haematologica
Journal of the Ferrata Storti Foundation

Autologous hematopoietic cell transplantation for T-cell prolymphocytic leukemia: a retrospective study on behalf of the Chronic Malignancies Working Party of the EBMT

by Joanna Drozd-Sokolowska, Luuk Gras, Linda Koster, Rodrigo Martino, María Queralt Salas, Urpu Salmenniemi, Teresa Zudaire, Lucrecia Yañez, Mar Bellido, Matthew Collin, Martin Kaufmann, Piotr Kozlowski, Xavier Poiré, Christelle Ferra, Antònia Sampol, Keith M.O. Wilson, Anne Cairoli, Tobias Gedde-Dahl, Eric Deconinck, Milena Mirabile, Felipe Suarez, Kavita Raj, Michel van Gelder, Ibrahim Yakoub-Agha, Olivier Tournilhac, and Donal P. McLornan

Received: September 24, 2023.
Accepted: January 2, 2024.

Citation: Joanna Drozd-Sokolowska, Luuk Gras, Linda Koster, Rodrigo Martino, María Queralt Salas, Urpu Salmenniemi, Teresa Zudaire, Lucrecia Yañez, Mar Bellido, Matthew Collin, Martin Kaufmann, Piotr Kozlowski, Xavier Poiré, Christelle Ferra, Antònia Sampol, Keith M.O. Wilson, Anne Cairoli, Tobias Gedde-Dahl, Eric Deconinck, Milena Mirabile, Felipe Suarez, Kavita Raj, Michel van Gelder, Ibrahim Yakoub-Agha, Olivier Tournilhac, and Donal P. McLornan. Autologous hematopoietic cell transplantation for T-cell prolymphocytic leukemia: a retrospective study on behalf of the Chronic Malignancies Working Party of the EBMT.
Haematologica. 2024 Jan 11. doi: 10.3324/haematol.2023.284359 [Epub ahead of print]

Autologous hematopoietic cell transplantation for T-cell prolymphocytic leukemia: a retrospective study on behalf of the Chronic Malignancies Working Party of the EBMT

Joanna Drozd-Sokolowska[1], Luuk Gras[2], Linda Koster[3], Rodrigo Martino[4], María Queralt Salas[5], Urpu Salmenniemi[6], Teresa Zudaire[7], Lucrecia Yañez[8], Mar Bellido[9], Matthew Collin[10], Martin Kaufmann[11], Piotr Kozlowski[12], Xavier Poiré[13], Christelle Ferra[14], Antònia Sampol[15], Keith M. O. Wilson[16], Anne Cairoli[17], Tobias Gedde-Dahl[18], Eric Deconinck[19], Milena Mirabile[20], Felipe Suarez[21], Kavita Raj[22], Michel van Gelder[23], Ibrahim Yakoub-Agha[24], Olivier Tournilhac[25], Donal P. McLornan[22]

[1] Central Clinical Hospital, The Medical University of Warsaw, Warsaw, Poland; jdrozd@wum.edu.pl

[2] EBMT Statistical Unit, Leiden, the Netherlands; luuk.gras@ebmt.org

[3] EBMT Leiden Study Unit, Leiden, the Netherlands; cmwpebmt@lumc.nl

[4] Hospital Santa Creu i Sant Pau, Barcelona, Spain; rmartino@santpau.cat

[5] Hematology Department (ICHMO). Hospital Clinic de Barcelona, Barcelona, Spain; mqsalas@clinic.cat

[6] Department of Hematology, Helsinki University Hospital Comprehensive Cancer Center, Helsinki, Finland; urpu.salmenniemi@hus.fi

[7] Unidad de Ensayos Clínicos de Hematología Pabellón A, bajo., Pamplona, Spain; teresa.zudaire.ripa@navarra.es

[8] Hospital U. Marqués de Valdecilla, Santander, Spain; lucrecia.yanez@scsalud.es

[9] University Medical Center Groningen (UMCG), Groningen, Netherlands; m.bellido@umcg.nl

[10] Adult HSCT unit, Newcastle, United Kingdom; matthew.collin@ncl.ac.uk

[11] Robert Bosch Krankenhaus, Stuttgart, Germany; martin.kaufmann@rbk.de

[12] Örebro University Hospital, Orebro, Sweden; piotr.kozlowski@regionorebrolan.se

[13] Cliniques Universitaires St. Luc, Brussels, Belgium; xavier.poire@uclouvain.be

[14] ICO-Hospital Universitari Germans Trias i Pujol, Badalona, Spain; cferra@iconcologia.net

[15] Hospital Son Espases, IDISBA, Palma de Mallorca, Balearic Islands, Spain; antonia.sampolm@ssib.es

[16] University Hospital of Wales, Cardiff, United Kingdom; keith.wilson@wales.nhs.uk

[17] Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland; anne.cairoli@chuv.ch

[18] Oslo University Hospital, Rikshospitalet, Oslo, Norway; tgeddeda@ous-hf.no

[19] Université de Franche-Comté, CHU Besançon, EFS, INSERM, UMR RIGHT, F-25000 Besançon, France; edeconinck@chu-besancon.fr

[20] Unità Operativa Di Medicina Interna, Civitanove, Italy; milena.mirabile@hotmail.it

[21] Adult hematology, Hôpital Necker-Enfants Malades, AP-HP.Centre Université Paris Cité, Paris, France; felipe.suarez@aphp.fr

[22] University College London Hospitals NHS Trust, London, United Kingdom; kavita.raj@nhs.net donal.mclornan@nhs.net

