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Long-term outcome of allogeneic hematopoietic cell transplantation for T-cell prolymphocytic leukemia – a study on behalf of the Chronic Malignancies Working Party of the EBMT

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Running title: Long-term outcome of allo-HCT for T-PLL

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CONFLICT OF INTEREST DISCLOSURE

The authors declare no competing interests related to the study.

AUTHOR CONTRIBUTION

JDS, OT, LG, DML, LGAB, and LK were involved in study design, analysis and drafting the paper. All other co-authors contributed data to the study, critically revised the paper and approved the submitted and final version.

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To the Editor,

T-cell prolymphocytic leukemia is a rare subtype of an aggressive T-cell lymphoma[1] associated with poor outcomes[2]. Intravenous Alemtuzumab is recommended as 1st line treatment[3] but with a high cumulative relapse incidence (RI) and short responses between 3-11 months. We recently published data on autologous hematopoietic cell transplantation which could be a consolidative option, though not curative[4]. Monocentric[5, 6] and registries studies[7-10] have found that allogeneic hematopoietic cell transplantation (allo-HCT) was associated with both high toxicity and high RI despite being the only hope of cure. Such studies, however, have a follow-up of <5 years and concerns remain about long-term efficacy and tolerance. Here we provide an update on the long-term outcome after allo-HCT in patients with verified T-PLL diagnoses whose short/medium term outcome were previously reported within two EBMT CMWP studies[11, 12]. In this study the findings indicate that long-term survival in patients with T-PLL remains disappointingly poor, and allo-HCT appears to be curative in fewer than 20% of patients.

This retrospective study was approved by the CMWP of the EBMT. We selected patients with verified T-PLL diagnoses undergoing allo-HCT between 1995 and 2012 from the EBMT registry who were described in 2 previous reports[11, 12]. Primary endpoint was overall survival (OS), and secondary endpoints were relapse-free survival (RFS), relapse, and non-relapse mortality (NRM). This retrospective study was approved by the CMWP of the EBMT.

Patients' characteristics are reported in Table 1. Data on previous treatment lines was available for 46 patients, of whom 31 (67.4%) had received 1 line, 9 (19.6%) 2 lines, and 6 (13.0%) ≥3 lines, including alemtuzumab in 91% of those treated (Figure 1). Median interval between initiation of 1st line therapy and allo-HCT was 5.5 (IQR, 4.6-8.1) months. Median time between the last alemtuzumab protocol initiation and allo-HCT was 5.0 (IQR, 4.2-6.6) months.

At time of transplantation, 47.2% of patients were in complete response (CR), 11.1% had progressive disease (PD) and the remainder partial response (PR) (33.3%) or stable disease (SD) (8.3%). Donors were mostly HLA-compatible, either related (45.5%) or unrelated (41.6%). Conditioning was myeloablative (MAC) in 51.4% and reduced intensity (RIC) in 48.6%. Total body irradiation (TBI) was not used or used <6 Gy in 46 (69.7%) and used ≥6 Gy in 20 (30.3%) patients. The distribution of TBI among MAC and RIC and the listing of conditioning are reported in Supplemental Table S1. In vivo T-cell depletion (TCD); mostly ATG was given in 32 (56.1%) patients. Source of stem cells was peripheral blood in 66 (85.7%). Graft-versus-host disease (GvHD) prophylaxis was conducted mostly with ciclosporin combined with a short course of methotrexate (47.3%) or with mycophenolate mofetil (21.8%) (Table 1).

With median follow-up after allo-HCT of 12.5 (IQR 6.0 to 14.4) years; the 6- and 10-year probabilities (95% CI) for OS were 29% (18-39) and 21% (11-31), for PFS 20% (10-29) and 9% (1-17), 6- and 10-

year cumulative incidence for relapse were 42% (31-54) and 46% (34-58) and for NRM 38% (27-49) and 40% (28-51) (Figure 2). Of note, relapse events regularly occurred throughout the whole duration of follow-up.

The respective cumulative incidence (95% CI) of acute GvHD (aGvHD) was 27% (17-37) at day 100, including 15% (7-23) grade III or higher and of chronic (c)GvHD at 1 year 39% (27-50), including 13% (5-21) extensive (Supplemental Figure S1).

