Clinical features and outcomes of peripheral T-cell lymphoma, not otherwise specified: A single institution retrospective analysis of 30 cases

MENG-XUE MA[1*], YA-LI ZHANG[2*], LI-NA XING[1], QIU-YI WANG[1] and SHUKAI QIAO[1]

[1]Department of Haematology, The Second Hospital of Hebei Medical University, Shijiazhuang, Hebei 050000, P.R. China;
[2]Department of General Medical, The Second Hospital of Hebei Medical University, Shijiazhuang, Hebei 050000, P.R. China

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Abstract. Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS) is the most common histological subtype of PTCL. PTCL-NOS has a relatively low incidence, and its pathogenesis and mechanisms of drug resistance remain unclear, leading to lagging research progress. The aim of the present study was to summarize the clinical features and outcomes of patients with PTCL-NOS. A total of 30 patients with treatment-naive PTCL-NOS who were admitted to The Second Hospital of Hebei Medical University (Shijiazhuang, China) between September 2013 and September 2023 were retrospectively analysed. The median age at diagnosis was 59 years (range, 17-70 years), and the male-to-female ratio was 2.75:1. The median follow-up duration was 59 months. The 3-year overall survival (OS) and progression-free survival (PFS) rates were 50.4 and 28.9%, respectively. Multivariate analysis showed that an Eastern Cooperative Oncology Group performance status >1, bone marrow involvement and a platelet count <150x10^9/l were independent risk factors for OS, whereas bone marrow involvement and albumin levels <35 g/l were independent risk factors for PFS. There was no significant difference between the cyclophosphamide, doxorubicin, vincristine, prednisone and etoposide regimen and the cyclophosphamide, vincristine, doxorubicin and prednisone regimen, whereas combinations with chidamide showed a trend toward an improved PFS. Within the cohort, 2 patients with relapsed and refractory CD30-positive PTCL-NOS received salvage chemotherapy with brentuximab vedotin (BV), a monoclonal antibody, and achieved complete metabolic remission, followed by sequential allogeneic haematopoietic stem-cell transplantation, resulting in long-term sustained remission. In conclusion, patients diagnosed with PTCL-NOS generally have a poor prognosis. Nevertheless, the use of innovative targeted therapies, such as chidamide and BV, shows potential to improve treatment outcomes in these patients.

Correspondence to: Dr Shukai Qiao, Department of Haematology, The Second Hospital of Hebei Medical University, 215 Heping Western Road, Shijiazhuang, Hebei 050000, P.R. China
E-mail: qiaoshukai@hebmu.edu.cn

*Contributed equally

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Introduction

Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS), is the most common histological subtype of PTCL (1); its clinical, immunophenotypic and genetic features are highly heterogeneous. The global incidence of PTCL-NOS is 0.5-1.7 cases per 100,000 person-years (2,3). The disease shows marked geographic variation; in China, PTCL-NOS accounts for 23-27% of all non-Hodgkin lymphoma cases, a figure notably higher than the 10% reported in Western countries (4). In the absence of distinctive immunophenotypic and molecular signatures, diagnosis is based on exclusion of other diseases (5). The clinical course is characteristically aggressive, with most patients presenting with advanced stage (III/IV) disease (5). Extranodal involvement is seen in ~50% of cases, most frequently in the bone marrow, skin and gastrointestinal tract (6). Typical laboratory abnormalities include anaemia, thrombocytopenia, elevated lactate dehydrogenase, increased β_2-microglobulin, eosinophilia and hypergammaglobulinemia (7). Histologically, diffuse effacement of lymph-node architecture is the most common pattern; residual B cells are often seen at the periphery of the infiltrate, and some cases show selective interfollicular or paracortical involvement. Tumour cells are not morphologically distinctive, consisting of medium- to large-sized pleomorphic lymphocytes with irregular nuclei, admixed with reactive elements, including eosinophils, neutrophils, histiocytes and plasma cells. Immunohistochemistry (IHC) may reveal loss of pan-T-cell antigens, most commonly CD5 and CD7. T-follicular helper (TFH)-associated markers [BCL6, CD10, inducible T-cell costimulator/CD278, serum amyloid P component, C-X-C motif chemokine ligand 13 and C-C chemokine receptor type 5 (CCR5)] can aid in identifying TFH-derived lymphoma; however, isolated positivity for a single TFH marker does not exclude a diagnosis of PTCL-NOS (8). PTCL-NOS is associated with poor outcomes, and no standard-of-care

therapy exists. Current management still borrows from B-cell lymphoma protocols, with the cyclophosphamide, vincristine, doxorubicin and prednisone (CHOP) regimen remaining the default first-line regimen. Although the initial objective response rate is modest, early relapse is common. For patients treated with CHOP regimen, the objective response rate (ORR) is 56%, and nearly one-half of the patients experienced relapse or progression within 6 months after primary therapy, with a 5-year progression-free survival (PFS) rate of only 29% (6,9,10). In recent years, increasing attention in lymphoma research has shifted toward molecular prognostic biomarkers and pathogenic mechanisms (11,12). In parallel, a wave of novel targeted agents has emerged for PTCL, including chidamide, romidepsin and brentuximab vedotin (BV), all of which have conferred measurable clinical benefit (8).

Nevertheless, the long-term outlook for relapsed/refractory PTCL-NOS remains poor. As the disease is rare, its molecular pathogenesis and mechanisms of drug resistance are still inadequately defined, and research progress has been slow; consequently, these patients face a therapeutic impasse. The present study was therefore designed to delineate the clinical characteristics of PTCL-NOS, identify potential prognostic determinants, and provide data to facilitate an earlier diagnosis and improve long-term survival.

Patients and methods

Patient selection. A retrospective analysis of 30 consecutive, previously untreated patients with newly diagnosed PTCL-NOS who attended the Department of Haematology, The Second Hospital of Hebei Medical University (Shijiazhuang, China) between September 2013 and September 2023 was conducted. The cohort consisted of 22 men and 8 women (male-to-female ratio, 2.75:1), with a median age of 59 years (age range, 17-70 years). The inclusion criteria for patient enrollment were as follows: i) Patients were diagnosed by histopathology and immunohistochemistry, in accordance with the 2017 World Health Organisation classification of haematolymphoid neoplasms (13); and ii) complete clinical and follow-up data were available. The exclusion criteria for patient enrollment were as follows: i) Patients with a second malignancy or a previous history of malignant tumor; and ii) patients with severe dysfunction of the heart, lung, liver, kidney or other vital organs. The study protocol was approved by the Clinical Research Ethics Committee of The Second Hospital of Hebei Medical University (approval no. 2024-R760), and written informed consent was obtained from each patient. All procedures were performed in accordance with the Institutional Review Board of The Second Hospital of Hebei Medical University and The Declaration of Helsinki. Clinical data were extracted from the electronic medical-record system and included demographics (age and sex), sites of involvement, Ann Arbor stage (14), Eastern Cooperative Oncology Group (ECOG) performance status (PS) (15), presence or absence of B symptoms, laboratory parameters (haemoglobin, platelet count, lactate dehydrogenase, albumin, β_2-microglobulin and Ki-67 proliferation index), imaging studies [positron emission tomography/computed tomography (CT), abdominal ultrasonography, superficial lymph-node ultrasonography, and chest and abdominal CT], histopathological and IHC findings, treatment regimens, response and long-term outcomes. All pathological diagnoses were independently reviewed and confirmed by two haematopathologists at The Second Hospital of Hebei Medical University. Any discrepancies were resolved via consensus consultation or by a third senior haematopathologist.

Treatment regimens. In this retrospective cohort, the treatment plans for the 30 patients with PTCL-NOS were formulated by a multidisciplinary team after comprehensive evaluation of each patient's PS, disease burden, Ann Arbor stage, International Prognostic Index (IPI)/PTCL-NOS Prognostic Index (PIT) score, molecular prognostic indicators and organ reserve function, in accordance with the current National Comprehensive Cancer Network Clinical Practice Guidelines and the Chinese Guidelines for the Diagnosis and Treatment of Adult Peripheral T-cell Lymphoma, and were adjusted according to real-world drug accessibility and patient preferences (16-19).

For first-line chemotherapy regimens, CHOP or CHOP-like protocols were primarily used. For younger patients with a good PS (ECOG PS ≤1) who displayed high-risk clinical features (advanced stage disease, high IPI/PIT score, bulky disease, central nervous system involvement and leukemic phase), a Ki-67 proliferation index ≥70% and a highly aggressive clinical course, the cyclophosphamide, doxorubicin, vincristine, prednisone and etoposide (CHOPE) regimen was preferred. Patients with low- or intermediate-risk disease without the aforementioned high-risk factors, elderly patients or those with a slightly poorer PS (ECOG PS ≥2) were recommended to receive CHOP. For patients with concomitant cardiovascular disease, anthracycline-containing agents were avoided where possible, and the gemcitabine, dexamethasone and cisplatin (GDP) regimen or the gemcitabine and oxaliplatin (GemOx) regimen was preferred. For patients with hepatic or renal insufficiency, a reduced-intensity CHOP regimen, GDP/GemOx regimens, bendamustine monotherapy or bendamustine-based combination protocols were used based on the patient's specific conditions.

