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Haematological Malignancy – Clinical

Long-term outcome of peripheral T-cell lymphomas: Ten-year follow-up of the International Prospective T-cell Project

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Summary
Peripheral T-cell lymphomas (PTCLs) are a heterogeneous group of haematological cancers with generally poor clinical outcomes. However, a subset of patients experience durable disease control, and little is known regarding long-term outcomes. The International T-cell Lymphoma Project (ITCLP) is the largest prospectively collected cohort of patients with PTCLs, providing insight into clinical outcomes at academic medical centres globally. We performed a long-term outcome analysis on patients from the ITCLP with available 10-year follow-up data ($n = 735$). The overall response rate to first-line therapy was 68%, while 5- and 10-year overall survival estimates were 49% and 40% respectively. Most deaths occurred prior to 5 years, and for patients alive at 5 years, the chance of surviving to 10 years was 84%. However, lymphoma remained the leading cause of death in the 5- to 10-year period (67%). Low-risk International Prognostic Index and Prognostic Index for T-cell lymphoma scores both identified patients with improved survival, while in multivariate analysis, age >60 years and Eastern Cooperative Oncology Group performance status 2–4 were associated with inferior outcomes. The favourable survival seen in patients achieving durable initial disease control emphasizes the unmet need for optimal front-line therapeutic approaches in PTCLs.

KEYWORDS
follow-up, outcome, T-cell lymphomas, TCP1

INTRODUCTION

Peripheral T-cell lymphomas (PTCLs) are an uncommon and heterogeneous group of haematological malignancies derived from post-thymic lymphoid cells at different stages of differentiation. PTCLs represent about 10%–15% of all lymphomas in Western countries, and 15%–25% in Asia.[1,2] In 2008, the International T-cell Lymphoma Project (ITCLP) conducted a retrospective analysis of 1314 cases of PTCL/natural killer T-cell lymphomas (NKTCL) and reported poor clinical outcomes with standard therapies for most subtypes. Across the most common subtypes (PTCL not otherwise specified [PTCL-NOS], angioimmunoblastic T-cell lymphoma [AITL] and all NKTCLs), the 5-year overall survival (OS) was 32%, compared with only 14% for adult T-cell leukaemia/lymphoma (ATLL). Anaplastic large-cell lymphoma (ALCL), ALK positive, demonstrated the best 5-year OS (70%), with ALCL, ALK negative, having an intermediate 5-year OS (49%).[1]

For affiliations refer to page 7.

The T-cell Project (TCP; NCT01142674) was a prospective cohort study initiated by the ITCLP aimed at better understanding the clinical characteristics and outcome of patients with PTCL. The TCP was initiated in September 2006 as a prospective registry of patients with mature PTCLs (PTCL-NOS; AITL; ALCL ALK+/−; extra-nodal natural killer (NK) T-cell lymphoma, ENKTL; hepatosplenic T-cell lymphoma (HSTCL), enteropathy associated T-cell lymphoma (EATL) and peripheral gamma delta T-cell lymphomas (PGDTCLs); and unclassifiable peripheral T-cell or NK lymphoma). Seventy-four institutions in 14 countries (Argentina, Australia, Brazil, Chile, France, Israel, Italy, South Korea, Slovakia, Spain, Switzerland, England, United States and Uruguay) served as enrolment sites. All consecutive patients with mature T-cell or natural killer-cell lymphomas diagnosed according to the World Health Organization classification of tumours of haematopoietic and lymphoid tissues (editions 2001, 2008 or 2017) were registered into the TCP at initial diagnosis before initiation of treatment. Unfortunately, even in the prospective series outcomes were no better than in the prior retrospective data. The 5-year OS was 32% for PTCL-NOS,[2] 44% for AITL[3] and ranged from 30% to 51% for rare subtypes.[4] Patients with ALCL ALK positive again had a favourable 5-year OS of 77%,[5] as compared to 49% for ALCL ALK negative.[6]

To the best of our knowledge, there are limited prospective long-term outcome data (i.e. 10 years) for PTCLs. To address this gap, we launched a survey to collect data and evaluate the outcomes of patients registered in the TCP who had reached this milestone.