Half of the 10 secondary malignancies reported during follow-up were PTLD (5, all within the first 13 months after allo-HCT), 2 were skin tumors, 1 pulmonary epidermoid carcinoma, 1 'other kidney tumor including renal cell carcinoma' and 1 other, unspecified, carcinoma. The cumulative incidence of secondary malignancies increased from 9% (95% CI, 2-16%) at 2 years to 14% (95% CI, 6-23%) at 10 years.

Fifty-nine (76.6%) patients succumbed after allo-HCT. Cause of death, unknown for 7 patients (11.9%) was in the remaining cases relapse/progression (n=23), infection (n=12), GvHD (n=8), secondary malignancy (n=3) or other (n=6). The 12 fatal infections were of bacterial (n=2), viral (n=2) , fungal (n=2) or unreported origin (n=6). The 2-year cumulative incidence of progression-related death was 22% (95%CI, 13-31%), followed by infection-related death (13%, 95%CI 6-21%), and GvHD (10%, 95% CI 4-17%) and other or unknown cause of death (5%, 95% 0-10%). The 10-year cumulative incidence of death due to relapse/progression and infection reached 32% (95% CI, 21-43%) and 16% (95% CI, 8-43%), respectively. No other causes of death were reported between 2 and 10 years except for unknown/other causes of death amounting to a 10-year cumulative incidence of 15% (95% CI, 6-23%).

Univariable analyses revealed a significant association of three variables with better outcome: more favorable disease status at allo-HCT (CR vs no CR), use of TBI (≥6 Gy vs no TBI or <6 Gy) and later calendar year of transplantation. (Supplemental Table S2) Exploratory multivariable analysis included those variables and additionally age at time of allo-HCT. Patients in CR at allo-HCT and those receiving TBI≥6 Gy showed significantly lower risk of relapse and longer PFS and OS. Older age at allo-HCT was also associated with lower risk of relapse and longer PFS. None of the analyzed factors were significantly associated with NRM. (Supplemental Table S2)

Results from this study rely on the same patients as previously published[11, 12] but with substantially longer follow-up and confirm findings from previous reports in T-PLL[1, 5-10] on the poor outcomes, highlighting that only a minority (10-20%) of T-PLL patients achieve long-term disease control of the disease that offers hope of a cure. However, considering the absence of available alternative such as fratricide-resistant CAR-T or bispecific antibodies, and given the natural poor prognosis, allo-HCT remains imperative in T-PLL treatment algorithms for eligible patients and should be optimized. Failures are related to high RI above 40% at 6 years, and high NRM also at almost 40% at 6 years, with infectious complications prevailing. These relapses after a massive incidence within the first year continue steadily with very late occurrences, translating into an RI much higher compared to other mature T-cell neoplasia, such as peripheral T-cell lymphoma (PTCL)[13].

With the usual precautions, given the retrospective nature and small sample size, these results point to 3 potential ways of improvement. A positive evolution of practices in the management of infections could improve the results which is suggested by the association of NRM with calendar year of allo-HCT albeit not confirmed in MVA. The quality of disease control at allo-HCT appears crucial. Unlike PTCL, for which the results of allo-HCT in PR/SD patients remain acceptable, the probability of achieving long-term survival in non-CR patients appears very low in T-PLL, with many patients experiencing both early and late relapses. Beyond alemtuzumab, it is essential to find new therapeutic approaches that can bridge patients successfully to allo-HCT. Choice of conditioning must be addressed. In line with the CIBMTR study[10] we did not find a benefit of MAC. However, applying the previously used cut-off[11], we confirmed the benefit of at least 6 Gy TBI on the risk of relapse. This result is in line with other studies of T-cell neoplasia, including acute lymphoblastic leukemia and PTCL[14, 15].

A paradoxical result was the association of older age at allo-HCT with better PFS and lower risk of relapse. We might hypothesize that older patients were selected based on stricter criteria for the absence of comorbidities compared to younger patients, or that the systematic use of reduced-intensity conditioning resulted in lower toxicity. However, unmeasured confounders may also have contributed to those findings.