[23] University Hospital Maastricht, Maastricht, Netherlands; m.van.gelder@mumc.nl

[24] CHU de Lille, Univ Lille, INSERM U1286, Infinite, 59000, Lille, France; ibrahim.yakoubagha@chru-lille.fr
[25] CHU Estaing, Clermont-Ferrand University Hospital, Clermont-Ferrand, France; otournilhac@chu-clermontferrand.fr

Running head: Auto-HCT for T-PLL

Corresponding author:
Ms Joanna E. Drozd-Sokolowska
Department of Hematology, Transplantation, and Internal Medicine
Central Clinical Hospital, The Medical University of Warsaw
Banacha 1a Str
Warsaw, 02-097, Poland
Tel. +48 22 599 28 48
e-mail address: joanna.drozd-sokolowska@wum.edu.pl

Data-sharing statement: The final analysis dataset will be available upon specific request to the Chronic Malignancies Working Party Chair.

Text word count: 1499
Number of tables and figures: 3
Number of supplementary tables and figures: 3

Funding statement: The research did not receive any grants from funding agencies in the public, commercial, or not-for-profit sectors.

ACKNOWLEDGEMENTS
We are indebted to all centers participating to the EBMT database, and especially the ones who contributed to this retrospective analysis.

AUTHOR CONTRIBUTION
JDS, OT, LG, DML, IYA 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.

COMPETING INTEREST STATEMENT:
The authors declare no competing interests directly related to the study.

Keywords: T-cell prolymphocytic leukemia, autologous hematopoietic cell transplantation, alemtuzumab, consolidation

T-cell prolymphocytic leukemia is a rare subtype of mature T-cell non-Hodgkin lymphoma[1,2] with poor prognosis. Recently the first consensus criteria have been proposed by the T-PLL International Study Group (TPLL-ISG)[3] to allow the systematic approach to the diagnosis, treatment, and response assessment.

Treatment of T-PLL is challenging. Alemtuzumab, an anti-CD52 monoclonal antibody, administered intravenously[4] is considered the mainstay of the first first-line treatment. Alemtuzumab is associated with objective response rates (ORR) higher than 90%, but with short duration of response and progression-free survival (PFS) between 8 and 11 months[3]. Therefore, despite the high ORR, it is recommended to offer consolidative treatment to all eligible patients. Allogeneic hematopoietic cell transplantation (allo-HCT) is considered the golden standard for this indication though it is associated with only modest long-term disease control[5-7]. Autologous hematopoietic cell transplantation (auto-HCT) is cited as an option[8,9]. The vague recommendation for auto-HCT is a result of extremely scarce data for this potential therapeutic option[10,11].

The current study aimed to study outcomes after auto-HCT using data from the EBMT, an organization comprising over 600 transplant centres from mainly Europe. EBMT centres commit to obtain informed consent according to the local regulations applicable at the time in order to report pseudonymized data.

Patients diagnosed with T-PLL undergoing their first auto-HCT between 2000 and 2019 were selected. Data to verify the diagnosis, as well as clarification on treatment pre and post auto-HCT and cause of death, was requested from participating centres.

T-PLL was diagnosed based on the TPLL-ISG consensus criteria[3]. In our study the diagnosis could be verified for patients for whom additional confirmatory data was provided by the participating centers.

The primary objective was to assess overall survival (OS). The secondary objectives were to examine PFS (the time between auto-HCT and relapse/progression of disease or death), relapse incidence (RI), non-relapse mortality (NRM), cause of death, incidence of second primary malignancies (SPM) and response to treatment. Response to treatment at day 100 was assessed according to TPLL-ISG recommendations[3].

We separately analysed a subset of patients for whom data was available to ascertain that these were patients who obtained a response to the first line alemtuzumab and who proceeded to consolidation with auto-HCT (the post-alemtuzumab consolidation group). A second, smaller subset consisted of those patients in the post-alemtuzumab consolidation group who had received alemtuzumab as monotherapy (the post-alemtuzumab monotherapy consolidation group).

The median follow-up was calculated using the reverse Kaplan–Meier estimator. The Kaplan-Meier estimator was used for OS and PFS, and the crude cumulative incidence estimator was used for the competing events – RI together with NRM, and SPM. The log-rank test was used to assess differences between groups in OS and PFS and Gray's test was used to assess differences in RI and NRM according to sex, age, disease status and Karnofsky performance status, year of auto-HCT, total body irradiation (TBI) and number of pre-treatment lines. All statistical tests were 2-sided and p-values

<0.05 were considered significant. All analyses were performed in R version 4.2.2 using 'survival', 'cmprsk', and 'prodlim' packages.

Forty-two patients were initially identified. Additional confirmatory data were obtained for 21 of these patients, among whom 19 fulfilled the diagnostic criteria for T-PLL. Two patients were excluded based on immunophenotype. Thus, 40 T-PLL patients from 31 centers form the "whole group" for this analysis (Table 1). In 25 of these 40 patients detailed information on pretreatment was available (Figure 1). Twenty-four patients of these 25 (96%) had been exposed to alemtuzumab before auto-HCT. Twenty patients (80%) received only 1 line of previous therapy.

In the 20 patients for whom auto-HCT was used as a first line consolidation, one patient did not receive alemtuzumab but fludarabine and cyclophosphamide. Thus, the "post-alemtuzumab first line consolidation group", as defined above, consisted of 19 patients including 15 patients who received alemtuzumab as monotherapy (the "post-alemtuzumab monotherapy first line consolidation group"). In these 15 patients, the median interval between start of first line alemtuzumab and auto-HCT was 8.1 (IQR 6.1-9.2) months.