For second-line chemotherapy regimens, the dexamethasone, ifosfamide, cisplatin and etoposide (DICE) regimen, the gemcitabine, vinorelbine and liposomal mitoxantrone (GVM) regimen, the GDP regimen, single-agent liposomal mitoxantrone, or the ifosfamide, carboplatin and etoposide (ICE) regimen were primarily used.

Regarding targeted agents, as chidamide has been approved for use in China, all newly diagnosed high-risk and relapsed/refractory patients in the present study were recommended to receive continuous chidamide until disease progression was reached or intolerable toxicity to chidamide occurred. For CD30-positive patients, BV in combination with chemotherapy or used as monotherapy was recommended; however, overall utilization of targeted drugs was constrained by multiple real-world factors.

Haematopoietic stem-cell transplantation (HSCT) was performed in high-risk young patients who achieved complete response (CR) after first-line induction, and sequential autologous HSCT as consolidation was considered. For relapsed/refractory patients who responded to salvage therapy, evaluation for allogeneic HSCT (allo-HSCT) was performed; due to the profound influence of real-world circumstances,

the proportion of patients undergoing transplantation in this cohort remained low.

Response assessment and adverse-event evaluation. Response was graded according to the Lugano criteria for malignant lymphoma (2014) (20) and classified as CR, partial response (PR), stable disease (SD) or progressive disease. Treatment-related adverse events were assessed and recorded with the Common Terminology Criteria for Adverse Events version 5.0 (21).

Follow-up. Follow-up was conducted via telephone, and review of outpatient and inpatient medical records, and concluded in September 2023. Overall survival (OS) was defined as the time from diagnosis to death or loss to follow-up for any reason, and PFS was defined as the time from diagnosis to disease progression, recurrence, death or last follow-up.

Statistical analysis. Statistical analysis of the case data was performed using SPSS version 29.0 (IBM Corp.). Continuous data are presented as the median (range), and categorical data are presented as n (%). Univariate survival analysis was performed using Kaplan-Meier analysis, and survival curves were plotted. Intergroup differences were compared using a log-rank test. Variables with a P-value <0.05 in the univariate analysis were included in the multivariate Cox regression model analysis. Hazard ratio (HR) and its 95% confidence interval (CI) values were calculated. The χ^2 test and Fisher's exact test were used for group comparisons in Tables V and VI. Graphs were generated using GraphPad Prism version 9.5 (Dotmatics). P<0.05 was considered to indicate a statistically significant difference.

Results

Clinical characteristics. The present study included 30 patients with PTCL-NOS. The most common presenting symptom was painless lymphadenopathy, although other symptoms included abdominal pain, nasal congestion, lower-limb oedema and limb weakness. A total of 13 patients presented with B symptoms, primarily fever. Pleural effusion was observed at initial diagnosis in 13 patients, with pleural, abdominal and pelvic effusions most commonly observed (data not shown). The majority of patients (26 out of 30) were diagnosed with advanced-stage disease (stage III/IV). Lesions originated from superficial or deep lymph nodes in 26 patients; in the remaining 4 cases, they were primary cases in extranodal sites and presented solely with extranodal involvement (2 in the gastrointestinal tract, 1 in the skin and 1 in skeletal muscle). At diagnosis, 23 patients had both nodal and extranodal involvement, of whom 12 had ≥2 extranodal sites affected (data not shown). Additional findings included splenomegaly in 14 patients, hepatomegaly in 8, bone marrow involvement in 11, and extranodal involvement at other sites, including the lungs and pleura (4 cases), skin (3 cases), thyroid gland (2 cases), kidney (1 case), and testis (1 case). A total of 3 patients had a history of immune abnormalities, including 2 with autoimmune diseases and 1 with acquired immunodeficiency due to human immunodeficiency virus infection. Additionally, 2 patients were diagnosed with hemophagocytic syndrome, and 1 patient was diagnosed with myelofibrosis (data not shonw). All laboratory tests were based on baseline levels at the first visit. Among the 30 patients, 16 had anaemia, 5 had thrombocytopenia, 20 had elevated lactate dehydrogenase levels, 19 had normal β_2-microglobulin levels and 12 had hypoalbuminemia (Table I).

Immunophenotype. The immunophenotypic features of all 30 patients were examined (initial pathology reports and stained sections obtained at The Second Hospital of Hebei Medical University were collated and re-reviewed; the panel of markers tested was determined by diagnostic requirements, so the number of evaluable cases varied between antigens). Antigens were assessed as follows: Pan-T-cell surface antigen CD2-positive in 100% (27/27), CD3-positive in 83.3% (20/24), CD5-positive in 56.7% (17/30) and CD7-positive in 40.0% (12/30) of cases; helper-T-cell subset CD4-positive in 73.3% (22/30) of cases; cytotoxic-T-cell subset CD8-positive in 46.7% (14/30) of cases; cytotoxic marker T-cell-restricted intracellular antigen-1 (TIA-1)-positive in 60.0% (15/25) of cases; TFH-associated marker BCL-6-positive in 23.1% (6/26) of cases; and CD30-positive in 53.8% (14/26) of cases (Table II).

Evaluation of treatment efficacy. In the present study, 28 patients received chemotherapy alone, whereas 2 patients received sequential radiotherapy after chemotherapy. Anthracycline-based regimens were the mainstay of treatment: 13 patients received CHOP, 13 received CHOPE and 4 received other chemotherapeutic regimens. Chidamide, an oral histone deacetylase inhibitor, was administered in combination to 18 patients: 8 received chidamide-based induction followed by maintenance and 10 received chidamide solely as maintenance after completing eight cycles of chemotherapy. After four cycles, the ORR among the 30 patients was 56.7% (17/30): 11 achieved a CR (36.7%) and 6 a PR (20.0%). A total of 6 patients were assessed as exhibiting SD (6/30; 20%). In the first-line chemotherapy arms, the CHOP-treated group of 13 patients achieved an ORR of 46.1% (6/13) with 5 patients attaining a CR (38.4%) and 1 patient a PR (7.7%), whereas the CHOPE-treated group of 13 patients achieved an ORR of 61.5% (8/13) with 5 patients attaining a CR (38.4%) and 3 patients achieving a PR (23.1%). In the chidamide-plus-chemotherapy subgroup of 8 patients, the ORR was 75.0% (6/8), 5 patients achieved a CR (62.5%) and 1 achieved a PR (12.5%). At the final efficacy evaluation, 9 of the aforementioned 11 patients who achieved a CR in the entire cohort maintained their CR (data not shown).

During the observation period, there were 21 relapsed/refractory patients, among whom 17 received at least one full cycle of salvage therapy, whereas 4 did not receive any systemic salvage treatment due to rapid disease progression. Salvage treatment was predominantly based on conventional combination chemotherapy, including the DICE regimen in 5 patients, the GVM regimen in 3 patients, the GDP regimen in 3 patients, the ICE regimen in 2 patients, the bendamustine plus liposomal mitoxantrone regimen in 1 patient, and liposomal mitoxantrone monotherapy in 3 frail patients who could not tolerate intensive chemotherapy. Within the cohort of 17 patients, 5 received chemotherapy (GDP/ICE/GVM regimens) combined with chidamide and 1 CD30-positive patient received BV in combination. After 2 cycles, a response evaluation was performed in

Table I. Clinical characteristics of 30 patients with peripheral T-cell lymphoma, not otherwise specified.

Clinical feature	Number of cases	Percentage
Sex		
Male	22	73.3
Female	8	26.7
Age, years		
≤60	21	70.0
>60	9	30.0
Ann Arbor stage		
I/II	4	13.3
III/IV	26	86.7
B symptoms		
Present	13	43.3
Absent	17	56.7
Presence of >1 extranodal involvement sites		
Yes	12	40.0
No	18	60.0
ECOG score		
<1	20	66.7
≥1	10	33.3
Serous cavity effusion		
Present	13	43.3
Absent	17	56.7
Hepatomegaly		
Present	8	26.7
Absent	22	73.3
Splenomegaly		
Present	14	46.7
Absent	16	53.3
Bone marrow involvement		
Present	11	36.7
Absent	19	63.3
HGB, g/l		
<110	16	53.3
≥110	14	46.7
PLTs		
$<150x10^9$/l	5	16.7
$≥150x10^9$/l	25	83.3
B2-MG, mg/l		
≤4.0	19	63.3
>4.0	11	36.7
ALB, g/l		
<35	12	40.0
≥35	18	60.0
LDH, U/l		
<245	10	33.3
≥245	20	66.7
Ki-67 index, %		
<70	11	36.7
≥70	19	63.3

ECOG, Eastern Cooperative Oncology Group; HGB, haemoglobin; PLT, platelet; B2-MG, β_2 microglobulin; ALB, albumin; LDH, lactate dehydrogenase.

Table II. Immunophenotypic characteristics of 30 patients with peripheral T-cell lymphoma, not otherwise specified.