Moreover, an important question not addressed by this study is the potential role of pretransplant alemtuzumab in allo-HCT failures. In the CIBMTR study[10], the authors did not analyze the impact of pretransplant alemtuzumab, however peri transplant *in vivo* TCD strategies (with ATG and/or alemtuzumab) resulted in an increased TRM and inferior disease-free survival. Unlike in other mature T-cell neoplasia, alemtuzumab is essential in T-PLL, since it is the only drug enabling achieving CR in most patients. In CLL, the use of alemtuzumab has been associated with unfavorable outcomes of allo-HCT, in both prospective and retrospective cohort studies. The risk of infection and higher NRM could be one of the main reasons. In addition, residual circulating alemtuzumab levels at the time of allo-HCT can be associated with a significant reduction in T-cell engraftment at day 100[16]. Thus, it could be concluded that the logically recommended alemtuzumab washout before allo-HCT, so as not to annihilate the graft versus leukemia (cGVL) effect, in fact allows the T-PLL to become progressive again at the time of allo-HCT. Despite its anti-neoplastic activity, alemtuzumab is complex to be used as a bridge and alternatives are warranted. The development of therapies specially targeting CD7 almost constantly expressed by T-PLL cells, as well as TRBC1 could be used alone or as a bridge to allo-HCT.

Finally, there is evidence that T-PLL is less susceptible to GVL effects than other lymphomas[5], questioning the role of allo-HCT in general and emphasizing the need for more effective cellular therapies in T-PLL. Auto-HCT[4] could also be an option for a proportion of patients, though more data is needed to establish its place in the T-PLL treatment algorithm.

In conclusion, this long-term analysis suggests that if we want to continue doing allo-HCT for eligible T-PLL patients, we need to optimize our practices in terms of infectious risk management and novel bridges to transplantation. Incorporating at least intermediate-dose TBI into conditioning could become a recommendation if its value is confirmed in larger, more recent cohorts of patients.

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Table 1 Patients' and transplantations' characteristics (n=77)

(allo-HCT – allogeneic hematopoietic cell transplantation, ATG – antithymocyte globulin, auto-HCT – autologous hematopoietic cell transplantation, CR – complete remission, CsA – cyclosporin A, HCT-CI – hematopoietic cell transplantation comorbidity index, IQR – interquartile range, KPS – Karnofsky performance status, MMF – mycophenolate mofetil, MMUD – mismatched unrelated donor, MTX – methotrexate, MUD – matched unrelated donor, Nb – number, PR – partial remission, UD – unrelated donor)

	Total N (%)
Total	77 (100)
Patient sex	
Male	54 (70.1)
Female	23 (29.9)
Year of diagnosis; median (IQR)	2005 (2003-2007)
Age at diagnosis; median (IQR); years	51.0 (46.7-58.6)
Lymphocyte count at diagnosis; median (IQR); $x10^9$/L; missing 58	44 (18-90)
Cytogenetics; missing 52	
Normal karyotype	3 (12.0)
Abnormal karyotype	22 (88.0)
Age at allo-HCT, median (IQR); years	53.6 (47.6-59.6)
(range); years	(23.6-71.1)
<50	27 (35.1)
50-60	34 (44.2)
≥60	16 (20.8)
KPS at allo-HCT; missing 40	
≤80	11 (29.7)
90 or 100	26 (70.3)
HCT-CI; missing 65	
low risk (0)	7 (58.3)
intermediate risk (1-2)	3 (25.0)
high risk (≥3)	2 (16.7)
Year of allo-HCT	
Median (IQR)	2006 (2004-2008)
<2005	22 (28.6)
≥2005	55 (71.4)
Interval diagnosis - allo-HCT; median (IQR); months	10.5 (6.0-17.2)
Disease stage at allo-HCT; missing 5	
CR	34 (47.2)
PR	24 (33.3)
Stable disease	6 (8.3)
Relapse / progression	8 (11.1)
Number of previous lines of therapy; missing 31	
1	31 (67.4)
2	9 (19.6)
≥3	6 (13.0)
Alemtuzumab before allo-HCT; missing 31	42 (91.3)
Auto-HCT before allo-HCT	2 (2.6)
Donor type	
Identical sibling	35 (45.5)
MUD	32 (41.6)
MMUD	6 (7.8)
UD, number of mismatches unknown	4 (5.2)
Donor: Female to male	17 (22.1)
Donor age; median (IQR); years; missing 21	43.8 (32.8-52.6)
Stem cell source	
BM	11 (14.3)
PB	66 (85.7)
CMV serostatus; missing 25	
Patient(-) / donor(-)	14 (26.9)
Patient(-) / donor(+)	6 (11.5)
Patient(+) / donor(-)	14 (26.9)
Patient(+) / donor(+)	18 (34.6)
T-cell depletion, missing 20	
No	24 (42.1)
Yes, *in vivo*	32 (56.1)