Data on mobilization was available for 13 patients. Twelve (92%) patients required only 1 mobilization attempt, while 1 (8%) required 2 mobilization attempts. The first mobilization was performed solely with granulocyte colony stimulating factor (G-CSF) in 7 (54%) patients, with G-CSF and plerixafor in 1 (8%) patient. In other patients, hematopoietic cells were collected after chemotherapy and G-CSF i.e., cyclophosphamide in 4 (31%) and DHAP in 1 (8%). Median time to mobilization from the initiation of alemtuzumab treatment was 25 weeks (range, 15-81).

Information on conditioning was available in 37 patients. Most received chemotherapy-based conditioning: BEAM (22, 59%), BEAC (6, 16%), and FEAM (3, 8%). In 3 patients alemtuzumab was incorporated into the conditioning regimen. Four (10%) patients received TBI (10.4-13 Gy). Engraftment was achieved in all evaluated patients.

For the whole group of evaluable patients (n=34), the ORR at 100 days post auto-HCT was 88% (95% CI 72-97%). Importantly 7 out of 34 patients (21%) improved their response after auto-HCT to complete remission (CR) while one (3%) partial remission (PR) patient experienced direct progression post-transplantation.

With a median follow-up of 87.7 months (IQR, 41.7-89.9) the 4-year OS, PFS, cumulative RI and NRM estimates were 34% (95% CI 19-50%), 29% (95% CI 14-44%), 66% (95% CI 50-81%), and 5% (95% CI 0-12%), respectively (Figure 1a-d).

For the post-alemtuzumab first-line consolidation group (n=19) the ORR at 100 days was 85% (95% CI 65-96%). OS, PFS and cumulative RI estimates after 4 years were: 39% (16-63%), 34% (11-56%), 66% (44-89%). There was no NRM (Figure 1a-d) in this group.

For the post-alemtuzumab monotherapy consolidation group (n=15) the 4-year OS and PFS were 47% (95% CI 21-72%) and 37% (95% CI 11-63%), respectively.

Table S1 shows probabilities of OS and PFS and cumulative incidences of RI and NRM at 2 years after auto-HCT for the evaluated prognostic factors. None of these were significantly associated with analyzed outcomes in univariable analyses. Only 3 patients with a death before relapse were observed during follow-up.

The most frequently reported cause of death among the 29 patients with data available on the cause of death was relapse/ progression (n=16), followed by infection (n=5), secondary malignancy (n=3) and other causes of death (n=5). In the whole group, 31 patients had data on SPM status available, the 4-year cumulative incidence of SPM was 19% (4-34%). Among the whole group of patients (n=40), there were 25 patients with data available on post-auto-HCT therapy. The cumulative incidence of having received post-auto treatment at 4 years was 73% (95% CI 56-91%). Alemtuzumab was given in 62% of patients who had received post-auto therapy. In 7 patients an allo-HCT was recorded after auto-HCT (Supplementary Table S2).

Summarizing, this retrospective study analyzed the outcomes of 40 T-PLL patients treated with auto-HCT. Unfortunately, we were not able to answer the question why patients with T-PLL underwent auto-HCT instead of allo-HCT as it was not part of the data collection.

As a large majority of patients received BEAM-like conditioning regimens, the effect of TBI-based conditioning on outcome after auto-HCT cannot be assessed. Further research is needed to answer the question of the role of TBI in HCT for T-PLL. While it is a well-known fact that T-PLL is refractory to conventional chemotherapy, it was surprising to find, high dose chemotherapy followed by auto-HCT was effective in T-PLL. ORR at +100 days for the whole group of evaluable patients post auto-HCT was 88%. Response after auto-HCT had improved to CR in 7 out of 34 (21%) evaluable patients. Among patients transplanted in CR, all patients retained their response after the treatment. For the entire cohort, efficacy of this approach was highlighted but additionally showed that improvements were required; the 4-year OS was 34%, the 4-year PFS 29%, the 4-year RI 66%, and the 4-year NRM 5%. These are important findings, ensuring that at least in the short-term auto-HCT appears safe and efficacious considering potential, deferred in time future therapeutic strategies.

Relapse or progression constituted the most prevalent cause of death in the whole cohort of patients. The occurrence of SPM in T-PLL patients was surprisingly high with a 4-year cumulative incidence of SPMs of 19% (but with wide confidence intervals). It cannot be elucidated whether this is the result of the T-PLL treatment, or an inherent feature of T-PLL. We were not able to find in the published papers any information on SPM in T-PLL[3,8,10,12,13].

When compared to reported results of allo-HCT performed for T-PLL, the outcomes of auto-HCT seem to be comparable, or only modestly worse[5-7,14-15] (Supplementary Table S3).

Limitations of the study are those applicable to retrospective, registry-based studies including missing data, lack of precise information on pre-treatment, diagnostic verification in all subjects. Nevertheless, this study, the first to report a significant number of patients, does suggest that high dose therapy followed by auto-HCT is a valid therapeutic option in the treatment of T-PLL with acceptable efficacy and low toxicity. Even if it probably does not represent a curative strategy, until new approaches are found, auto-HCT can be proposed as consolidation to extend response duration specially after alemtuzumab.