Immune phenotype	Cases, n/total n[a]	Percentage
CD2	27/27	100.0
CD3	20/24	83.3
CD4	22/30	73.3
CD5	17/30	56.7
CD7	12/30	40.0
CD8	14/30	46.7
CD30	14/26	53.8
TIA-1	15/25	60.0
BCL-6	6/26	23.1

[a]The panel of markers tested was determined by diagnostic requirements, so the number of evaluable cases varied between antigens. TIA-1, T-cell-restricted intracellular antigen-1.

the 17 patients who received salvage therapy, yielding an ORR of 23.5% (4/17), with 2 patients achieving a CR (11.8%) and 2 achieving a PR (11.8%) (data not shown).

A total of 5 patients underwent HSCT: 3 received autologous stem-cell transplantation after achieving CR, and all 3 experienced a sustained CR at the time of last follow-up. Another 2 patients received allo-HSCT after achieving a PR following salvage therapy for relapsed disease, and both experienced a CR after transplantation; 1 patient remained alive with a continued CR and 1 succumbed due to severe bloodstream infection post-transplant (Table III).

Survival and prognostic analysis. Follow-up ended in September 2023; among the 30 patients, 15 were alive and 15 had died, 14 of whom succumbed to disease progression or relapse and 1 who had succumbed to severe infection after transplantation. The median follow-up duration was 59.0 months. For the entire cohort, the 3-year OS and PFS rates were 50.4 and 28.9%, respectively, while the 5-year OS and PFS rates were 44.8 and 21.7% (Fig. 1).

Among the 21 relapsed/refractory patients, the 3-year OS and PFS rates calculated from the date of documented relapse/refractoriness were 21.8 and 17.9%, respectively

Table III. Treatment information and follow-up outcomes of patients post-transplant.

Case no.	Age, years	Sex	Ann Arbor stage	First-line therapy	Short-term therapeutic effect	Second-line therapy	Pre-transplant condition	Transplant type	Donor	Conditioning regimen	Best response after transplantation	Outcome of follow-up
1	35	Male	IV	CHOP regimen x2	SD	Chidamide + ICE regimen x2	CR2	AHCT	/	BEAM regimen	CR	Survival status
2	31	Female	IV	Chidamide + CHOPE regimen x6	CR	/	CR1	AHCT	/	BEAM regimen	CR	Survival status
3	54	Male	IV	CHOP regimen x6	CR	Chidamide + GDP regimen x4	CR2	AHCT	/	CBV regimen	CR	Survival status
4	44	Male	IV	Chidamide + CHOP regimen x4	SD	Chidamide + GDP regimen x6	PR	Allo-HSCT	Younger brother	Bu/Cy regimen	CR	Mortality due to transplant complications
5	19	Male	IV	DA-EPOCH regimen x2	SD	BV + ICE regimen x2	PR	Allo-HSCT	Father	Bu/Cy regimen	CR	Survival status

CHOP, cyclophosphamide, vincristine, doxorubicin and prednisone; CHOPE, cyclophosphamide, doxorubicin, vincristine, prednisone and etoposide; ICE, ifosfamide, carboplatin and etoposide; BV, brentuximab vedotin; GDP, gemcitabine, dexamethasone and cisplatin; DA-EPOCH, dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide and doxorubicin; BEAM, carmustine, etoposide, cytarabine and melphalan; CBV, cyclophosphamide, carmustine and etoposide; Bu/Cy, busulfan plus cyclophosphamide. SD, stable disease; CR, complete response; CR1, first complete response; CR2, second complete response; PR, partial response; AHCT, autologous hematopoietic cell transplantation; allo-HSCT, allogeneic haematopoietic stem-cell transplantation.

Table IV. Descriptive comparison of baseline clinical characteristics between patients in the salvage therapy group (n=17) and non-salvage therapy group (n=4).

Clinical characteristic	Salvage therapy group, n (%)	Non-salvage therapy group, n (%)
Male sex	11 (64.7)	4 (100.0)
Age >60 years	11 (64.7)	3 (75.0)
Ann Arbor stage III/IV	14 (82.4)	4 (100.0)
B symptoms	10 (58.8)	3 (75.0)
Extranodal involvement sites >1	10 (58.8)	2 (50.0)
ECOG score ≥1	10 (58.8)	2 (50.0)
Serous cavity effusion present	11 (64.7)	4 (100.0)
Hepatomegaly	4 (23.5)	1 (20.0)
Splenomegaly	8 (47.1)	1 (20.0)
Bone marrow involvement	10 (58.8)	2 (50.0)
HGB <110 g/l	9 (52.9)	4 (100.0)
PLTs <150x10^9/l	15 (88.2)	2 (50.0)
B2-MG >4.0 mg/l	6 (35.3)	3 (75.0)
ALB <35 g/l	8 (47.1)	3 (75.0)
LDH ≥245 U/l	12 (70.6)	3 (75.0)
Ki-67 index ≥70%	10 (58.8)	4 (100.0)

ECOG, Eastern Cooperative Oncology Group; HGB, haemoglobin; PLT, platelet; B2-MG, β2 microglobulin; ALB, albumin; LDH, lactate dehydrogenase.

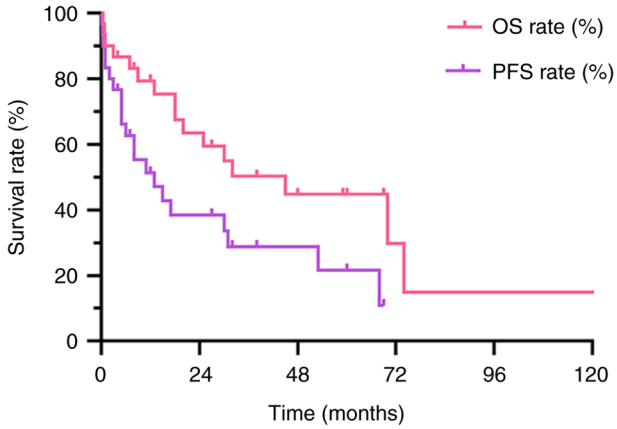

Figure 1. OS and PFS curves of 30 patients with peripheral T-cell lymphoma, not otherwise specified. OS, overall survival; PFS, progression-free survival.

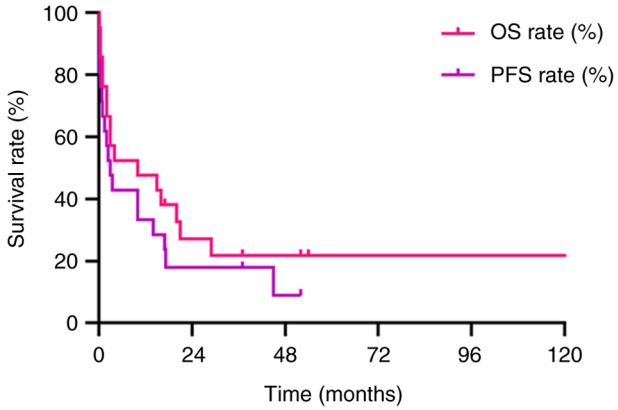

Figure 2. OS and PFS curves of 21 patients with relapsed/refractory peripheral T-cell lymphoma, not otherwise specified. OS, overall survival; PFS, progression-free survival.

(Fig. 2). Based on whether salvage therapy was administered, these 21 patients were divided into two groups; given the extremely small sample size of the untreated group (n=4), no statistical analysis was performed and the data are presented for descriptive comparison only; baseline characteristics were compared only descriptively (Table IV). All 4 patients who did not receive salvage therapy were male, had serous effusion, haemoglobin <110 g/l and Ki-67 ≥70%, and were all stage III/IV; the two groups were similar with respect to PS, number of extranodal sites and bone marrow involvement. Survival analysis showed that the salvage-treatment group had 3-year OS and PFS rates of 26.9 and 15.7%, respectively, whereas every patient in the non-salvage therapy group experienced rapid progression and died; their median PFS time was only 0.22 months and median OS time was 0.50 months (Fig. 3). Survival analyses were performed for patients who received CHOP vs. CHOPE (baseline characteristics had no significant differences; Table V). The CHOP cohort had a 3-year OS rate of 56.4% and a 3-year PFS rate of 29.3%, whereas the CHOPE cohort had a 3-year OS rate of 54.8% and a 3-year PFS rate of 25.2%. Neither OS (HR, 0.786; 95% CI, 0.268-2.334; P=0.647) nor PFS (HR, 1.384; 95% CI, 0.549-3.531; P=0.471) differed significantly between the two groups (Fig. 4).

Survival analyses were performed for patients who received chidamide vs. those who did not (baseline characteristics had no significant differences; Table VI). The chidamide group had a 3-year OS rate of 51.1% and a 3-year PFS rate of 35.4%, whereas the non-chidamide group had a 3-year OS rate of 46.9%

Table V. Comparison of baseline clinical characteristics between the CHOP (n=13) and CHOPE (n=13) regimen groups.

