
Treatment Arm		
AC	1.00 (reference)	0.51
TMS	0.86 (0.55-1.35)	
HCT-CI Score		
0-2	1.00 (reference)	**0.0047**
3+	2.08 (1.25-3.47)	

Supplementary Table 12: Factors associated with moderate-severe chronic GVHD-free survival (CFS) in univariate analysis.

Description	Category	Median Survival (years) (95% CI)	1-Year Survival Probability (95% CI)	2-Year Survival Probability (95% CI)	5-Year Survival Probability (95% CI)	p-value
Treatment Arm	AC	1.0 (0.7-2.7)	0.500 (0.346-0.636)	0.386 (0.245-0.536)	0.273 (0.152-0.488)	0.059
	TMS	0.9 (0.7-1.0)	0.385 (0.235-0.532)	0.179 (0.079-0.313)	0.077 (0.02-0.187)	
Sex	Male	0.8 (0.5-1.0)	0.358 (0.233-0.486)	0.226 (0.125-0.346)	0.132 (0.058-0.237)	0.060
	Female	1.0 (1.0-3.0)	0.633 (0.436-0.778)	0.400 (0.228-0.567)	0.267 (0.126-0.430)	
AC Arm	Male	0.9 (0.5-2.9)	0.448 (0.265-0.616)	0.379 (0.209-0.549)	0.241 (0.107-0.405)	0.68
	Female	1.0 (0.5-7.3)	0.667 (0.375-0.846)	0.400 (0.165-0.628)	0.333 (0.122-0.564)	
TMS Arm	Male	0.7 (0.5-1.0)	0.250 (0.102-0.431)	0.042 (0.003-0.176)	NR	**0.0023**
	Female	1.0 (0.7-3.0)	0.600 (0.318-0.797)	0.400 (0.165-0.628)	0.200 (0.049-0.424)	
HCT-CI	0-1	1.5 (0.9-3.0)	0.600 (0.384-0.761)	0.400 (0.213-0.581)	0.240 (0.098-0.417)	0.074
	2+	0.8 (0.6-1.0)	0.397 (0.272-0.519)	0.241 (0.141-0.357)	0.155 (0.076-0.259)	
AC Arm	0-1	1.8 (0.8-NE)	0.643 (0.343-0.833)	0.500 (0.229-0.722)	0.357 (0.130-0.594)	0.16
	2+	1.0 (0.5-2.7)	0.467 (0.284-0.630)	0.333 (0.175-0.500)	0.233 (0.103-0.394)	
TMS Arm	0-1	1.0 (0.5-2.0)	0.545 (0.229-0.780)	0.273 (0.065-0.539)	0.091 (0.005-0.333)	0.29
	2+	0.8 (0.5-1.0)	0.321 (0.161-0.493)	0.143 (0.045-0.295)	0.071 (0.013-0.204)	
Disease Status at Transplant	No Disease	1.0 (0.9-3.0)	0.483 (0.295-0.648)	0.414 (0.237-0.583)	0.276 (0.131-0.443)	0.062
	Active/Minimal Residual Disease	0.8 (0.5-1.0)	0.431 (0.294-0.561)	0.216 (0.116-0.336)	0.118 (0.048-0.222)	
AC Arm	No Disease	1.5 (0.8-NE)	0.500 (0.245-0.710)	0.500 (0.245-0.710)	0.438 (0.198-0.656)	0.14
	Active/Minimal Residual Disease	1.0 (0.4-1.5)	0.538 (0.333-0.706)	0.308 (0.146-0.485)	0.154 (0.048-0.315)	
TMS Arm	No Disease	1.0 (0.7-2.7)	0.462 (0.192-0.696)	0.308 (0.095-0.554)	0.077 (0.001-0.292)	0.23
	Active/Minimal Residual Disease	0.7 (0.5-1.0)	0.320 (0.152-0.502)	0.120 (0.03-0.277)	0.08 (0.001-0.225)	
Disease Chemosensitivity	Chemosensitive	1.0 (1.0-1.7)	0.531 (0.383-0.658)	0.368 (0.236-0.500)	0.224 (0.120-0.348)	**0.030**
	Chemoresistant	0.6 (0.4-1.0)	0.333 (0.175-0.515)	0.167 (0.061-0.328)	0.100 (0.025-0.236)	
AC Arm	Chemosensitive	1.0 (0.9-7.3)	0.593 (0.386-0.750)	0.444 (0.256-0.617)	0.333 (0.168-0.509)	0.21
	Chemoresistant	0.6 (0.3-2.9)	0.429 (0.177-0.660)	0.286 (0.088-0.524)	0.143 (0.023-0.366)	
TMS Arm	Chemosensitive	1.0 (0.7-1.7)	0.455 (0.244-0.643)	0.273 (0.111-0.464)	0.091 (0.016-0.251)	0.084
	Chemoresistant	0.7 (0.2-0.9)	0.250 (0.078-0.472)	0.063 (0.004-0.247)	0.063 (0.004-0.247)	
Donor-Recipient Sex Match	Other	1.0 (0.8-1.3)	0.500 (0.378-0.610)	0.329 (0.222-0.439)	0.200 (0.116-0.300)	0.10
	Female Donor, Male Recipient	0.7 (0.3-1.0)	0.231 (0.056-0.475)	0.077 (0.005-0.292)	0.077 (0.005-0.292)	
AC Arm	Other	1.0 (0.8-2.9)	0.564 (0.396-0.702)	0.410 (0.257-0.558)	0.282 (0.153-0.427)	0.37
	Female Donor, Male Recipient	0.3 (0.3-NE)	0.200 (0.008-0.582)	0.200 (0.008-0.582)	0.200 (0.008-0.582)	
TMS Arm	Other	0.9 (0.6-1.0)	0.419 (0.247-0.583)	0.226 (0.100-0.383)	0.097 (0.025-0.229)	0.27
	Female Donor, Male Recipient	0.8 (0.1-1.0)	0.250 (0.037-0.558)	NR	NR	
HLA Match	7/8	0.7 (0.3-1.0)	0.235 (0.073-0.449)	0.176 (0.043-0.383)	0.118 (0.020-0.312)	**0.041**
	8/8	1.0 (0.8-1.5)	0.515 (0.389-0.627)	0.318 (0.210-0.431)	0.197 (0.112-0.300)	
AC Arm	7/8	0.5 (0.3-7.3)	0.222 (0.034-0.513)	0.222 (0.034-0.513)	0.222 (0.034-0.513)	0.15
	8/8	1.1 (0.9-2.9)	0.600 (0.420-0.740)	0.429 (0.264-0.583)	0.286 (0.149-0.438)	
TMS Arm	7/8	0.8 (0.1-1.0)	0.250 (0.037-0.558)	0.125 (0.007-0.423)	NR	0.20
	8/8	1.0 (0.7-1.0)	0.419 (0.247-0.583)	0.194 (0.079-0.346)	0.097 (0.025-0.229)	