METHODS

Study design and patients

Between 2006 and 2018, 1669 patients were registered in the TCP. Eligible patients for this report were adults (age ≥18 years) with adequate tissue biopsy specimens for diagnosis and available clinical data, including baseline information on disease staging, laboratory parameters at diagnosis, treatment regimens received and follow-up for at least 5 years. Full inclusion and exclusion criteria are provided in the study protocol (Supporting Information). The study was done in compliance with the Declaration of Helsinki and approved by research ethics committees and institutional review boards at each participating institution. The TCP used a central dedicated database (http://www.tcellproject.org; now inactive) to store all patient data. All patients provided written informed consent before study entry. In September 2022, a survey was launched requesting centres to provide long-term follow-up data on patients previously registered at their sites for the purpose of reporting long-term PFS and OS. For patients with available data, prognostic indices, including the International Prognostic Index (IPI) and Prognostic Index for T-cell lymphoma (PIT), were calculated.[7,8]

Study end-points and statistical methods

The primary end-point of the study was OS at 10 years, measured from the date of diagnosis until death from any cause or the date of the last known contact for living patients. The key secondary end-point was PFS at 10 years, measured from the time of diagnosis to the date of progressive disease assessment or death from any cause. If no events occurred, observations were censored at the time of last follow-up. To reduce potential selection bias based on reporting institutions, an analysis of 5-year OS and PFS was performed on patients from the TCP who did not have 10-year outcome data available. Survival curves were calculated with the Kaplan–Meier method, and time-to-event distributions were compared with the log-rank test (univariate regression). The median duration of follow-up was estimated by the Kaplan–Meier method. Cox models were used to investigate the association between survival outcomes and covariates with hazard ratios (HRs), with 95% CIs used as a summary measure. All reported tests were two-sided, and $p \leq 0.05$ was considered to indicate moderate strength of evidence against the null hypothesis. p Values were not adjusted for multiple comparisons. Statistical analyses were performed using SPSS (version 20.0).

RESULTS

Patient characteristics

Between December 2006 and March 2018, 1553 (91.4%) of 1669 registered patients were eligible for the current study. To date, 19 of the 74 participating institutions have provided long-term follow-up data on 735 cases. Specifically, 255 patients had PTCL-NOS (35%), 133 AITL (18%), 124 (17%) ALCL ALK–, 62 (8%) ALCL ALK+ and 64 (9%) with NKTCL. The remaining 97 (13%) were diagnosed with rare histological subtypes (HSTCL 3%, EATL 5%, subcutaneous panniculitis-like T-cell lymphoma 2%, PGDTCL 1% and unclassifiable T cell 2%). The geographic distribution was notable for less frequent AITL (9% vs. 25%–28%) and more frequent ALCL ALK– (29% vs. 15%–17%) among South American institutions as compared to Europe and the United States, similar to prior reports.[9] The median age was 56 years (range, 18–88), with a slight male predominance (58%). B symptoms were present in 50% and extranodal involvement in 60% of patients. Patient characteristics are summarized in Table 1.

For institutions that did not provide long-term data, frequent reasons included a lack of research resources, unavailable clinical follow-up or limited interest in the current study. To evaluate for potential bias based on institutional participation, we compared the clinical characteristics and 5-year outcomes of patients from the 55 institutions without updated 10-year follow-up ($n = 818$) to those with long-term data ($n = 735$). The baseline characteristics of patients without long-term follow-up were not significantly different, including a similar distribution of histological subtypes and clinical parameters (Table 1).

TABLE 1 Baseline clinical characteristics for patients with long-term follow-up data ($n = 735$) or for whom long-term data was unavailable ($n = 818$). For clinical factors available for a subset of long-term patients, the number of evaluable patients is reported.