APPENDIX

Corrado Tarella, European Institute of Oncology, Milano, Italy; Ben Carpenter, University College London Hospital, London, United Kingdom; Charles Crawley, Addenbrookes Hospital, Cambridge, United Kingdom; Dries Deeren, AZ Delta, Roeselare, Belgium; Giovanni Grillo, ASST GRANDE OSPEDALE METROPOLITANO NIGUARDA, Milano, Italy; Maija Itäla-Remes, Turku University Hospital, Turku, Finland; Patrick Medd, University Hospitals Plymouth NHS Trust, Plymouth, United Kingdom; Maria del Mar Perera Alvarez, Hospital de Gran Canaria Dr Negrin, Las Palmas, Spain; Péter Reményi, Dél-pesti Centrumkórház, Budapest, Hungary; Carlos Solano Vercet, Hospital Clínico de Valencia, Valencia, Spain; Eva Maria Wagner-Drouet, University Medical Center Mainz, Mainz, Germany;

References

1. Alaggio R, Amador C, Anagnostopoulos I, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. Leukemia. 2022;36(7):1720-1748.
2. Swerdlow SH, Campo E, Pileri SA, et al. The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood. 2016;127(20):2375-2390.
3. Staber PB, Herling M, Bellido M, et al. Consensus criteria for diagnosis, staging, and treatment response assessment of T-cell prolymphocytic leukemia. Blood. 2019;134(14):1132-1143.
4. Dearden CE, Khot A, Else M, et al. Alemtuzumab therapy in T-cell prolymphocytic leukemia: comparing efficacy in a series treated intravenously and a study piloting the subcutaneous route. Blood. 2011;118(22):5799-5802.
5. Wiktor-Jedrzejczak W, Drozd-Sokolowska J, Eikema DJ, et al. EBMT prospective observational study on allogeneic hematopoietic stem cell transplantation in T-prolymphocytic leukemia (T-PLL). Bone Marrow Transplant. 2019;54(9):1391-1398.
6. Wiktor-Jedrzejczak W, Dearden C, de Wreede L, et al. Hematopoietic stem cell transplantation in T-prolymphocytic leukemia: a retrospective study from the European Group for Blood and Marrow Transplantation and the Royal Marsden Consortium. Leukemia. 2012;26(5):972-976.
7. Murthy HS, Ahn KW, Estrada-Merly N, et al. Outcomes of Allogeneic Hematopoietic Cell Transplantation in T Cell Prolymphocytic Leukemia: A Contemporary Analysis from the Center for International Blood and Marrow Transplant Research. Transplant Cell Ther. 2022;28(4):187.e10.
8. Dearden C. Management of prolymphocytic leukemia. Hematology Am Soc Hematol Educ Program. 2015;2015:361-367.
9. Horwitz SM AS, Ai WZ, Barnes J, et al. T-Cell Prolymphocytic Leukemia (TPLL-1). In: T-Cell Lymphomas. In: NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) . Version 1.2023 — January 5, 2023. 2023 [Available from: https://www.nccn.org/professionals/physician_gls/pdf/t-cell.pdf.

10. Dearden CE, Matutes E, Cazin B, et al. High remission rate in T-cell prolymphocytic leukemia with CAMPATH-1H. Blood. 2001;98(6):1721-1726.
11. Krishnan B, Else M, Tjonnfjord GE, et al. Stem cell transplantation after alemtuzumab in T-cell prolymphocytic leukaemia results in longer survival than after alemtuzumab alone: a multicentre retrospective study. Br J Haematol. 2010;149(6):907-910.
12. Jain P, Aoki E, Keating M, et al. Characteristics, outcomes, prognostic factors and treatment of patients with T-cell prolymphocytic leukemia (T-PLL). Ann Oncol. 2017;28(7):1554-1559.
13. Rose A, Zhang L, Jain AG, et al. Delineation of clinical course, outcomes, and prognostic factors in patients with T-cell prolymphocytic leukemia. Am J Hematol. 2023;98(6):913-921.
14. Guillaume T, Beguin Y, Tabrizi R, et al. Allogeneic hematopoietic stem cell transplantation for T-prolymphocytic leukemia: a report from the French society for stem cell transplantation (SFGM-TC). Eur J Haematol. 2015;94(3):265-269.
15. Yamasaki S, Nitta H, Kondo E, et al. Effect of allogeneic hematopoietic cell transplantation for patients with T-prolymphocytic leukemia: a retrospective study from the Adult Lymphoma Working Group of the Japan Society for hematopoietic cell transplantation. Ann Hematol. 2019;98(9):2213-2220.

Table 1 Patients' and T-PLL characteristics at diagnosis and at auto-HCT. The characteristics are provided for all patients, for the subset of the post-alemtuzumab consolidation group of patients, and for the smallest subset of the post-alemtuzumab monotherapy consolidation group of patients (see Figure 1). Patient-, disease-, and transplant-related variables are expressed as median and interquartile range (IQR) for continuous variables and frequencies for categorical variables.