Supplementary Table 13: Factors associated with moderate-severe CFS in multivariable analysis. Model resulted from backward selection from factors identified in univariate analysis.

Parameter	HR (95% CI)	p-value
Treatment Arm		
AC	1.00 (reference)	**0.021**
TMS	1.79 (1.09-2.93)	
Sex		
Male	1.00 (reference)	**0.0061**
Female	0.48 (0.29-0.81)	
HCT-CI Score		
0-2	1.00 (reference)	**0.02**
3+	1.90 (1.11-3.26)	

Supplementary Table 14: Factors associated with cumulative incidence of relapse (CIR) of underlying malignancy competing with death in univariate analysis.

Description	Category	Cumulative Incidence at 1 Year (95% CI)	Cumulative Incidence at 2 Years (95% CI)	Cumulative Incidence at 5 Years (95% CI)	p-value
Treatment Arm	AC	0.341 (0.205-0.482)	0.477 (0.322-0.617)	0.523 (0.363-0.660)	**0.0027**
	TMS	0.205 (0.095-0.345)	0.205 (0.095-0.345)	0.205 (0.095-0.345)	
Kahl Relapse Risk	Low	0.180 (0.088-0.298)	0.280 (0.163-0.409)	0.300 (0.179-0.431)	**0.041**
	Intermediate/ Standard or High	0.424 (0.252-0.587)	0.455 (0.277-0.616)	0.485 (0.303-0.645)	
AC Arm	Low	0.167 (0.050-0.341)	0.375 (0.183-0.567)	0.417 (0.214-0.608)	0.051
	Intermediate/ Standard or High	0.550 (0.303-0.742)	0.600 (0.342-0.784)	0.650 (0.383-0.824)	
TMS Arm	Low	0.192 (0.068-0.364)	0.192 (0.068-0.364)	0.192 (0.068-0.364)	0.79
	Intermediate/ Standard or High	0.231 (0.050-0.487)	0.231 (0.050-0.487)	0.232 (0.050-0.487)	
CD34+ Cell Dose (*10^6 cells)	2.0-7.0	0.197 (0.108-0.305)	0.262 (0.159-0.388)	0.279 (0.172-0.395)	0.0064
	>7.0	0.476 (0.248-0.673)	0.571 (0.325-0.757)	0.619 (0.365-0.796)	
AC Arm	2.0-7.0	0.276 (0.128-0.446)	0.414 (0.231-0.588)	0.448 (0.259-0.621)	0.24
	>7.0	0.429 (0.166-0.671)	0.571 (0.254-0.796)	0.643 (0.297-0.851)	
TMS Arm	2.0-7.0	0.125 (0.038-0.265)	0.125 (0.038-0.265)	0.125 (0.038-0.265)	0.012
	>7.0	0.571 (0.131-0.857)	0.571 (0.131-0.857)	0.571 (0.131-0.857)	
Number of Prior Treatment Regimens	0-2	0.205 (0.095-0.344)	0.205 (0.095-0.344)	0.231 (0.113-0.373)	**0.013**
	3+	0.341 (0.205-0.482)	0.477 (0.322-0.617)	0.500 (0.342-0.639)	
AC Arm	0-2	0.267 (0.077-0.505)	0.267 (0.077-0.505)	0.333 (0.113-0.575)	0.079
	3+	0.379 (0.205-0.553)	0.586 (0.378-0.745)	0.621 (0.409-0.775)	
TMS Arm	0-2	0.167 (0.050-0.342)	0.167 (0.050-0.342)	0.167 (0.050-0.342)	0.50
	3+	0.267 (0.076-0.507)	0.267 (0.076-0.507)	0.267 (0.076-0.507)	