	Long-term cohort		Long-term data unavailable		
Parameters	**Patients evaluable**	***N* (%)**	**Patients evaluable**	***N* (%)**	***p* Values**
Median age, years (range)		56 (18–88)		55 (18–88)	0.9
Age ≥60	735	173 (24%)	818	191 (23%)	0.9
Male gender	735	428 (58%)	818	494 (60%)	0.9
B symptoms	696	348 (50%)	818	366 (49%)	0.9
Extra-nodal sites ≥2	713	428 (60%)	818	431 (53%)	0.71
Stage	638		673		
I–II		189 (30%)		203 (30%)	0.9
III–IV		449 (70%)		470 (70%)	0.9
ECOG PS > 1	696	195 (28%)	720	144 (20%)	0.8
LDH > ULN	648	285 (44%)	623	293 (47%)	0.6
Albumin <35 g/L	640	288 (45%)	634	260 (41%)	0.4
Haemoglobin >12 g/dL	683	294 (43%)	715	315 (44%)	0.8
Platelet count $<150 \times 10^9$ cells/L	683	123 (18%)	736	140 (19%)	0.8
ANC $>6.5 \times 10^3/mm^3$	518	202 (39%)	817	319 (39%)	0.9
IPI ≥3	520	341 (66)	676	414 (61%)	0.9
PIT ≥2	520	218 (42)	676	294 (43%)	0.9
Overall survival 5 years	735	44% (95% CI 23–65)	818	44% (95% CI 22–66)	Log rank 0.78
Progression-free survival 5 years	735	37% (95% CI 19–55)	818	35% (95% CI 17–53)	Log rank 0.88

Abbreviations: ANC, absolute neutrophil count; ECOG PS, Eastern Cooperative Oncology Group performance status; IPI, International Prognostic Index; LDH, lactate dehydrogenase; PIT, Prognostic Index for T-cell lymphoma; ULN, upper limit of normal.

Treatment regimens and outcomes

Treatment details were available for 658 patients (90%), of whom 58 (9%) received only the best supportive care (Table 2). Of the remaining 600 patients, 499 (83%) received chemotherapy (CHT) alone, 10 (2%) received radiotherapy (RT) alone and 91 (15%) received CHT + RT. Specifically, for patients treated with curative intent, 392 (65%) received anthracycline-based CHT, 120 (20%) anthracycline/etoposide, 58 (10%) etoposide-based therapy and 30 (5%) L-asparaginase therapy for ENKTL. The overall response rate (ORR) to first-line therapy (as assessed by local investigators) was 68% ($n = 448$): 345 patients (52%) achieved a complete response (CR) and 103 patients (16%) achieved a partial response (PR). Initial treatment regimens and response rates did not significantly differ for patients without long-term follow-up (Table 2).

After a median follow-up of 81 months (range 1–198), 373 (51%) patients in the long-term cohort had died. The 5-year OS and PFS were similar for patients with or without long-term follow-up (OS 44% vs. 44%, PFS 37% vs. 35%) (Table 1; Figure S1A,B). For the long-term cohort, OS at 10 years was 40% (95% CI 22–58) and PFS 27% (95% CI 17–37) (Figure 1A,B), with similar decreases seen across major histological subtypes (Table 3). The majority of deaths in the long-term cohort were due to lymphoma ($n = 263$, 70%), followed by infections ($n = 42$, 11%), treatment-related toxicity ($n = 25$, 7%), second malignancies ($n = 19$, 5%) and other causes ($n = 24$, 7%) (Table 2). Detailed data were not available regarding a second cancer diagnosis or type of infection.