	Whole group	**Post-alemtuzumab consolidation group**	**Post-alemtuzumab monotherapy consolidation group**
	N (%)	**N (%)**	**N (%)**
Total	40 (100)	19 (100)	15 (100)
Patient sex			
Male	23 (58)	11 (58)	8 (53)
Female	17 (42)	8 (42)	7 (47)
Age at diagnosis; median (IQR); years	61 (50.3-66.2)	64 (60-68)	65 (61-68)
Year of diagnosis; median (IQR)	2009 (2006-2013)	2012 (2007-2014)	2012 (2007-2015)
WBC count at diagnosis; median (IQR); $x10^9$/L; missing 22	56.6 (24-232.8)	62 (51-237)	58 (52-204)
Cytogenetics; missing 19			
Normal karyotype	5 (24)	3 (21)	2 (18)
Abnormal karyotype	16 (76)	11 (79)	9 (82)
Specific abnormalities*			
abn14q23	9 (56)	6 (55)	4 (44)
abnXq28	2 (12.5)	2 (18)	1 (11)
neither abn14q23 nor abnXq28	5 (31)	4 (36)	4 (44)
abn11q22.3	4 (25)	2 (18)	1 (11)
complex karyotype	9 (56)	7 (64)	5 (56)
Age at auto-HCT, median (IQR)	62 (53-67)	66 (61-69)	66 (62-69)
<65	24 (60)	9 (47)	7 (47)
65-70	12 (30)	7 (37)	6 (40)
70 or more	4 (10)	3 (16)	2 (13)
KPS at auto-HCT; missing 8			
≤80	7 (22)	3 (16)	2 (13)
90 or 100	25 (78)	16 (84)	13 (87)
HCT-CI; missing 14			
low risk (0)	14 (54)	8 (47)	6 (46)
intermediate risk (1-2)	5 (19)	3 (18)	2 (15)
high risk (≥3)	7 (27)	6 (35)	5 (38)
Year of auto-HCT			
<2010	17 (42)	6 (32)	5 (33)
2010-2019	23 (58)	13 (68)	10 (67)
Interval diagnosis - auto-HCT; median (IQR); months	8.8 (6.4-17.7)	9 (7.3-16.9)	9.7 (7.7-16.9)

Disease stage at auto-HCT			
CR	27 (67)	11 (58)	9 (60)
PR	10 (25)	6 (32)	4 (27)
Stable disease	2 (5)	2 (10)	2 (13)
Relapse / progression	1 (3)		
Number of previous lines of therapy; missing 15			
1	20 (80)	19 (100)	15 (100)
2	5 (20)		
Alemtuzumab before auto-HCT; missing 15	24 (96)	19 (100)	15 (100)
Months between start of the first pretreatment and auto-HCT, median (IQR), missing 15	7.4 (6-11.8)	7.4 (6.1-9.2)	8.1 (6.1-9.2)

***** More than one category possible for each patient, hence percentages do not add up to 100%. (Percentage calculated as the percentage among patients with an abnormal karyotype)

auto-HCT- autologous hematopoietic cell transplantation, CR – complete remission, HCT-CI – hematopoietic cell transplantation comorbidity index, IQR - interquartile range, KPS – Karnofsky performance status, PR – partial remission, WBC - white blood cells

Figure Legends

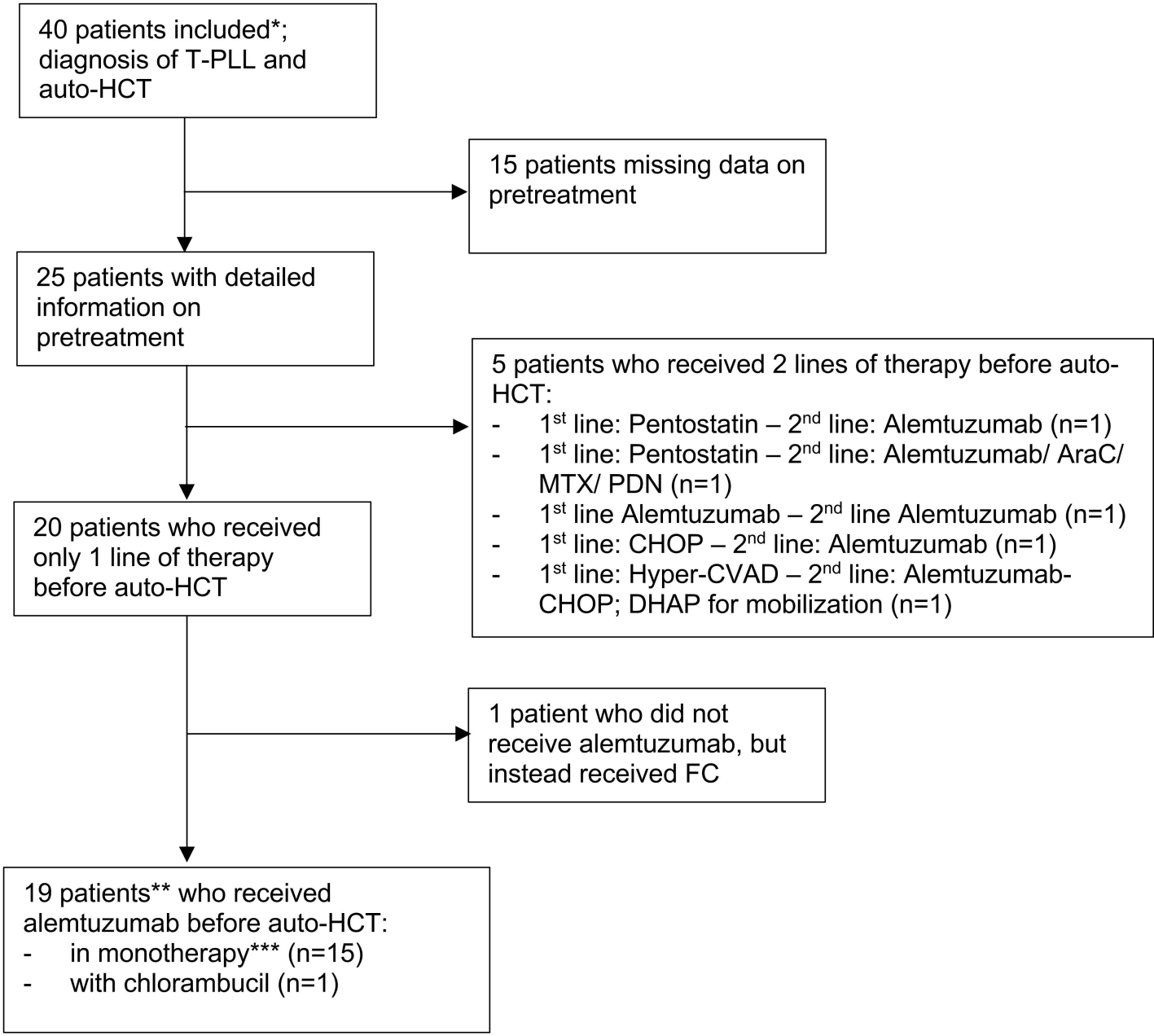
Figure 1 Flow diagram depicting the number of patients with different types of treatment before auto-HCT (AraC – cytarabine, CHOP – cyclophosphamide/ doxorubicine/ vincristine/ prednisone, DHAP – dexamethasone/ cisplatin/ cytarabine, FC – fludarabine/ cyclophosphamide, Hyper-CVAD – cyclophosphamide/ doxorubicin/ vincristine/ dexamethasone, MTX – methotrexate, PDN – prednisone)