Parameters not associated with cumulative incidence of relapse were sex (p=0.81), recipient age at transplant (20-59 vs. 60+; p=0.45), donor age group (4 groups; global p=0.60), prior transplant (none vs. any; p=0.73), disease status at transplant (no disease vs. active disease or minimal residual disease; p=0.22), chemosensitivity (sensitive vs. resistant; p=0.22), HLA match (7/8 vs. 8/8; p=0.23), Karnofsky performance status at transplant (60-80 vs. 90 vs. 100; global p=0.37 // 60-80 vs. 90-100; p=0.93 // 60-90 vs. 100; p=0.18), HCT-CI score (0-1 vs. 2. vs. 3. vs. 4; global p=0.86 // 0-1 vs. 2.-4; p=0.66 // 0-3 vs. 4; p=0.74, CMV match (mismatch vs. match; p=0.15), donor-recipient sex match (female donor, male recipient vs. other; p=0.28), recipient CMV status (negative vs. positive; p=0.65), and CD3+ cell dose (quartiles; p=0.86).

Supplementary Table 15: Factors associated with relapse in multivariable analysis. Model resulted from backward selection from factors identified in univariate analysis.

Parameter	HR (95% CI)	p-value
Treatment Arm		
AC	1.00 (reference)	**0.022**
TMS	0.38 (0.17-0.87)	
Number of Prior Treatment Regimens		
0-2	1.00 (reference)	**0.018**
3+	2.70 (1.19-6.13)	
Kahl Relapse Risk		
Low	1.00 (reference)	**0.023**
Intermediate/Standard or High	2.32 (1.13-4.79)	
CD34+ Cell Dose (*10^6 cells)		
2.0-7.0	1.00 (reference)	0.0046
>7.0	2.90 (1.39-6.07)	

Supplementary Table 16: Factors associated with cumulative incidence of relapse-related mortality (RRM) in univariate analysis.