For patients in the long-term cohort alive at 5 years ($n = 324$), the chance of surviving the subsequent 5 years was 84% (95% CI 61–105) (Figure 2). Furthermore, for patients in CR at 5 years, the probability of remaining disease-free in the subsequent 5 years was 74% (95% CI 60–96) (Figure 2). Patients who experienced late relapse (during years 5–10, $n = 37$) had superior subsequent OS than patients who relapsed prior to 5 years ($n = 32$, Figure 3, $p = 0.05$). By histology, the respective 10-year OS and PFS rates for patients alive at 5 years were: PTCL-NOS 78% (95% CI 43–113) and 73% (95% CI 31–115); AITL 85% (95% CI 39–131) and 76% (95% CI 36–116); ALCL ALK– 88% (95% CI 42–134) and 87% (95% CI 40–134); ALCL ALK+ 100% (95% CI n.e.) and 100% (95% CI n.e.); NKTCL 80% (95% CI 45–115) and 78% (95% CI 45–111). A comparison across subtypes was notable only for significantly superior 10-year PFS and OS in ALCL ALK+ (global p value for difference $p < 0.001$ by multigroup Mantel-Cox tests for PFS/OS, pairwise comparisons by log-rank test in Table S1A,B).

Among patients achieving CR, only 19% ($n = 66$) received consolidative autologous stem cell transplantation (ASCT) in first remission. Of these patients, 44 (67%) were alive at 5 years, with a 10-year OS of 62% and a PFS of 52% (median follow-up = 79 months).

TABLE 2 Treatment regimens and clinical outcomes for patients with long-term follow-up data ($n = 735$) or for whom long-term data were unavailable ($n = 818$). For clinical factors available for a subset of long-term patients, the number of evaluable patients is reported.

	Long-term cohort		Long-term data unavailable		
Parameters	**Patients evaluable**	***N* (%)**	**Patients evaluable**	***N* (%)**	***p* Values**
Therapy	658		710		
Best supportive care		58 (9%)		31 (4%)	0.6
CHT alone		499 (67%)		531 (75%)	0.7
RT alone		10 (2%)		21 (3%)	0.9
CHT/RT		91 (15%)		127 (18%)	0.8
HDT/ASCT consolidation	658	66 (11%)	818	89 (11%)	0.8
CHT regimens	600		679		
Anthracycline		392 (65%)		423 (62%)	0.9
Anthracycline/etoposide		120 (20%)		140 (21%)	0.4
Etoposide		58 (10%)		76 (11%)	0.8
Asparaginase		30 (5%)		40 (6%)	0.5
Response to treatment	658		710		
CR		345 (53%)		391 (55%)	0.7
PR		103 (15%)		118 (16%)	0.7
PD		210 (32%)		201 (29%)	0.8
Relapsed	735		818		
Yes		326 (44%)		338 (41%)	0.8
No		409 (56%)		480 (59%)	0.8
Death	373		365		
Cause of death					
Lymphoma		263 (70%)		244 (67%)	0.7
Toxicity		25 (7%)		15 (4%)	0.8
Other cancers		19 (5%)		22 (6%)	0.8
Infection		42 (11%)		54 (15%)	0.7
Other/unknown		24 (7%)		30 (8%)	0.7

Abbreviations: CHT, chemotherapy; CR, complete response; HDT/ASCT, high-dose chemotherapy/autologous stem cell transplantation; PD, progressive disease; PR, partial response; RT, radiotherapy.