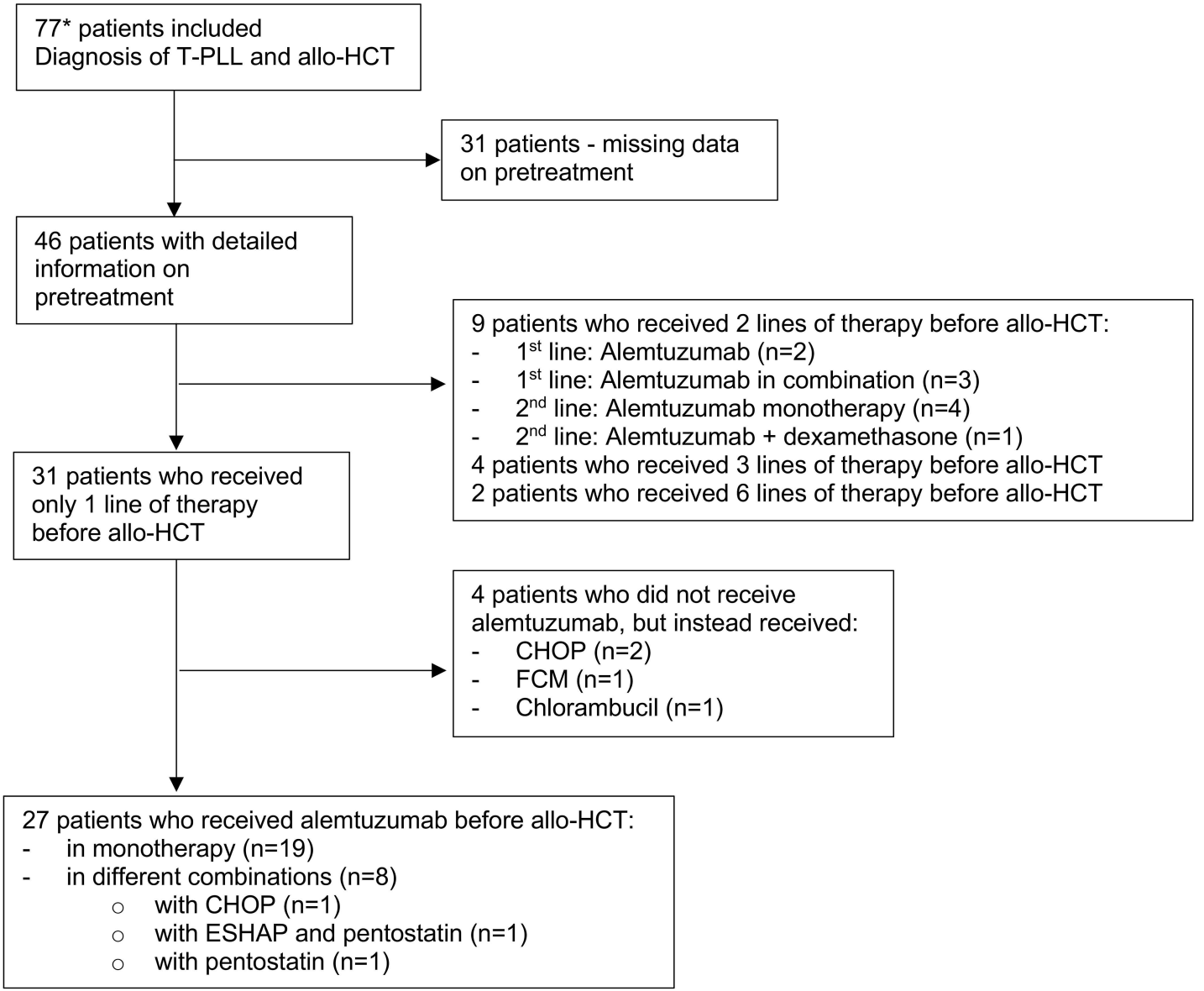
Yes, *ex vivo*	1 (1.8)
ATG given as conditioning at allo-HCT; missing 21	16 (28.6)
GvHD prophylaxis, missing 22	
CsA+MTX	26 (47.3)
CsA+MMF	12 (21.8)
CsA alone	8 (14.5)
Other	8 (14.5)
Nb of infused CD34(+) cells; median (IQR) x 10^6/kg body weight; missing 32	5.9 (3.9-7.5)