Description	Category	Cumulative Incidence at 1 Year (95% CI)	Cumulative Incidence at 2 Years (95% CI)	Cumulative Incidence at 5 Years (95% CI)	p-value
Treatment Arm	AC	0.227 (0.116-0.361)	0.273 (0.150-0.410)	0.341 (0.204-0.482)	0.064
	TMS	0.104 (0.032-0.226)	0.104 (0.032-0.226)	0.157 (0.062-0.291)	
Donor Age	18-34	0.119 (0.043-0.237)	0.119 (0.043-0.237)	0.168 (0.783-0.297)	0.051
	35+	0.220 (0.107-0.357)	0.268 (0.143-0.411)	0.341 (0.200-0.488)	
AC Arm	18-34	0.182 (0.054-0.368)	0.182 (0.054-0.368)	0.273 (0.107-0.470)	0.29
	31 5+	0.273 (0.107-0.470)	0.364 (0.168-0.564)	0.409 (0.200-0.608)	
TMS Arm	1018-34	0.050 (0.003-0.211)	0.050 (0.003-0.211)	0.050 (0.003-0.211)	0.064
	35+	0.158 (0.036-0.358)	0.158 (0.036-0.358)	0.263 (0.089-0.478)	
Number of Prior Treatment Regimens	0-2	0.128 (0.046-0.254)	0.128 (0.046-0.254)	0.128 (0.046-0.254)	**0.023**
	3+	0.206 (0.101-0.337)	0.253 (0.134-0.390)	0.370 (0.227-0.514)	
AC Arm	0-2	0.133 (0.020-0.355)	0.133 (0.020-0.355)	0.133 (0.020-0.355)	**0.033**
	3+	0.276 (0.128-0.447)	0.345 (0.178-0.519)	0.448 (0.259-0.621)	
TMS Arm	0-2	0.125 (0.030-0.291)	0.125 (0.030-0.291)	0.125 (0.030-0.291)	0.85
	3+	0.072 (0.004-0.290)	0.072 (0.004-0.290)	0.217 (0.046-0.469)	
CMV Match	Mismatch	0.304 (0.131-0.498)	0.391 (0.193-0.585)	0.391 (0.193-0.585)	**0.036**
	Match	0.117 (0.051-0.212)	0.117 (0.051-0.212)	0.202 (0.110-0.313)	
AC Arm	Mismatch	0.417 (0.140-0.677)	0.583 (0.241-0.816)	0.583 (0.241-0.816)	**0.044**
	Match	0.156 (0.056-0.303)	0.156 (0.056-0.303)	0.250 (0.115-0.411)	
TMS Arm	Mismatch	0.182 (0.025-0.456)	0.182 (0.025-0.456)	0.182 (0.025-0.456)	0.30
	Match	0.071 (0.012-0.208)	0.071 (0.012-0.208)	0.147 (0.044-0.308)	
Kahl Relapse Risk	Low	0.101 (0.036-0.203)	0.121 (0.048-0.229)	0.203 (0.104-0.326)	0.054
	Intermediate/ Standard or High	0.273 (0.134-0.432)	0.303 (0.156-0.465)	0.333 (0.179-0.496)	
AC Arm	Low	0.125 (0.031-0.291)	0.167 (0.050-0.324)	0.250 (0.098-0.438)	0.094
	Intermediate/ Standard or High	0.350 (0.151-0.559)	0.400 (0.185-0.608)	0.450 (0.222-0.655)	
TMS Arm	Low	0.079 (0.013-0.227)	0.079 (0.013-0.227)	0.160 (0.048-0.330)	0.55
	Intermediate/ Standard or High	0.154 (0.022-0.401)	0.154 (0.022-0.401)	0.154 (0.022-0.401)	

Parameters not associated with relapse-related mortality were sex (p=0.81), recipient age at transplant (20-59 vs. 60+; p=0.39), prior transplants (none vs. any; p=0.82), disease status at transplant (no disease vs. active disease or minimal residual disease; p=0.24), chemosensitivity (sensitive vs. resistant; p=0.90), HLA match (7/8 vs. 8/8; p=0.16), donor-recipient sex match (female donor, male recipient vs. other; p=0.36), CD3+ cell dose (quartiles; p=0.30), CD34+ cell dose (quartiles; p=0.45), Karnofsky performance status at transplant (60-80 vs. 90 vs. 100; global p=0.48 // 60-80 vs. 90-100; p=0.74 // 60-90 vs. 100; p=0.23), HCT-CI score (0-1 vs. 2. vs. 3. vs. 4; global p=0.93 // 0-1 vs. 2.-4; p=0.61 // 0-3 vs. 4; p=0.74), and recipient CMV status (negative vs. positive; p=0.95)

Supplementary Table 17: Factors associated with relapse-related mortality (RRM) in multivariable analysis. Model resulted from backward selection from factors identified in univariate analysis.

Parameter	HR (95% CI)	p-value
Treatment Arm		
AC	1.00 (reference)	0.22
TMS	0.56 (0.23-1.41)	
Donor Age		
18-34	1.00 (reference)	**0.041**
35+	2.54 (1.04-6.20)	
Number of Prior Treatment Regimens		
0-2	1.00 (reference)	0.058
3+	2.52 (0.97-6.56)	

Supplementary Table 18: Cox regression of OS using cytokines measured at 6 months. All cytokines have the same measuring unit of pg/mL. The association of TNF-α with survival was only maintained as a dichotomized factor separated at the median of all measured patients after considering the respective Kaplan-Meier curves of OS.

Factor	**Univariate**			**Multivariable (adjusted for treatment arm, age ≥60, recipient CMV status, HCT-CI ≥2)**		
	HR	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**
TNF-α	1.256	1.011 to 1.538	**0.03**			
TNF-α ≥2.7 pg/mL (median)	4.499	1.893 to 12.39	**0.001**	3.771	1.522 to 10.78	**0.007**
IL-6	1.523	1.148 to 1.979	**0.002**	1.501	1.063 to 2.066	**0.01**
ST2	1.000	0.9998 to 1.000	0.94			
CXCL9	0.9999	0.9987 to 1.000	0.58			
CXCL10	1.000	0.9992 to 1.001	0.85			
BAFF	1.000	0.9997 to 1.000	0.71			