Clinical characteristic	CHOP regimen group, n (%)	CHOPE regimen group, n (%)	P-value[a]
Male sex	9 (69.2)	10 (76.9)	>0.999
Age >60 years	3 (23.1)	4 (30.8)	>0.999
Ann Arbor stage III/IV	12 (92.3)	11 (84.6)	>0.999
B symptoms	3 (23.1)	6 (46.2)	0.236
Extranodal involvement sites >1	3 (23.1)	7 (53.8)	0.226
ECOG score ≥1	4 (30.8)	2 (15.4)	0.649
Serous cavity effusion present	5 (38.5)	3 (23.1)	0.673
Hepatomegaly	2 (15.4)	3 (23.1)	0.645
Splenomegaly	4 (30.8)	7 (53.8)	0.428
Bone marrow involvement	3 (23.1)	6 (46.2)	0.411
HGB <110 g/l	4 (30.8)	8 (61.5)	0.238
PLTs <150x10^9/l	1 (7.7)	2 (15.4)	>0.999
B2-MG >4.0 mg/l	3 (23.1)	6 (46.2)	0.411
ALB <35 g/l	3 (23.1)	7 (53.8)	0.226
LDH ≥245 U/l	9 (69.2)	8 (61.5)	>0.999
Ki-67 index ≥70%	6 (46.2)	11 (84.6)	0.094

[a]χ^2/Fisher's exact test. CHOP, cyclophosphamide, vincristine, doxorubicin and prednisone; CHOPE, cyclophosphamide, doxorubicin, vincristine, prednisone and etoposide; ECOG, Eastern Cooperative Oncology Group; HGB, haemoglobin; PLT, platelet; B2-MG, β_2 microglobulin; ALB, albumin; LDH, lactate dehydrogenase.

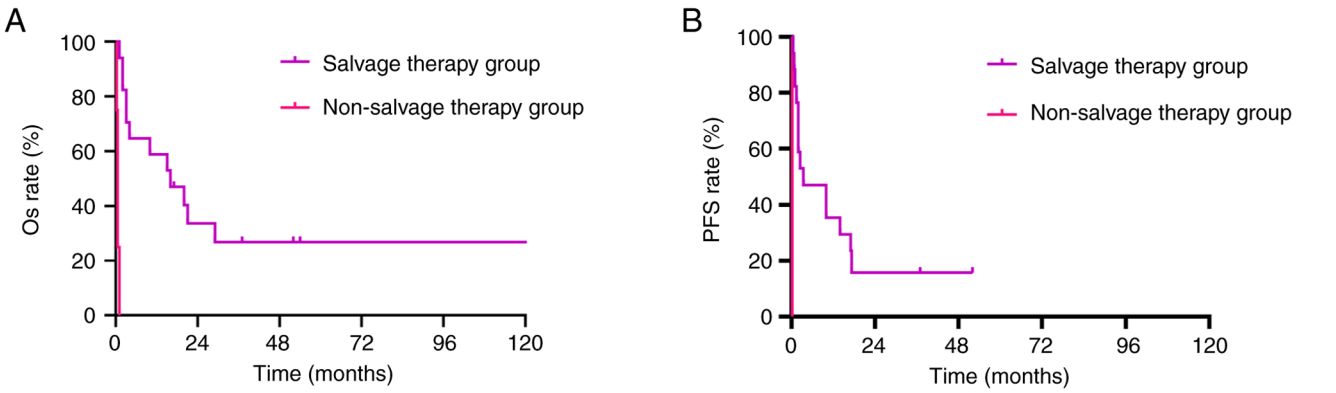

Figure 3. (A) OS and (B) PFS curves of relapsed/refractory patients in the salvage therapy group and the non-salvage therapy group. OS, overall survival; PFS, progression-free survival.

and a 3-year PFS rate of 20%. Neither OS (HR, 0.786; 95% CI, 0.268-2.334; P=0.364) nor PFS (HR, 1.384; 95% CI, 0.549-3.531; P=0.088) differed significantly between the two groups, although a trend toward improved PFS was observed (Fig. 5).

Prognostic-factor analysis

Univariate analysis. Univariate analysis of the clinical characteristics of the 30 patients (sex, age, disease stage, B symptoms, number of extranodal sites, ECOG PS, serous effusion, hepatosplenomegaly, bone marrow involvement and laboratory parameters), showed that an ECOG PS >1, serous effusion, bone marrow involvement, a platelet count <150x10^9/l and decreased ALB were significantly associated with worse OS (P<0.05), whereas ECOG PS, bone marrow involvement, a platelet count <150x10^9/l, β_2-microglobulin levels >4.0 mg/l, and albumin levels <35 g/l were significantly associated with worse PFS (P<0.05) (Table VII).

Multivariate analysis. Factors significant in the univariate analysis were entered into a Cox regression model. ECOG PS >1, bone marrow involvement and platelet count <150x10^9/l were independent predictors of OS (Table VIII), whereas bone marrow involvement and albumin levels <35 g/l were independent predictors of PFS (Table IX).

Adverse events. All 30 patients experienced treatment-related adverse events. Grade 3-4 toxicities were predominantly haematological in nature (leukopenia, anaemia and thrombocytopenia). Each episode was managed with supportive care [subcutaneous granulocyte-colony stimulating factor (G-CSF) or recombinant human thrombopoietin, or blood product

Table VI. Comparison of baseline characteristics between the chidamide treatment group (n=18) and the non-chidamide treatment group (n=12).

Clinical characteristic	Chidamide treatment group, n (%)	Non-chidamide treatment group, n (%)	P-value[a]
Male sex	12 (66.7)	10 (83.3)	0.419
Age >60 years	6 (33.3)	3 (25.0)	0.704
Ann Arbor stage III/IV	14 (77.8)	11 (91.7)	0.622
B symptoms	8 (44.4)	5 (41.7)	>0.999
Extranodal involvement sites >1	9 (50.0)	3 (25.0)	0.264
ECOG score ≥1	8 (44.4)	2 (16.7)	0.235
Serous cavity effusion present	9 (50.0)	4 (33.3)	0.465
Hepatomegaly	6 (33.3)	2 (16.7)	0.419
Splenomegaly	10 (55.6)	4 (33.3)	0.284
Bone marrow involvement	7 (38.9)	4 (33.3)	>0.999
HGB <110 g/l	10 (55.6)	6 (50.0)	>0.999
PLTs $<150x10^9$/l	3 (16.7)	2 (16.7)	>0.999
B2-MG >4.0 mg/l	7 (38.9)	4 (33.3)	>0.999
ALB <35 g/l	5 (27.8)	7 (58.3)	0.130
LDH ≥24 5U/l	11 (61.1)	9 (75.0)	0.694
Ki-67 index ≥70%	11 (61.1)	8 (66.7)	>0.999

[a]χ^2/Fisher's exact test. ECOG, Eastern Cooperative Oncology Group; HGB, haemoglobin; PLT, platelet; B2-MG, β2 microglobulin; ALB, albumin; LDH, lactate dehydrogenase.

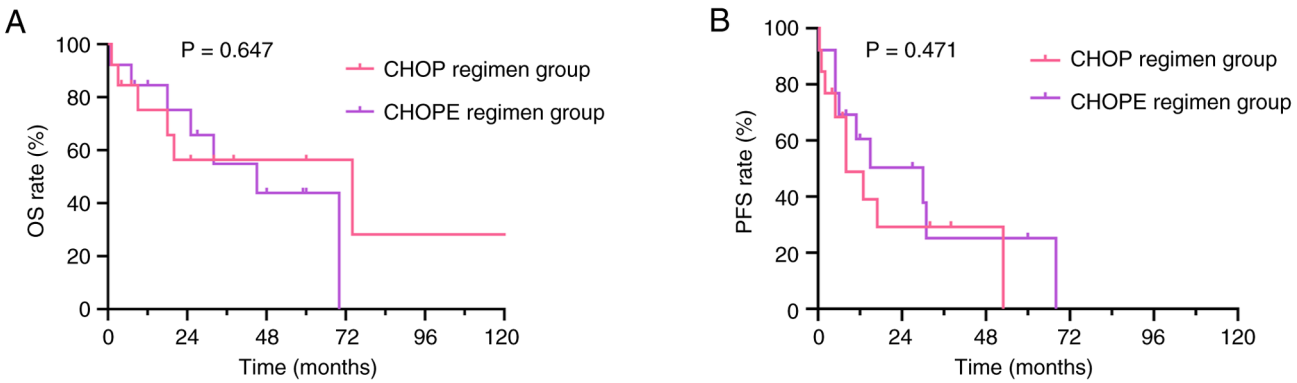

Figure 4. (A) OS and (B) PFS curves of patients in the CHOP and CHOPE regimen groups. CHOP, cyclophosphamide, vincristine, doxorubicin and prednisone; CHOPE, cyclophosphamide, doxorubicin, vincristine, prednisone and etoposide; OS, overall survival; PFS, progression-free survival.