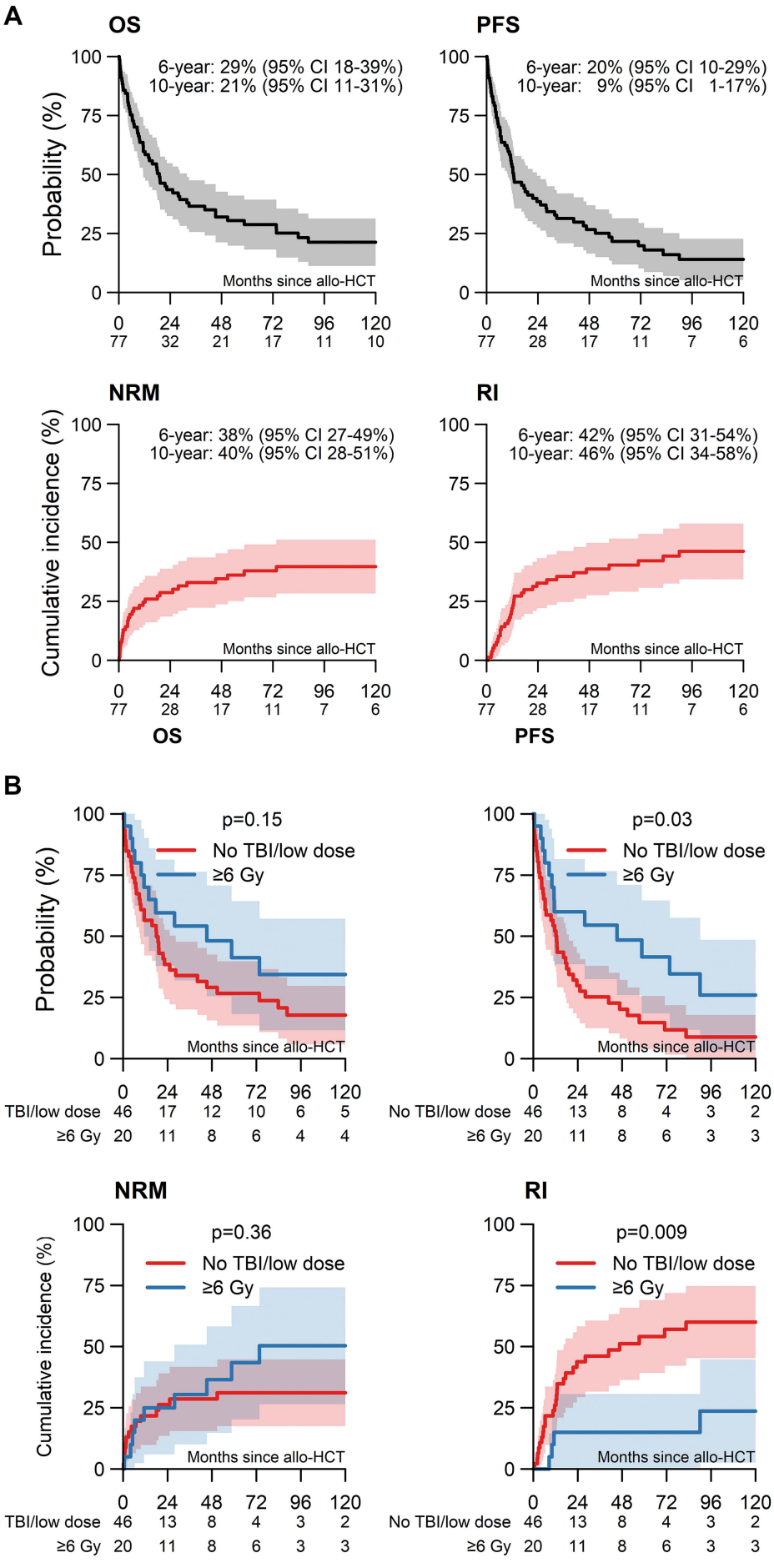
Figure legends

Figure 1 Flow diagram depicting the number of patients with different number of lines of therapy and different types of treatment before allo-HCT (CHOP – cyclophosphamide, doxorubicine, vincristine, prednisone; FCM – Fludarabine, Cyclophosphamide, Mitoxantrone)