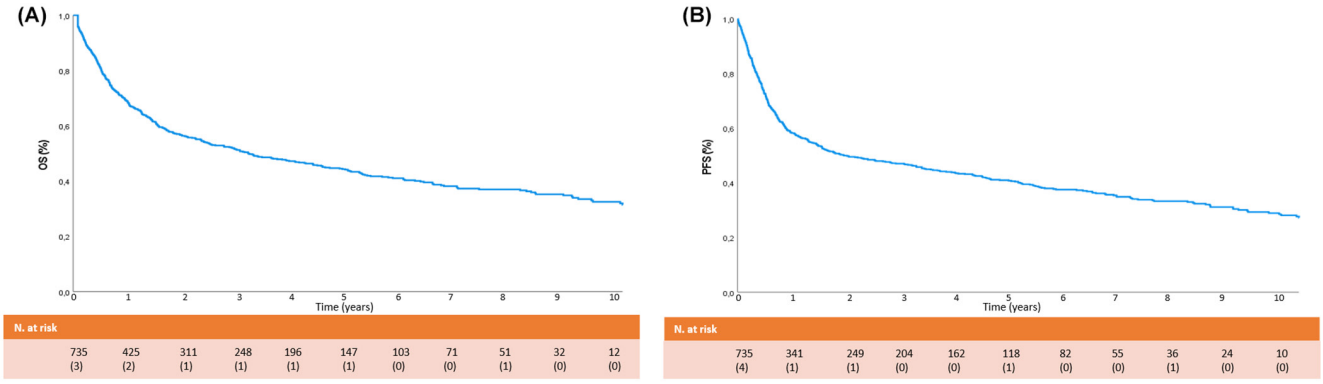

FIGURE 1 (A, B) Ten-year overall survival and progression-free survival of long-term cohort patients ($n = 735$).

Clinical prognostic factors

Of 735 patients in the long-term cohort, 520 had data available to calculate prognostic indices, including the IPI and PIT.[7,8] Both prognostic indices identified high-risk subgroups with inferior OS compared with low-risk patients. Patients with high-risk IPI or PIT scores (66% and 42% of patients, respectively) had 10-year OS estimates of 21% and 31%. By comparison, patients with low-risk IPI and PIT scores had 10-year OS estimates of 48% and 43% respectively (Table S2).

TABLE 3 Comparison of 5- and 10-year OS and PFS for major PTCL subtypes.

	OS		PFS	
Subtype	**5 year (95% CI)**	**10 year (95% CI)**	**5 year (95% CI)**	**10 year (95% CI)**
PTCL-NOS	31 (26–36)	23 (18–28)	26 (17–35)	18 (9–27)
AITL	44 (31–57)	31 (26–36)	39 (33–45)	24 (14–34)
ALCL, ALK–	49 (37–61)	40 (34–46)	42 (33–51)	36 (29–43)
ALCL, ALK+	79 (65–93)	69 (62–76)	71 (60–82)	63 (53–73)
NK TCL	45 (37–53)	32 (23–41)	40 (32–48)	28 (20–36)

Abbreviations: OS, overall survival; PFS, progression-free survival; PTCL, peripheral T-cell lymphoma.

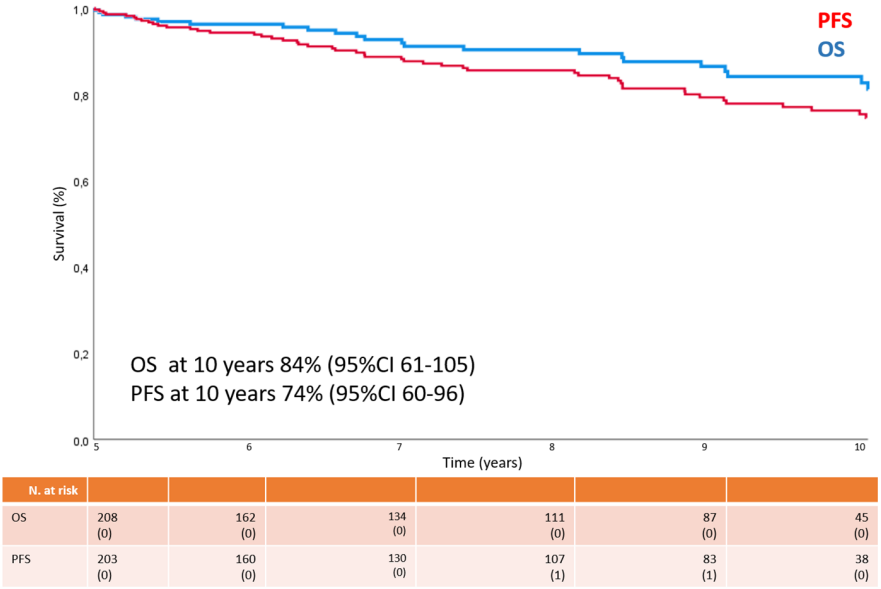

FIGURE 2 Ten-year overall survival and progression-free survival of long-term cohort patients alive and in remission after the initial 5 years ($n = 208$).