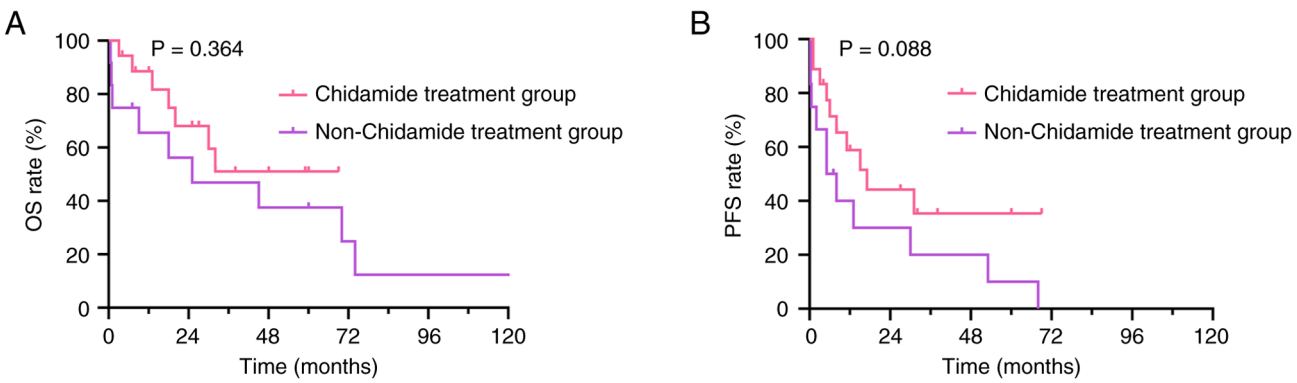

Figure 5. (A) OS and (B) PFS curves of patients in the chidamide treatment group and the non-chidamide treatment group. OS, overall survival; PFS, progression-free survival.

Table VII. Influence of different factors on OS and PFS.

	OS			PFS		
Clinical characteristic	Median time, months	P-value	HR (95% CI)	Median time, months	P-value	HR (95% CI)
Sex						
Male	30	0.850	1.119 (0.349-3.586)	8	0.067	2.824 (0.932-8.559)
Female	45			31		
Age, years						
≤60	32	0.814	1.130 (0.408-3.130)	17	0.947	0.970 (0.388-2.423)
>60	45			13		
Ann Arbor stage		0.644	0.739 (0.205-2.660)			
I/II	45			11	0.700	1.278 (0.367-4.455)
III/IV	30			13		
B symptoms						
Present	25	0.312	1.665 (0.620-4.469)	5	0.057	2.412 (0.973-5.979)
Absent	70			30		
Presence of >1 extranodal involvement sites						
Yes	74	0.533	0.713 (0.247-2.064)	31	0.401	0.673 (0.267-1.695)
No	30			8		
ECOG score						
≤1	7	0.001[a]	6.327 (2.090-19.152)	1	0.021[a]	2.922 (1.178-7.249)
>1	70			15		
Serous cavity effusion						
Present	3	0.025[a]	3.507 (1.167-10.536)	5	0.261	1.642 (0.691-3.901)
Absent	30			15		
Hepatomegaly						
Present	-	0.831	0.870 (0.242-3.124)	1	0.729	1.199 (0.429-3.351)
Absent	32			5		
Splenomegaly						
Present	30	0.637	1.269 (0.471-3.418)	11	0.441	1.426 (0.578-3.518)
Absent	70			17		
Bone marrow involvement						
Present	9	0.003[a]	4.705 (1.679-13.183)	2	<0.001[a]	6.391 (2.514-16.248)
Absent	70			30		
HGB, g/l						
<110	20	0.276	1.759 (0.636-4.862)	5	0.139	1.955 (0.805-4.750)
≥110	70			31		
PLTs						
<150x10^9/l	3	0.002[a]	11.474 (2.484-52.997)	1	0.014[a]	4.438 (1.353-14.559)
≥150x10^9/l	70			15		
B2-MG, mg/l						
≤4.0	70	0.087	2.524 (0.873-7.296)	30	0.031[a]	2.276 (1.098-6.765)
>4.0	13			3		
ALB, g/l						
<35	18	0.035[a]	2.969 (1.077-8.183)	6	0.016[a]	3.152 (1.243-7.995)
≥35	70			53		
LDH, U/l						
<245	30	0.176	2.226 (0.698-7.102)	8	0.108	2.264 (0.806-6.361)
≥245	70			30		

Table VII. Continued.

	OS			PFS		
Clinical characteristic	Median time, months	P-value	HR (95% CI)	Median time, months	P-value	HR (95% CI)
Ki-67 index, %						
<70	45	0.776	0.857 (0.296-2.478)	13	0.365	1.529 (0.599-3.905)
≥70	75			17		

[a]P<0.05. OS, overall survival; PFS, progression-free survival; ECOG, Eastern Cooperative Oncology Group; HGB, haemoglobin; PLT, platelet; B2-MG, β2 microglobulin; ALB, albumin; LDH, lactate dehydrogenase; HR, hazard ratio; CI, confidence interval.

Table VIII. Multivariate analysis of OS with Cox proportional hazards regression.

	OS		
Clinical characteristic	HR	95% CI	P-value
ECOG score >1	4.223	1.089-16.383	0.037[a]
Serous cavity effusion present	2.705	0.730-10.029	0.137
Bone marrow involvement	3.354	1.016-11.065	0.047[a]
PLTs <150x10^9/l	7.353	1.096-49.330	0.040[a]
ALB <35 g/l	2.648	0.787-8.915	0.116

[a]P<0.05. OS, overall survival; ECOG, Eastern Cooperative Oncology Group; PLT, platelet; ALB, albumin; HR, hazard ratio; CI, confidence interval.

Table IX. Multivariate analysis of PFS with Cox proportional hazards regression.

	PFS		
Clinical characteristic	HR	95% CI	P-value
ECOG score >1	1.154	0.340-3.916	0.819
Bone marrow involvement	6.140	1.982-19.018	0.002[a]
PLTs <150x10^9/l	3.887	0.897-16.841	0.070
B2-MG >4.0 mg/l	2.090	0.669-6.531	0.205
ALB <35 g/l	3.595	1.159-11.154	0.027[a]

[a]P<0.05. PFS, progression-free survival; ECOG, Eastern Cooperative Oncology Group; PLT, platelet; B2-MG, β2 microglobulin; ALB, albumin; HR, hazard ratio; CI, confidence interval.

transfusion], and blood counts recovered to acceptable levels before the next cycle. Non-haematological toxicities were primarily grade 1-2. Every patient developed some degree of gastrointestinal symptoms (nausea, vomiting or loss of appetite); symptomatic management (oral or parenteral vitamin B6 or 5-HT_3 receptor antagonists) led to improvement. A total of 10 patients had pneumonia, 2 of which were grade 3-4 and delayed the next chemotherapy cycle. Neurotoxic events consisted primarily of mild peripheral neuropathy; follow-up of 6 patients showed gradual resolution after drug withdrawal. A total of 3 patients developed grade 1-2 hepatic dysfunction; only 1 episode occurred during active treatment, which resolved after suspension of chemotherapy and addition of glycyrrhizin preparations. None of the patients discontinued therapy due to severe adverse events (Table X).

Discussion

PTCL-NOS is the most common subtype of PTCL, accounting for 21-27% of all PTCL cases (22). Although PTCL-NOS

Table X. Adverse events during treatment of 30 patients with peripheral T-cell lymphoma, not otherwise specified.

Adverse event	Number of cases	Percentage	Cumulative percentage
Hematological toxicity			
Leukopenia			80.0
Grade 1-2	15	50.0	
Grade 3-4	9	30.0	
Anemia			56.7
Grade 1-2	12	40.0	
Grade 3-4	5	16.7	
Thrombocytopenia			86.7
Grade 1-2	12	40.0	
Grade 3-4	6	20.0	
Non-haematological toxicity			
Gastrointestinal reactions			100.0
Grade 1-2	28	93.3	
Grade 3-4	2	6.7	
Peripheral neuropathy			20.0
Grade 1-2	6	20.0	
Grade 3-4	0	0.0	
Pneumonia			36.7
Grade 1-2	9	30.0	
Grade 3-4	2	6.7	
Abnormal liver function			10.0
Grade 1-2	3	10.0	
Grade 3-4	0	0.0	

remains defined as a heterogeneous collection of tumours that cannot be assigned to any other recognized PTCL category, recent advances in PTCL genomics have led to the reclassification of cases exhibiting a TFH phenotype or Epstein-Barr virus (EBV) positivity as distinct entities, thereby narrowing the diagnostic scope of PTCL-NOS (23).

In the present study, the clinical characteristics of 30 patients with PTCL-NOS were analysed; the median age at diagnosis was 59 years, and the disease was more common among men (73.3%). The majority of patients presented with painless peripheral lymphadenopathy, and approximately one-half (43%) had B symptoms (fever, night sweats or weight loss). Occasional co-occurrence of hemophagocytic syndrome and myelofibrosis was also observed, which is consistent with a previous report (6). PTCL-NOS typically arises in the lymph nodes, but the present cohort also included rare primary extranodal cases involving the gastrointestinal tract, skin and muscle. Previous research has shown that the primary site influences outcome: Tumours originating in the kidney or gastrointestinal tract are associated with poorer survival than nodal disease, whereas primary bone, skin or soft-tissue involvement confers a better prognosis (24).