* 1 patient of the former retrospective study (Wiktor-Jedrzejczak W, Leukemia, 2012) was excluded (no T-PLL)

Figure 2 Outcomes after allogeneic hematopoietic cell transplantation for T-cell prolymphocytic leukemia. a**)** Overall survival (OS), progression free survival (PFS), non-relapse mortality (NRM), cumulative relapse incidence (RI) for all patients, b**)** OS, PFS, NRM and RI stratified by TBI ≥6 Gy. Numbers below the graphs show the number of patients at risk. Shaded areas show the 95% confidence intervals.


77* patients included
Diagnosis of T-PLL and allo-HCT
31 patients - missing data on pretreatment
46 patients with detailed information on pretreatment
9 patients who received 2 lines of therapy before allo-HCT:
- 1st line: Alemtuzumab (n=2)
- 1st line: Alemtuzumab in combination (n=3)
- 2nd line: Alemtuzumab monotherapy (n=4)
- 2nd line: Alemtuzumab + dexamethasone (n=1)
4 patients who received 3 lines of therapy before allo-HCT
2 patients who received 6 lines of therapy before allo-HCT
31 patients who received only 1 line of therapy before allo-HCT
4 patients who did not receive alemtuzumab, but instead received:
- CHOP (n=2)
- FCM (n=1)
- Chlorambucil (n=1)
27 patients who received alemtuzumab before allo-HCT:
- in monotherapy (n=19)
- in different combinations (n=8)
o with CHOP (n=1)
o with ESHAP and pentostatin (n=1)
o with pentostatin (n=1)


A
OS
6-year: 29% (95% CI 18-39%)
10-year: 21% (95% CI 11-31%)
Probability (%)
Months since allo-HCT
0 24 48 72 96 120
77 32 21 17 11 10
PFS
6-year: 20% (95% CI 10-29%)
10-year: 9% (95% CI 1-17%)
Months since allo-HCT
0 24 48 72 96 120
77 28 17 11 7 6
NRM
6-year: 38% (95% CI 27-49%)
10-year: 40% (95% CI 28-51%)
Cumulative incidence (%)
Months since allo-HCT
0 24 48 72 96 120
77 28 17 11 7 6
OS
RI
6-year: 42% (95% CI 31-54%)
10-year: 46% (95% CI 34-58%)
Months since allo-HCT
0 24 48 72 96 120
77 28 17 11 7 6
PFS
B
p=0.15
No TBI/low dose
≥6 Gy
Probability (%)
Months since allo-HCT
0 24 48 72 96 120
No TBI/low dose 46 17 12 10 6 5
≥6 Gy 20 11 8 6 4 4
p=0.03
No TBI/low dose
≥6 Gy
Months since allo-HCT
0 24 48 72 96 120
No TBI/low dose 46 13 8 4 3 2
≥6 Gy 20 11 8 6 3 3
NRM
p=0.36
No TBI/low dose
≥6 Gy
Cumulative incidence (%)
Months since allo-HCT
0 24 48 72 96 120
No TBI/low dose 46 13 8 4 3 2
≥6 Gy 20 11 8 6 3 3
RI
p=0.009
No TBI/low dose
≥6 Gy
Months since allo-HCT
0 24 48 72 96 120
No TBI/low dose 46 13 8 4 3 2
≥6 Gy 20 11 8 6 3 3

Supplemental Table S1: Additional patients' and transplantations' characteristics on TBI implementation in conditioning.