On univariate analysis, several clinical variables had a significant negative impact on 10-year OS, including age ≥60 years (HR 2.3, 95% CI 1.7–3.1; $p = 0.001$), ECOG performance status >2 (HR 1.9, 95% CI 1–3.4; $p = 0.03$), elevated CRP (HR 1.93, 95% CI 1.1–3.2 $p = 0.001$), IPI ≥3 (HR 1.83, 95% CI 1.5–2.1; $p = 0.001$) and PIT ≥2 (HR 2.39, 95% CI 1.9–2.9; $p = 0.001$) (Table S1). Similar clinical risk factors were observed for 5-year OS, with low albumin (HR 2.4, 95% CI 1.9–3.1, $p = 0.001$) and elevated LDH (HR 2.1, 95% CI 1.7–2.6, $p = 0.04$) also significant in univariate analysis (Table S1). In multivariate analysis, age ≥60 years (HR 1.2, 95% CI 1–1.4; $p = 0.03$), ECOG performance status >2 (HR 2.1, 95% CI 1.6–2.8; $p < 0.001$) and elevated CRP (HR 1.5, 95% CI 1.1–2.1, $p = 0.01$) retained an independent prognostic significance for 10-year OS (Table 4).

DISCUSSION

The International TCP is the largest prospectively collected cohort of patients with PTCLs, providing insight into clinical outcomes with real-world therapies at academic medical centres globally. In prior publications addressing major PTCL subtypes, we have described heterogeneous but overall poor 3- and 5-year outcomes.[2–6] From the TCP, we have also reported that salvage therapies for patients who relapse are at best marginally effective.[10] For the subset of individuals who experience durable disease control, there is a paucity of data regarding long-term outcomes. To the best of our knowledge, the present study, describing 735 patients at a median follow-up of 81 months, represents the largest prospective cohort investigating clinical outcomes >5 years in patients with PTCL.

Although the OS at 10 years was only 40%, the majority of events occurred early, with only 16% of deaths occurring in the period from 5 to 10 years. While deaths were most commonly due to lymphoma (70%), infections (11%) and treatment-related toxicity (7%) were also major sources of mortality. In the late period (5–10 years), lymphoma remained the leading cause of death (67%), followed by other malignancies (4%), with treatment toxicity (1%) and infections (1%) playing a lesser role. For patients alive without recurrence at 5 years, the estimated probability of surviving to 10 years postdiagnosis is 84%. In comparison to the variable outcomes seen at 3–5 years,[2–6] for patients alive at 5 years, outcomes were not significantly different across histological subtypes except for a sustained superior PFS/OS in ALK+ ALCL.