Immunophenotypically, all patients in the present cohort exhibited partial or complete loss/downregulation of pan-T-cell antigens, most frequently CD7 and CD5. Overall, 60% of cases were positive for the cytotoxic marker TIA-1, a figure considerably higher than the 32% reported in Western countries (North America and Europe) (6) and further evidence that cytotoxic PTCL-NOS (cPTCL-NOS) is more common in Asian populations (25). cPTCL-NOS is defined by expression of ≥1 cytotoxic marker (TIA-1, granzyme B or perforin) in ≥50% of tumour cells (25). These patients often have an immunocompromised background, such as a history of malignancy or autoimmune disease, and the pathogenesis is linked to mutations in epigenetic regulators, including tet methylcytosine dioxygenase 2 and DNA methyltransferase 3α. Studies have shown that cPTCL-NOS typically expresses the T-helper 1-associated transcription factors TBX21 and C-X-C chemokine receptor type 3 (CXCR3), and belongs to the PTCL-TBX21 subgroup, which is associated with a poor prognosis (26). PTCL-TBX21 is driven by the transcription factor TBX21 and characterized by aberrant activation of the STAT3 pathway; another subgroup identified by gene expression profiling is PTCL-GATA3, which is driven by the transcription factor GATA3. Compared with PTCL-TBX21, PTCL-GATA3 exhibits a more aberrant genomic expression profile and is associated with PI3K pathway activation, with a worse overall prognosis (27). An IHC algorithm using TBX21/CXCR3 and GATA3/CCR4 as markers has been developed to distinguish PTCL-TBX21 and PTCL-GATA3 in clinical practice (28). Due to the lack of fresh, formalin-fixed, paraffin-embedded pathological samples, it was not possible to perform supplementary IHC staining for the aforementioned markers and gene-expression profiling

in the present study, thereby limiting the ability to validate the prognostic value of molecular subtypes and specific gene mutations in cPTCL-NOS in the real-world setting. Notably, previous cohort studies of cPTCL-NOS primarily included EBV-positive cases (28,29); these have now been reclassified as distinct entities. Large-scale investigations are urgently needed to determine whether EBV-negative cPTCL-NOS exhibits clinical features and survival outcomes that differ from those of non-cPTCL-NOS (30). In the present study, the CD30 positivity rate was 53.8%, which is higher than that reported in an earlier study (22), likely reflecting differences in the CD30 positivity cutoff and the limited sample size. This finding indicates that BV, an antibody-drug conjugate targeting CD30, could be a therapeutic option for these patients.

Currently, the clinical prognostic indices most frequently used for PTCL-NOS are the IPI, the PIT and the modified PIT; all three models stratify patients according to age, ECOG PS, LDH level, number of extranodal sites and Ki-67 expression (6,19,31,32). The present study confirmed that an ECOG PS >1, bone marrow involvement and platelet count $<150x10^9$/l are independent predictors of OS, which is consistent with previous reports (6,31,32). In addition to bone marrow involvement, albumin levels <35 g/l were an independent predictor of PFS. Low serum albumin levels have been linked to poor outcomes in a variety of malignancies, including gastric, small-cell lung and breast cancer (33-35), and its prognostic value across PTCL subtypes has been confirmed by multiple studies (36-39). Albumin reflects not only systemic nutritional status but also the inflammatory burden and tumour load. Pro-inflammatory cytokines released within the tumour microenvironment, such as IL-6 and tumour necrosis factor-α, suppress hepatic albumin synthesis, whereas increased capillary leakage accelerates the development of hypoalbuminemia. Raj *et al* (40) analysed 149 patients with large B-cell lymphoma and demonstrated that C-reactive protein and IL-6 levels were inversely associated with serum albumin level, confirming that albumin behaves as a negative acute-phase protein that mirrors the high inflammatory state of lymphoma. Further mechanistic studies have shown that IL-6 is a key component of a positive inflammatory feedback loop, activating the JAK1-STAT3 pathway, and thereby promoting proliferation and migration of PTCL cells (41,42). Federico *et al* (36) incorporated the prognostic value of serum albumin into a T-cell scoring system that combines serum albumin level, ECOG PS, disease stage and absolute neutrophil count, and validated its ability to predict both OS and PFS. Although this model, derived from a large prospective dataset, achieved greater predictive accuracy than earlier indices, it remains limited to clinical variables and offers limited guidance for treatment selection. In the present study, albumin was measured only once prior to treatment initiation, precluding any dynamic assessment of its relationship with therapeutic response. Owing to the retrospective nature of the data, inflammatory markers such as C-reactive protein and IL-6 were excluded from the model; therefore, the proposed link between hypoalbuminemia and systemic inflammation could not be formally validated. Large prospective cohorts are still needed to clarify how pretreatment albumin levels are associated with nutritional status and inflammatory burden in real-world PTCL-NOS, with the ultimate goal of developing robust predictive algorithms that can reliably identify high-risk patients.

In the present cohort, anthracycline-based chemotherapy was the primary strategy, yielding an ORR of 56.7% and a 5-year OS of 44.8%, figures that mirror historical data (6). CHOP-like regimens perform poorly in PTCL-NOS. Although first-line response rates are acceptable, early relapse often occurs, and long-term outlook remains poor. The value of anthracyclines is itself debated; several studies have found no notable survival difference between anthracycline-containing and anthracycline-free schedules (6,43). In the present study, the outcomes between patients receiving CHOP and those receiving CHOPE were compared, and no statistically significant difference in either OS or PFS was observed. A previous report has suggested that CHOPE may improve PFS rate in patients <60 years old, possibly as elderly or frail individuals are less tolerant of the myelosuppressive effects of etoposide (44); therefore, age-stratified analyses are required to clarify the true benefit of the CHOPE regimen.

Chidamide, a selective histone deacetylase inhibitor developed in China, is now widely used to manage PTCL and shows favourable activity (45). In the present study, patients who received chidamide exhibited higher 3-year OS and PFS rates compared with those who did not receive the treatment, with a notable trend toward improved PFS. However, this difference did not reach statistical significance, likely due to the limited sample size. The small sample size also precluded stratified analysis of outcomes based on different chidamide treatment strategies, such as up-front combination therapy vs. maintenance therapy. Additionally, clinicians tend to initiate chidamide treatment earlier in patients deemed high-risk. Furthermore, financial constraints prevent some patients from completing the planned number of treatment cycles. These factors may bias the efficacy estimates toward the null, potentially obscuring the true therapeutic benefits of chidamide. The small cohort and variable follow-up duration further reduced the statistical power in the present study. Consequently, the negative result observed did not refute the therapeutic value of chidamide, rather, it simply documents the heterogeneity of its real-world use. Large prospective studies are required to define the precise role of chidamide as first-line and maintenance therapy, and to determine whether molecular subgroups derive differential benefit. BV, an anti-CD30 antibody-drug conjugate, has demonstrated therapeutic potential in CD30-positive lymphoma (46,47). In the present study, 1 patient who relapsed (repeat lymph-node biopsy confirming CD30 positivity) received BV combined with chemotherapy as salvage therapy, and achieved PR, before proceeding to allo-HSCT. This single-case experience suggests that BV is active in PTCL-NOS. Beyond improving drug accessibility (such as reducing economic burden), an evidence-based CD30 cutoff must be established, and prospective real-world studies on the efficacy and safety of BV in China are urgently needed to inform clinical decision-making.

A total of 3 patients in the present study underwent autologous stem-cell transplantation after achieving CR, and all remain alive at the latest follow-up. The precise value of upfront autologous stem-cell transplantation in PTCL-NOS is still contested. A large retrospective study showed improved

OS when patients aged <65 years with stage II-IV disease received autologous stem-cell transplantation as consolidation (48), whereas a prospective trial found no survival benefit for sequential autologous stem-cell transplantation in first-remission PTCL-NOS (49). Although existing data are conflicting, and large-scale studies specific to the PTCL-NOS subtype are lacking, current guidelines and clinical practice continue to favour sequential autologous stem-cell transplantation for chemotherapy-sensitive patients, on the assumption that it may achieve long-term disease control.

Patients with relapsed or refractory PTCL-NOS have poor outcomes, effective agents are limited, and they remain in a challenging therapeutic situation. In the present cohort, the 3-year OS was only 21.8%, and 4 of the 21 patients died from rapid progression, within a median OS time of 0.50 months, without ever receiving salvage therapy. Although the sample is too small to identify statistically robust high-risk features, all four had high stage disease, serous effusion, anaemia and a Ki-67 index ≥70%, suggesting that an inherently aggressive biology, rather than poor PS, drives the fulminant course. Larger studies integrated with molecular genetics are required to determine whether an ultra-high-risk molecular subset exists. Salvage regimens in the present study were highly heterogeneous; conventional chemotherapy (GDP and ICE) conferred only a modest survival benefit, which is consistent with previous reports (50-52). Notably, the mere opportunity to receive salvage therapy emerged as a survival 'watershed', implying that published response rates may be systemically overestimated. Additionally, the use of targeted agents (chidamide and BV) in Chinese patients with relapsed/refractory PTCL-NOS was piloted, providing preliminary experience for individualized, targeted combination strategies. Transplant-related mortality is undeniable, yet allo-HSCT remains the only curative option for relapsed/refractory PTCL-NOS. In the present study, only 2 patients were bridged to allo-HSCT; most younger individuals never achieved a response adequate for transplant, and the need to locate a suitable donor and secure costly procedures before further progression created additional, real-world barriers. More effective pre-transplant salvage regimens are urgently required, while frail patients who are ineligible for transplants need lower-intensity alternatives that can meaningfully prolong survival. As the genetic understanding of PTCL pathogenesis improves, novel targeted agents, such as the JAK1 inhibitor golidocitinib, the PI3K inhibitor linperlisib and the programmed cell death protein 1 inhibitor pembrolizumab, are emerging, offering patients with relapsed/refractory PTCL-NOS additional therapeutic options. Thus, patients with PTCL-NOS may achieve sustained remission or even disease-free status with effective targeted therapies.