	Whole group	No TBI	TBI 2-4 Gy	TBI ≥6 Gy	Unknown TBI dose
	N (%)	N (%)	N (%)	N (%)	N (%)
Total	77	42	4	20	11
Myeloablative Conditioning	**38 (51.4)**	**14 (33.3)**		**16 (80.0)**	**8 (100.0)**
BuCy +/- others	1 (1.4)	1 (2.4)			
FluBu +/- others	1 (1.4)	1 (2.4)			
TBI +/- Cy +/- others	24 (32.4)			16 (80.0)	8 (100.0)
Others	12 (16.2)	12 (28.6)			
Reduced Intensity Conditioning	**36 (48.6)**	**28 (66.7)**	**4 (100.0)**	**4 (20.0)**	
FluBu +/- others	4 (5.4)	4 (9.5)			
FluMel +/- others	13 (17.6)	13 (31.0)			
FluTreo +/- others	1 (1.4)	1 (2.4)			
TBI +/- Cy +/- Flu +/- others	8 (10.8)		4 (100.0)	4 (20.0)	
Others	10 (13.5)	10 (23.8)			
Intensity description missing	*3*				*3*

Supplemental Table S2:

Univariable analysis of probability of overall survival (OS) and progression free survival (PFS) and cumulative non-relapse mortality (NRM) incidence and relapse incidence (RI) at 6 years after allo-HCT with (95% confidence intervals). The probabilities of OS and PFS were obtained using Kaplan-Meier methods and cumulative incidence of NRM and RI was obtained using the crude cumulative incidence estimator. P-values measure the probability that curves are similar (so do not just compare the 6-year estimates) and were obtained with the log-rank test for OS and PFS, Gray's test for NRM and RI and censoring events after 10 years. Analysis of post-transplant variables was done using a 100-day and 1-year landmark models for acute graft-versus-host disease (aGvHD) and chronic graft-versus-host disease (cGvHD), respectively. CI: confidence interval; CR: complete response; TBI: total body irradiation,. ALZ: alemtuzumab. Pt: patients, Dr: donors. Conso: consolidation.

Multivariable analysis (MVA). Estimates were obtained using Cox (cause-specific) proportional hazards models for overall survival (OS), progression free survival (PFS), risk of non-relapse mortality (NRM) and risk of relapse.

Univariable analysis									
						6-Year			
		OS (95% CI)	***P***	**PFS (95% CI)**	***P***	**NRM (95% CI)**	***P***	**RI (95% CI)**	***P***
All patients		29 (18-39)		20 (10-29)		38 (27-49)		42 (31-54)	
Pre-transplant variables									
Age at allo-HCT			0.31		0.46		0.44		0.22
	<50 y.	24 (7-40)		12 (0-25)		35 (16-53)		53 (34-73)	
	50-60 y.	28 (13-44)		25 (10-40)		45 (28-61)		30 (15-46)	
	≥60 y.	39 (14-65)		26 (2-49)		27 (4-51)		47 (21-73)	
Sex			0.21		0.23		0.18		0.59
	Male	24 (12-36)		16 (5-26)		44 (30-58)		40 (27-54)	
	Female	40 (18-61)		29 (9-50)		24 (5-42)		47 (25-69)	
Year of allo-HCT			**0.04**		0.11		**0.01**		0.16
	<2005	14 (0-28)		9 (0-21)		59 (39-80)		32 (12-51)	
	≥2005	35 (22-49)		25 (13-38)		29 (16-41)		46 (32-60)	
Conso. post ALZ 1st line			0.29		0.82		0.11		0.13
	yes	43 (24-62)		24 (7-40)		23 (7-39)		53 (34-72)	
	other	34 (12-57)		28 (7-50)		38 (15-60)		34 (12-57)	
ALZ single agent 1st line			0.66		0.90		0.07		0.09
	yes	45 (22-68)		23 (4-43)		16 (0-33)		60 (38-83)	
	no	35 (16-53)		26 (8-44)		38 (20-57)		36 (17-55)	
Previous lines of therapy			0.44		0.85		0.63		0.72
	1 line	40 (23-58)		24 (9-39)		30 (13-46)		46 (28-64)	
	≥2 lines	37 (11-63)		29 (4-54)		27 (4-49)		44 (17-71)	
Karnofsky score at HCT			0.05		0.09		0.71		0.56
	≤80%	27 (1-54)		18 (0-41)		36 (8-65)		45 (16-75)	
	90-100%	48 (28-68)		31 (12-50)		32 (13-50)		38 (18-57)	
Interval diagnosis-HCT			0.98		0.68		0.62		0.48
	<12 m.	29 (15-42)		22 (9-34)		40 (26-55)		38 (24-52)	
	≥12 m.	29 (11-47)		16 (0-32)		36 (17-55)		48 (30-67)	
Disease status at allo-HCT			**0.008**		**0.01**		0.42		0.55
	CR	48 (30-65)		33 (15-50)		27 (12-42)		41 (22-59)	
	Other	18 (5-30)		12 (2-23)		38 (22-53)		50 (34-66)	
Donor type			0.42		0.53		0.49		0.25
	MRD	36 (20-52)		24 (9-39)		41 (24-57)		35 (19-51)	
	Other	22 (8-36)		16 (4-29)		36 (20-51)		48 (32-64)	
Age of donor			0.20		0.40		0.05		0.26
	<45 y.	20 (5-36)		13 (0-26)		51 (32-69)		37 (19-55)	
	≥45 y.	43 (24-62)		28 (10-45)		23 (7-39)		49 (30-69)	
Conditioning intensity			0.55		0.67		0.38		0.25
	Standard	27 (13-42)		24 (10-39)		41 (25-57)		35 (20-50)	
	Reduced	33 (17-49)		16 (2-30)		29 (14-44)		55 (37-73)	
TBI in conditioning			0.15		**0.03**		0.36		**0.009**
	≥6 Gy	41 (18-64)		42 (19-65)		43 (20-67)		57 (42-72)	