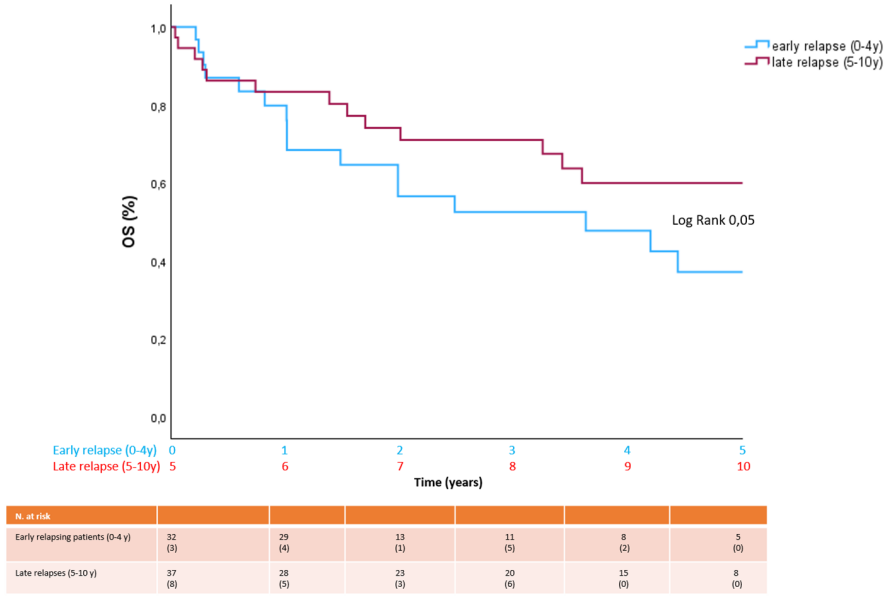

FIGURE 3 Superimposed Kaplan–Meier curves demonstrate the subsequent 5-year overall survival of patients experiencing relapse in the early post-treatment period ($n = 32$, blue, survival from diagnosis to year 5) versus patients with late relapse ($n = 37$, red, survival from years 5–10).

TABLE 4 Multivariate analysis of risk factors for overall survival.

			5 year OS HR multivariate			10 year OS HR multivariate	
Factor	**Status**	**5 year OS (95% CI)**	**HR (95 CI)**	***p* Value**	**10 year OS (95% CI)**	**HR (95 CI)**	***p* Value**
Age	<60	46 (25–67)			46 (31–61)		
	≥60 year	22 (14–30)	1.20 (0.99–1.62)	0.05	13 (4–22)	1.22 (1.01–1.42)	0.033
ECOG PS	0–1	51 (29–73)			41 (31–51)		
	2–4	22 (12–32)	2.41 (1.50–3.92)	0.001	19 (13–25)	2.12 (1.61–2.80)	0.001
CRP	≤ULN	53 (30–76)			39 (23–55)		
	>ULN	19 (12–26)	1.32 (0.73–2.13)	0.33	19 (11–27)	1.51 (1.19–2.12)	0.01
Albumin, g/L	≥35	56 (33–79)			40 (15–65)		
	<35	30 (13–47)	1.81 (1.20–2.83)	0.02	25 (14–36)	1.22 (0.04–1.31)	0.9

Abbreviations: ECOG PS, Eastern Cooperative Oncology Group performance status; ULN, upper limit of normal.

As in follicular lymphoma and diffuse large B-cell lymphoma, where POD24 and EFS24 are defined surrogate markers for long-term outcomes, the favourable long-term survival observed for patients in remission at 5 years suggests that early disease progression may serve as a clinically useful surrogate end-point in PTCLs.[11,12] We have previously reported POD24 as a significant prognostic factor in AITL, where patients progressing within 24 months had a 5-year OS of 6% as compared to 63% for patients without POD24.[3] Similarly, a large international retrospective study of systemic PTCL reported 5-year OS with or without EFS24 as 11% and 78% respectively.[13] An Italian study previously described clinical prognostic factors associated with 5-year OS in PTCL patients, including high-risk IPI ≥3, ECOG PS >2 and PIT >2.[8] In the current cohort, while similar associations were seen for 10-year OS in univariate analysis, multivariate analysis demonstrated independent prognostic value for age >60 years, ECOG PS >2 and elevated CRP.

Our results are comparable to the recently reported long-term follow-up of the phase II Nordic NLG-T-01 trial ($n = 160$, median follow-up 10.7 years).[14] In the latter, the 10-year OS (41%), PFS (38%) and rates of death from lymphoma (76%) and treatment toxicity (10%) were similar to our cohort, and late lymphoma-related deaths were also rare. Regarding clinical risk factors, a similar adverse prognostic impact was observed for age (OS: HR 1.03 per year, 95% CI 1.00–1.06; $p = 0.004$) and ECOG PS ≥2 (OS: HR 1.71, 95% CI 1.08–2.72; $p = 0.023$).[14]

While our study provides a unique insight into long-term outcomes from major academic centres, reflecting a global real-world treatment population, there are several limitations. Long-term outcome data was only available for 735 of the 1553 patients initially enrolled in the TCP. To evaluate for potential biases, we compared baseline clinical characteristics and 5-year PFS/OS, which did not differ between the long-term cohort and patients without available 10-year data.