In the present study, treatment-related toxicities were generally manageable; the most common grade 3-4 adverse events were myelosuppression-neutropenia (30%), anaemia (16.7%) and thrombocytopenia (20%). These rates are largely consistent with those of a previous report (53). Pneumonia was the leading cause of treatment delay, and the two grade 3-4 pulmonary infections were both neutropenia-related. Clearly, maintaining chemotherapy intensity to achieve remission while avoiding severe myelosuppression-related complications remains a formidable clinical challenge. Prophylactic G-CSF can reduce the incidence of serious infections and maintain cycle schedules, but cumulative toxicity, dynamic blood count trends and individual infection histories must all be considered. Therefore, a multidisciplinary consultation should be sought promptly when necessary. Overall, the regimens used in the present study were considered safe, and no treatment-related deaths occurred.

The present study has several important limitations that restrict the generalizability of the findings. First, the overall sample size and the sizes of individual subgroups are small, limiting statistical power and increasing the risk of type II errors; comparisons of survival between groups must therefore be interpreted with caution. Second, the study is a single-centre retrospective analysis and is subject to inherent selection and recall biases; although baseline clinical characteristics were compared across all subgroups, potential confounders such as socioeconomic factors, patient treatment preferences and individual physician choices may still have influenced survival outcomes. Third, the absence of an external validation cohort means that the results are exploratory only; they provide clinical evidence and generate preliminary hypotheses for this rare disease, but a large, multicentre, prospective study is required for confirmation.

In summary, PTCL-NOS predominantly affects middle-aged and elderly men, follows an aggressive clinical course and is associated with poor overall outcomes. Conventional CHOP-like regimens provide sub-optimal disease control; relapse is common and robust prognostic tools are lacking. Multicentre prospective studies with larger patient cohorts are urgently required, together with comprehensive mapping of the PTCL-NOS molecular landscape, to elucidate the biological basis of its clinical heterogeneity and to develop effective targeted combination strategies that improve long-term survival for patients with this disorder.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

MM and YZ contributed equally to this work. MM and YZ were involved in the conception and design of the study, data analysis and interpretation, drafting of the manuscript and preparation of the figures. LX and QW participated in data collection, data collation and data curation. SQ contributed to the conception and design of the study, supervised the research, critically revised the manuscript for important intellectual content, and gave final approval of the version to be

published. MM and YZ confirm the authenticity of all the raw data. All authors have read and approved the final manuscript, and agree to be accountable for all aspects of the work.

Ethics approval and consent to participate

All procedures involved in this study were approved by the Institutional Review Board and Ethics Committee of The Second Hospital of Hebei Medical University (Shijiazhuang, China; approval no. 2024R760). Written informed consent was obtained from each patient.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Swerdlow SH, Campo E, Pileri SA, Harris NL, Stein H, Siebert R, Advani R, Ghielmini M, Salles GA, Zelenetz AD and Jaffe ES: The 2016 revision of the World Health Organization classification of lymphoid neoplasms. Blood 127: 2375-2390, 2016.
2. Adams SV, Newcomb PA and Shustov AR: Racial patterns of peripheral T-cell lymphoma incidence and survival in the United States. J Clin Oncol 34: 963-971, 2016.
3. Sant M, Allemani C, Tereanu C, De Angelis R, Capocaccia R, Visser O, Marcos-Gragera R, Maynadié M, Simonetti A, Lutz JM, *et al*: Incidence of hematologic malignancies in Europe by morphologic subtype: Results of the HAEMACARE project. Blood 116: 3724-3734, 2010.
4. Shi Y: Current status and progress of lymphoma management in China. Int J Hematol 107: 405-412, 2018.
5. d'Amore F, Gaulard P, Trümper L, Corradini P, Kim WS, Specht L, Bjerregaard Pedersen M and Ladetto M; ESMO Guidelines Committee: Peripheral T-cell lymphomas: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 26 (Suppl 5): v108-v115, 2015.
6. Weisenburger DD, Savage KJ, Harris NL, Gascoyne RD, Jaffe ES, MacLennan KA, Rüdiger T, Pileri S, Nakamura S, Nathwani B, *et al*: Peripheral T-cell lymphoma, not otherwise specified: A report of 340 cases from the international peripheral T-cell lymphoma project. Blood 117: 3402-3408, 2011.
7. Oluwasanjo A, Kartan S, Johnson W, Alpdogan O, Gru A, Mishra A, Haverkos BM, Gong J and Porcu P: Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS). Cancer Treat Res 176: 83-98, 2019.
8. Pileri SA, Tabanelli V, Fiori S, Calleri A, Melle F, Motta G, Lorenzini D, Tarella C and Derenzini E: Peripheral T-cell lymphoma, not otherwise specified: Clinical manifestations, diagnosis, and future treatment. Cancers (Basel) 13: 4535, 2021.
9. Sorial M, Aniagboso K, Buttermore E, Lei M, Kendall E, Nasto K, Koh MJ, Han JX, Boussi L, Malpica L, *et al*: Early time-to-relapse as a predictor of survival in mature T-cell/NK-cell lymphomas: Results from the PETAL consortium. Blood 146 (Suppl 1): S889, 2025.
10. Broccoli A and Zinzani PL: Peripheral T-cell lymphoma, not otherwise specified. Blood 129: 1103-1112, 2017.
11. Lee C and An Y: Deciphering the genetic complexity of classical hodgkin lymphoma: Insights and effective strategies. Curr Genomics 25: 334-342, 2024.
12. Lyu G and Li D: PLEKHG7 expression: A biomarker for prognosis and targeted therapy in diffuse large B-cell lymphoma. Protein Pept Lett 32: 657-666, 2025.
13. Swerdlow SH, Campo E, Harris NL, Jaffe ES, Pileri SA, Stein H, Thiele J and Vardiman JW: WHO classification of tumours of haematopoietic and lymphoid tissues. International agency for research on cancer Lyon, France, 2017.
14. Carbone PP, Kaplan HS, Musshoff K, Smithers DW and Tubiana M: Report of the committee on Hodgkin's disease staging classification. Cancer Res 31: 1860-1861, 1971.
15. Oken MM, Creech RH, Tormey DC, Horton J, Davis TE, McFadden ET and Carbone PP: Toxicity and response criteria of the eastern cooperative oncology group. Am J Clin Oncol 5: 649-656, 1982.
16. International Non-Hodgkin's Lymphoma Prognostic Factors Project. A predictive model for aggressive non-Hodgkin's lymphoma. N Engl J Med 329: 987-994, 1993.
17. Horwitz SM, Ansell S, Ai WZ, Barnes J, Barta SK, Brammer J, Clemens MW, Dogan A, Foss F, Ghione P, *et al*: NCCN Clinical Practice Guidelines in Oncology. T-Cell Lymphomas, Version 2.2022. J Natl Compr Canc Netw 20: 285-308, 2022.
18. Zhang QY, Feng JF, Wang HQ, Huang HQ, Zhang HL, Li XC, Gao YY, Song YP, Li ZM, *et al*: China Anti-Cancer Association (CACA) guidelines for holistic integrative management of lymphoma (version 2022). Holist Integ Oncol 2: 41, 2023.
19. Gallamini A, Stelitano C, Calvi R, Bellei M, Mattei D, Vitolo U, Morabito F, Martelli M, Brusamolino E, Iannitto E, *et al*: Peripheral T-cell lymphoma unspecified (PTCL-U): A new prognostic model from a retrospective multicentric clinical study. Blood 103: 2474-2479, 2004.
20. Cheson BD, Fisher RI, Barrington SF, Cavalli F, Schwartz LH, Zucca E, Lister TA; Alliance, Australasian Leukaemia and Lymphoma Group; Eastern Cooperative Oncology Group, *et al*: Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: The Lugano classification. J Clin Oncol 32: 3059-3068, 2014.
21. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. U.S. Department of Health and Human Services, Washington, DC, 2017.
22. Chen NC, Chang H, Kuo MC, Lin TL, Shih LY, Chuang WY and Kao HW: Predictive model for treatment outcomes of peripheral T-cell lymphoma, not otherwise specified, in Taiwanese patients. J Formos Med Assoc 123: 188-197, 2024.
23. Khoury JD, Solary E, Abla O, Akkari Y, Alaggio R, Apperley JF, Bejar R, Berti E, Busque L, Chan JKC, *et al*: The 5th edition of the World Health Organization classification of haematolymphoid tumours: Myeloid and histiocytic/dendritic neoplasms. Leukemia 36: 1703-1719, 2022.
24. Davis O, Truong D, Day S, Pandey M, Ibrahimi S, Khawandanah M, Holter-Chakrabarty J, Asch A and Al-Juhaishi T: Impact of primary organ site of involvement by peripheral T-cell lymphoma not otherwise specified on survival. Cancer Med 12: 21770-21778, 2023.
25. Nicolae A, Bouilly J, Lara D, Fataccioli V, Lemonnier F, Drieux F, Parrens M, Robe C, Poullot E, Bisig B, *et al*: Nodal cytotoxic peripheral T-cell lymphoma occurs frequently in the clinical setting of immunodysregulation and is associated with recurrent epigenetic alterations. Mod Pathol 35: 1126-1136, 2022.
26. Herek TA, Bouska A, Lone W, Sharma S, Amador C, Heavican TB, Li Y, Wei Q, Jochum D, Greiner TC, *et al*: DNMT3A mutations define a unique biological and prognostic subgroup associated with cytotoxic T cells in PTCL-NOS. Blood 140: 1278-1290, 2022.
27. Iqbal J, Wright G, Wang C, Rosenwald A, Gascoyne RD, Weisenburger DD, Greiner TC, Smith L, Guo S, Wilcox RA, *et al*: Gene expression signatures delineate biological and prognostic subgroups in peripheral T-cell lymphoma. Blood 123: 2915-2923, 2014.
28. Amador C, Greiner TC, Heavican TB, Smith LM, Galvis KT, Lone W, Bouska A, D'Amore F, Pedersen MB, Pileri S, *et al*: Reproducing the molecular subclassification of peripheral T-cell lymphoma-NOS by immunohistochemistry. Blood 134: 2159-2170, 2019.
29. Asano N, Suzuki R, Kagami Y, Ishida F, Kitamura K, Fukutani H, Morishima Y, Takeuchi K and Nakamura S: Clinicopathologic and prognostic significance of cytotoxic molecule expression in nodal peripheral T-cell lymphoma, unspecified. Am J Surg Pathol 29: 1284-1293, 2005.
30. Kato S, Takahashi E, Asano N, Tanaka T, Megahed N, Kinoshita T and Nakamura S: Nodal cytotoxic molecule (CM)-positive Epstein-Barr virus (EBV)-associated peripheral T cell lymphoma (PTCL): A clinicopathological study of 26 cases. Histopathology 61: 186-199, 2012.
31. Went P, Agostinelli C, Gallamini A, Piccaluga PP, Ascani S, Sabattini E, Bacci F, Falini B, Motta T, Paulli M, *et al*: Marker expression in peripheral T-cell lymphoma: A proposed clinical-pathologic prognostic score. J Clin Oncol 24: 2472-2479, 2006.
32. Gutiérrez-García G, García-Herrera A, Cardesa T, Martínez A, Villamor N, Ghita G, Martínez-Trillos A, Colomo L, Setoain X, Rodríguez S, *et al*: Comparison of four prognostic scores in peripheral T-cell lymphoma. Ann Oncol 22: 397-404, 2011.