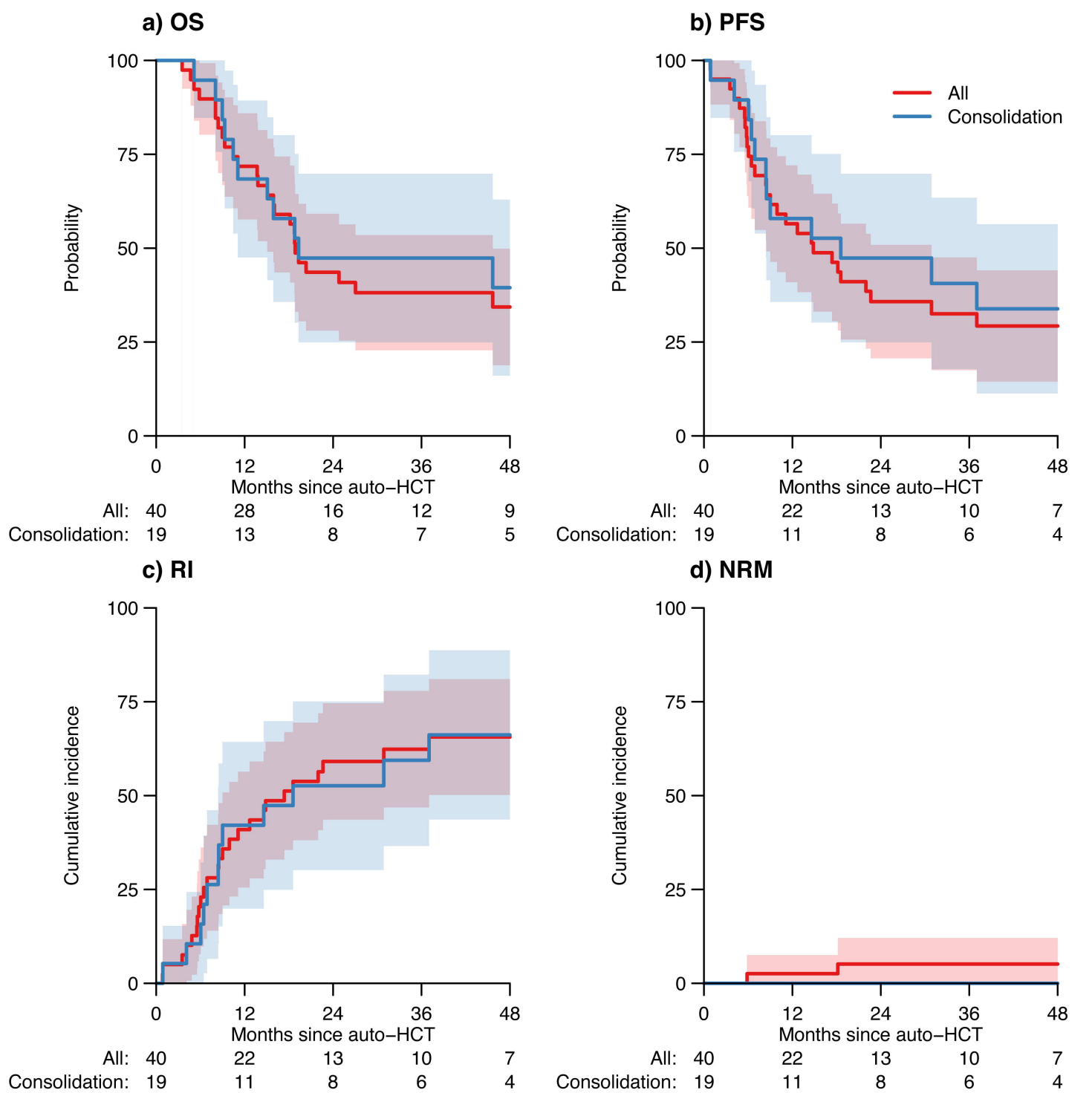
* whole group

** post-alemtuzumab first line consolidation group

*** the post-alemtuzumab monotherapy consolidation group

Figure 2 Outcome after auto-HCT, a) Overall survival (OS), **b)** progression-free survival (PFS), **c)** relapse incidence (RI) and **d)** non-relapse mortality (NRM) of patients undergoing autologous hematopoietic cell transplantation (auto-HCT). Shaded areas represent the 95% confidence intervals. The figures below the graph are the number of patients at risk. The “Consolidation" patients (blue line) are patients with available detailed data receiving auto-HCT as a consolidation of response after first line alemtuzumab (either in monotherapy or in combination). This group is a subset of “All” patients representing the whole group (red line). Hence the groups cannot be compared using a statistical test.