The role of ASCT in first remission is controversial. In retrospective studies reporting improved outcomes, patients frequently have favourable baseline characteristics,[15] while no benefit was seen for ASCT in either a propensity-matched analysis (HR = 1.08; 95% CI 0.68–1.69 for OS)[16] or the only randomized prospective study (5-year OS 40% with ASCT vs. 45% without, $p = 0.98$).[17] In our dataset, only 66 patients (representing 19% of patients in CR) underwent ASCT. While outcomes appear somewhat superior (62% vs. 40% 10-year OS), these numbers are too small to make any definitive conclusions. The ongoing randomized TRANSCRIPT study (NCT05444712) will attempt to answer this more definitively.

For patients in remission at 5 years, the lymphoma relapse risk of 26% is almost threefold higher than rates reported in DLBCL, and outcomes were only modestly superior in late versus early relapse. Continued clinical follow-up even for patients achieving long-term remission is appropriate, and further investigation into the biological mechanisms of late PTCL relapse is required. Despite a subset of long-term survivors, the majority of patients in our study died of PTCL (64%), which underscores the critical need for improved risk stratification and novel therapeutic approaches. While this cohort reflects a global population of patients receiving standard-of-care therapies, only a minority of patients received brentuximab vedotin (BV). The recently approved front-line regimen of BV-CHP has demonstrated an OS advantage in ECHELON-2,[18] although applicability to all PTCL subtypes is questionable as the majority of patients in the latter trial had ALCL. HDAC inhibitors (romidepsin, belinostat) are approved for relapsed/refractory disease, but unfortunately have not yet established a role in front-line treatment, and the addition of romidepsin to CHOEP induction did not improve PFS in the phase IB/II PTCL13 study.[19] The recent identification of T follicular helper phenotype as an independent prognostic factor for response to HDACi in relapsed PTCL suggests that biological patient selection could potentially improve response rates.[20] Several studies have identified additional biological subsets associated with clinical outcomes, that is *DUSP22* translocations associated with favourable prognosis in ALCL ALK–,[21] or GATA3 expression associated with poor outcomes in PTCL-NOS.[22] These data are not currently universally available in clinical care and were not reported in our cohort, but they may help patient stratification to individualize therapies.

In conclusion, the 10-year outcomes for patients with PTCL remain poor; however, most events occur early (<5 years) with a gradual but continuous attrition of lymphoma relapses between years 5 and 10. This underscores the importance of developing better individualized front-line therapy based on both lymphoma biology and patient characteristics, taking into account the heterogeneity of PTCL, as a 'one size fits all' approach is clearly suboptimal.

AUTHOR CONTRIBUTIONS

R.A., M.C., J.G.S.-M. and M.F. designed the research, interpreted the data and wrote the manuscript. M.M., A.L., Y.S. and T.S. collected and analysed the data. All other authors provided patients and study materials, and all authors reviewed and approved the manuscript.

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CONFLICT OF INTEREST STATEMENT

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Myeloid Therapeutics, ONO Pharmaceuticals, Seattle Genetics, SecuraBio, Shoreline Biosciences, Inc, Takeda, Trillium Therapeutics, Tubulis, Verastem and Vividion Therapeutics. The remaining authors declare no competing financial interests.

DATA AVAILABILITY STATEMENT

Deidentified data will be available on reasonable request. Requests for original data should be sent to the corresponding author and Monica Civallero (mcivallero@unimo.it).

ETHICS STATEMENT

The study was done in compliance with the Declaration of Helsinki and approved by research ethics committees and institutional review boards at each participating institution. The TCP used a central dedicated database (http://www.tcellproject.org; now inactive) to store all patient data.

PATIENT CONSENT STATEMENT

All patients provided written informed consent before study entry.

CLINICAL TRIAL REGISTRATION (INCLUDING TRIAL NUMBER)

The T-Cell Project (TCP; NCT01142674) was a prospective cohort study initiated by the ITCLP aimed at better understanding of clinical characteristics and outcome of patients with PTCL.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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