	no / low dose	27 (14-40)		12 (2-22)		31 (18-45)		15 (0-31)	
Source of stem cells			0.47		0.17		0.61		0.08
	BM	36 (8-65)		36 (8-65)		45 (16-75)		18 (0-41)	
	PB	28 (16-39)		17 (7-27)		36 (24-48)		47 (34-60)	
CMV Serostatus (Pt/Dr) (-): negative (+): positive			0.07		0.11		0.12		0.32
	- / -	14 (0-33)		7 (0-21)		43 (17-69)		50 (24-76)	
	- / +	33 (0-71)		33 (0-71)		33 (0-71)		33 (0-71)	
	+ / -	36 (11-61)		29 (5-52)		50 (24-76)		21 (0-43)	
	+ / +	58 (33-82)		30 (5-55)		13 (0-31)		57 (30-83)	
Post-transplant variables									
aGvHD at 100 days			0.20		0.65		0.28		0.55
	no	39 (25-54)		29 (14-43)		28 (14-42)		47 (31-63)	
	yes	26 (3-48)		18 (0-40)		39 (14-64)		42 (18-67)	
cGvHD at 1 year			0.58		0.67		0.33		0.19
	no	43 (21-64)		38 (15-61)		34 (12-56)		28 (7-49)	
	yes	63 (42-85)		42 (17-67)		11 (0-26)		47 (22-72)	

Multivariable analysis (MVA)

		OS		**PFS**		**NRM**		**Relapse**	
		HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
TBI									
	low dose/no TBI	1.0		1.0		1.0		1.0	
	≥6 Gy	0.49 (0.25-0.97)	***0.04***	0.37 (0.19-0.73)	***0.004***	0.77 (0.31-1.90)	*0.57*	0.17 (0.06-0.51)	***0.002***
Age at allo-HCT (per 10 year older)		0.77 (0.57-1.04)	*0.08*	0.74 (0.55-0.99)	***0.04***	0.87 (0.55-1.36)	*0.54*	0.60 (0.40-0.91)	***0.02***
Year of allo-HCT (per year later)		0.97 (0.87-1.08)	*0.59*	0.98 (0.88-1.08)	*0.64*	0.95 (0.82-1.10)	*0.50*	1.00 (0.87-1.15)	*0.98*
Disease status at allo-HCT									
	CR	0.53 (0.29-0.97)	***0.04***	0.50 (0.28-0.89)	***0.02***	0.54 (0.22-1.30)	*0.17*	0.45 (0.21-0.96)	***0.04***
	Other	1.0		1.0		1.0		1.0	

HR: hazard ratio; CI: confidence interval; CR: complete response; TBI: total body irradiation

Figure legends

Supplemental Figure S1 Graft versus host disease (GvHD). Cumulative incidence of a**)** acute, and b) chronic GvHD. The number below the graph show the number of patients at risk for an event. The individual cumulative incidence curves are stacked on top of each other.

Supplemental Figure S1