40 patients included*; diagnosis of T-PLL and auto-HCT
15 patients missing data on pretreatment
25 patients with detailed information on pretreatment
5 patients who received 2 lines of therapy before auto-HCT:
- 1st line: Pentostatin – 2nd line: Alemtuzumab (n=1)
- 1st line: Pentostatin – 2nd line: Alemtuzumab/ AraC/ MTX/ PDN (n=1)
- 1st line Alemtuzumab – 2nd line Alemtuzumab (n=1)
- 1st line: CHOP – 2nd line: Alemtuzumab (n=1)
- 1st line: Hyper-CVAD – 2nd line: Alemtuzumab-CHOP; DHAP for mobilization (n=1)
20 patients who received only 1 line of therapy before auto-HCT
1 patient who did not receive alemtuzumab, but instead received FC
19 patients** who received alemtuzumab before auto-HCT:
- in monotherapy*** (n=15)
- with chlorambucil (n=1)


a) OS
b) PFS
c) RI
d) NRM
All
Consolidation
Probability
Cumulative incidence
100
75
50
25
0
0
12
24
36
48
Months since auto−HCT
All: 40 28 16 12 9
Consolidation: 19 13 8 7 5
All: 40 22 13 10 7
Consolidation: 19 11 8 6 4

Supplementary Table S1 Univariable probabilities/cumulative incidences (95% confidence intervals) at 2 years after auto-HCT for overall survival (OS), progression free survival (PFS), non-relapse mortality (NRM) and relapse incidence (RI). For the whole group of evaluable patients the 1-year and 2-year OS was estimated at 72% (95% CI 58-86%) and 44% (95% CI 28-59%), and the 1-year and 2-year PFS at 56% (95% CI 41-72%) and 36% (95% CI 21-51%). The 6-month, 1-year and 2-year RI was 20% (95% CI 8-33%), 41% (95% CI 26-56%), and 59% (95% CI 44-75%), while the 1-year, and 2-year NRM was 3% (95% CI 0-8%), and 5% (95% CI, 0-12%) respectively. The 1- and 2-year probabilities of OS and PFS were obtained using Kaplan-Meier methods and the 1- and 2-year cumulative incidence of NRM and RI was obtained using the crude cumulative incidence estimator. P-values were obtained with the log-rank test for OS and PFS and Gray's test for NRM and RI and events artificially censored at 4 years. BEAM: carmustine, etoposide, cytarabine and melphalan; CR: complete response; TBI: total body irradiation.

		2-year OS	p	2-year PFS	p	2-year NRM	p	2-year RI	p
Age	<65 years	52% (32-73%)	0.50	39% (19-59%)	0.39	0% (0-0%)	0.09	61% (41-81%)	0.98
	≥65 years	31% (9-54%)		31% (9-54%)		12% (0-29%)		56% (32-81%)	
Sex	Male	50% (29-71%)	0.69	41% (20-61%)	0.67	9% (0-21%)	0.21	50% (29-71%)	0.33
	Female	35% (13-58%)		29% (8-51%)		0% (0-0%)		71% (49-92%)	
Year of auto-HCT	<2010	59% (35-82%)	0.19	46% (22-70%)	0.3	0% (0-0%)	0.21	54% (30-78%)	0.65
	≥2010	32% (12-51%)		27% (9-46%)		9% (0-21%)		63% (43-84%)	
Karnofsky score at auto-HCT	≤80	43% (6-80%)	0.86	43% (6-80%)	0.79	14% (0-40%)	0.07	43% (6-80%)	0.42
	90-100	46% (26-66%)		42% (22-61%)		0% (0-0%)		58% (39-78%)	
Interval between diagnosis and auto-HCT	<12 months	42% (22-61%)	0.36	38% (18-57%)	0.63	8% (0-19%)	0.26	54% (34-74%)	0.99
	≥12 months	47% (21-72%)		33% (10-57%)		0% (0-0%)		67% (43-90%)	
Number of previous lines of therapy	1	50% (28-72%)	0.96	50% (28-72%)	0.45	0% (0-0%)	*	50% (28-72%)	0.45
	2-3	40% (0-83%)		20% (0-55%)		0% (0-0%)		80% (45-100%)	
Status of T-PLL at auto-HCT	CR	46% (27-65%)	0.56	38% (20-57%)	0.31	4% (0-11%)	0.60	58% (39-77%)	0.53
	Other	38% (12-65%)		31% (6-56%)		8% (0-22%)		62% (35-88%)	
Conditioning	BEAM	38% (17-59%)	0.75	38% (17-59%)	0.91	5% (0-14%)	0.90	57% (36-78%)	0.97
	Other	50% (27-73%)		33% (12-55%)		6% (0-16%)		61% (39-84%)	
TBI in conditioning	yes	75% (33-100%)	0.88	50% (1-99%)	0.86	0% (0-0%)	0.73	50% (1-99%)	0.96
	no	41% (25-58%)		35% (19-51%)		3% (0-9%)		62% (46-78%)	

***: no NRM observed in the group of patients with data on the number of previous therapy lines available.**

Supplementary Table S2 Allo-HCT (second transplant) after auto-HCT

	Timing of relapse after auto-HCT (months)	Timing of allo-HCT after auto-HCT (months)	Timing (months) of last follow (status at last follow-up; cause of death)
After relapse after auto-HCT (n=2)			
	0.8	2.7	4.7 (dead; relapse)
	37	41.5	45.7 (dead; relapse)
Without recorded relapse after auto HCT (n=5)			
	/ /	2.8 3.0	5.8 (dead; GvHD) 87.7 (alive)
	/ / /	11.2 15.9 27.4	51.5 (alive) 18.2 (dead; 2nd malignancy) 42.3 (alive)

Supplementary Table S3 Efficacy of allo-HCT for T-PLL in published reports (ALWP JS - Adult Lymphoma Working Group of the Japan Society, IQR – interquartile range, NR – not reported, OS – overall survival, PLL – prolymphocytic leukemia, PFS – progression-free survival, SFGM-TC - French society for stem cell transplantation, T-PLL – T-cell PLL, yr – year)

Reference	Type of HCT	Number of patients	Median follow-up (IQR), months	Median OS (95% CI), months	OS (95% CI) at time point X	Median PFS (95% CI), months	PFS (95% CI) at time point X
Current study	Auto	40	87.7 (IQR, 42 -90)	18.9 (95% CI 15.1-45.7)	4-yr 34% (19-50%)	14.9 (95% CI 8.5-30.9)	4-yr 29% (14-44%)
EBMT, Wiktor-Jedrzejczak, 2019 (1)	Allo	37	50 (range, 12-78)	27.8 (NR)	4-yr 42% (25–59%)	19.2 (11.6–46.7)	4-yr 30% (14–46%)
EBMT, Wiktor-Jedrzejczak, 2012 (2)	Allo	41	36 (18-72)	12 (NR)	3-yr 21% (7-34%)	10 (NR)	3-yr 19% (6-31%)
CIBMTR, Murthy, 2022 (3)	Allo	266	49 (range, 3-117)	NR	4-yr 30% (24- 36.5%)	NR	4-yr DFS 26% (20-32%)
CIBMTR, Kalaycio, 2010 (4)	Allo	21 among 47 PLL patients reported	NR	NR	NR	5.1 (NR)	NR
SFGM-TC, Guillaume, 2015 (5)	Allo	27	33 (range, 6-103)	26 (NR)	3-yr 36% (17-54%)	16.5 (NR)	3-yr 26% (14-45%)
Moffitt Cancer Center, Dholaria, 2018 (6)	Allo	11	48 (range, 6-123)	56 (95% CI 15–56)	4-yr 56% (24-89%)	15 (95% CI 12–99)	4-yr 45% (13-78%)
ALWP JS, Yamasaki, 2019 (7)	Allo	20	51 (range, 12-68)	NR	1-yr 58% (33–76%) 3-yr 40% (18–61%)	NR	1-yr 53% (29–72%) 3-yr 53% (29–72%)
Heildelberg Sellner, 2017 (8)	Allo	10	NR	NR	3-yr 50% (19-81%)	NR	3-yr 40% (10-70%)

References:

1. Wiktor-Jedrzejczak W, Drozd-Sokolowska J, Eikema DJ et al. EBMT prospective observational study on allogeneic hematopoietic stem cell transplantation in T-prolymphocytic leukemia (T-PLL). Bone Marrow Transplant. 2019;54(9):1391-8.
2. Wiktor-Jedrzejczak W, Dearden C, de Wreede L et al. Hematopoietic stem cell transplantation in T-prolymphocytic leukemia: a retrospective study from the European Group for Blood and Marrow Transplantation and the Royal Marsden Consortium. Leukemia. 2012;26(5):972-6.
3. Murthy HS, Ahn KW, Estrada-Merly N et al. Outcomes of Allogeneic Hematopoietic Cell Transplantation in T Cell Prolymphocytic Leukemia: A Contemporary Analysis from the Center for International Blood and Marrow Transplant Research. Transplant Cell Ther. 2022;28(4):187.e1-.e10.
4. Kalaycio ME, Kukreja M, Woolfrey AE et al. Allogeneic hematopoietic cell transplant for prolymphocytic leukemia. Biol Blood Marrow Transplant. 2010;16(4):543-7.
5. Guillaume T, Beguin Y, Tabrizi R et al. Allogeneic hematopoietic stem cell transplantation for T-prolymphocytic leukemia: a report from the French society for stem cell transplantation (SFGM-TC). Eur J Haematol. 2015;94(3):265-9.
6. Dholaria BR, Ayala E, Sokol L et al. Allogeneic hematopoietic cell transplantation in T-cell prolymphocytic leukemia: A single-center experience. Leuk Res. 2018;67:1-5.
7. Yamasaki S, Nitta H, Kondo E et al. Effect of allogeneic hematopoietic cell transplantation for patients with T-prolymphocytic leukemia: a retrospective study from the Adult Lymphoma Working Group of the Japan Society for hematopoietic cell transplantation. Ann Hematol. 2019;98(9):2213-20.
8. Sellner L, Brüggemann M, Schlitt M et al. GvL effects in T-prolymphocytic leukemia: evidence from MRD kinetics and TCR repertoire analyses. Bone Marrow Transplant. 2017;52(4):544-551