33. Zhang H, Shi J, Xie H, Liu X, Ruan G, Lin S, Ge Y, Liu C, Chen Y, Zheng X, *et al*: Superiority of CRP-albumin-lymphocyte index as a prognostic biomarker for patients with gastric cancer. Nutrition 116: 112191, 2023.
34. Liu X, Meng QH, Ye Y, Hildebrandt MAT, Gu J and Wu X: Prognostic significance of pretreatment serum levels of albumin, LDH and total bilirubin in patients with non-metastatic breast cancer. Carcinogenesis 36: 243-248, 2015.
35. Guo Y, Wei L, Patel SH, Lopez G, Grogan M, Li M, Haddad T, Johns A, Ganesan LP, Yang Y, *et al*: Serum albumin: Early prognostic marker of benefit for immune checkpoint inhibitor monotherapy but not chemoimmunotherapy. Clin Lung Cancer 23: 345-355, 2022.
36. Federico M, Bellei M, Marcheselli L, Schwartz M, Manni M, Tarantino V, Pileri S, Ko YH, Cabrera ME, Horwitz S, *et al*: Peripheral T cell lymphoma, not otherwise specified (PTCL-NOS). A new prognostic model developed by the international T cell project network. Br J Haematol 181: 760-769, 2018.
37. Kaito S, Kanemasa Y, Sasaki Y, Okuya T, Yamaguchi T, Funasaka C, Shimoyama T, Omuro Y, Hishima T and Maeda Y: A new prognostic score comprising lactate dehydrogenase, albumin and neutrophil to lymphocyte ratio to predict sensitivity to first-line chemotherapy in patients with peripheral T-cell lymphomas. Int J Hematol 107: 451-459, 2018.
38. Chen H, Tao Y, Zhou Y, Liu P, Yang J, He X, Zhou S, Qin Y, Song Y, Gui L, *et al*: The clinical features, treatment, and prognostic factors for peripheral T-cell lymphomas: A single-institution analysis of 240 Chinese patients. Asia Pac J Clin Oncol 19: e202-e214, 2023.
39. Shen HR, Tang J, Li WY, Liang JH, Li Y, Wu JZ, Wang L, Li JY, Gao R, Yin H and Xu W: 25-Hydroxy vitamin D deficiency is an inferior predictor of peripheral T-cell lymphomas. Ann Hematol 103: 565-574, 2024.
40. Raj SS, Fei T, Fried S, Ip A, Fein JA, Leslie LA, Alarcon Tomas A, Leithner D, Peled JU, Corona M, *et al*: An inflammatory biomarker signature of response to CAR-T cell therapy in non-Hodgkin lymphoma. Nat Med 31: 1183-1194, 2025.
41. Zhu F, Wang KB and Rui L: STAT3 activation and oncogenesis in lymphoma. Cancers (Basel) 12: 19, 2019.
42. Jaeger A, Gambheer SMM, Sun X, Chernyakov D, Skorobohatko O, Mack T, Kissel S, Pfeifer D, Zeiser R, Fisch P, *et al*: Activated granulocytes and inflammatory cytokine signaling drive T-cell lymphoma progression and disease symptoms. Blood 141: 2824-2840, 2023.
43. Vose J, Armitage J and Weisenburger D; International T-Cell Lymphoma Project: International peripheral T-cell and natural killer/T-cell lymphoma study: Pathology findings and clinical outcomes. J Clin Oncol 26: 4124-4130, 2008.
44. Ellin F, Landström J, Jerkeman M and Relander T: Real-world data on prognostic factors and treatment in peripheral T-cell lymphomas: A study from the Swedish lymphoma registry. Blood 124: 1570-1577, 2014.
45. Wang J, Su N, Fang Y, Ma S, Zhang Y, Cai J, Zou Q, Tian X, Xia Y, Liu P, *et al*: Comparison of chemotherapy combined with chidamide versus chemotherapy in the frontline treatment for peripheral T-cell lymphoma. Front Immunol 13: 835103, 2022.
46. Horwitz S, O'Connor OA, Pro B, Illidge T, Fanale M, Advani R, Bartlett NL, Christensen JH, Morschhauser F, Domingo-Domenech E, *et al*: Brentuximab vedotin with chemotherapy for CD30-positive peripheral T-cell lymphoma (ECHELON-2): A global, double-blind, randomised, phase 3 trial. Lancet 393: 229-240, 2019.
47. Sureda A, García-Sanz R, Domingo-Domenech E, Capote FJ, Gutiérrez A, Rodriguez A, Aguiar D, Giraldo P, Infante MS, López-Jiménez J, *et al*: Retreatment with brentuximab vedotin in patients with relapsed/refractory CD30+ malignancies: A retrospective medical chart review study in Spain-The BELIEVE study. Cancers (Basel) 17: 1137, 2025.
48. Brink M, Meeuwes FO, van der Poel MWM, Kersten MJ, Wondergem M, Mutsaers PGNJ, Böhmer LH, Woei-A-Jin FSH, Visser O, Oostvogels R, *et al*: Impact of etoposide and ASCT on survival among patients aged <65 years with stage II to IV PTCL: A population-based cohort study. Blood 140: 1009-1019, 2022.
49. Park SI, Horwitz SM, Foss FM, Pinter-Brown LC, Carson KR, Rosen ST, Pro B, Hsi ED, Federico M, Gisselbrecht C, *et al*: The role of autologous stem cell transplantation in patients with nodal peripheral T-cell lymphomas in first complete remission: Report from COMPLETE, a prospective, multicenter cohort study. Cancer 125: 1507-1517, 2019.
50. Meeuwes FO, Serroukh YIM, van der Poel MWM, Plattel WJ and Nijland M: Relapsed and refractory peripheral T-cell lymphoma; treatment, challenges and future perspectives. Leuk Lymphoma 66: 2341-2356, 2025.
51. Qi F, Dong M, He X, Li Y, Wang W, Liu P, Yang J, Gui L, Zhang C, Yang S, *et al*: Gemcitabine, dexamethasone, and cisplatin (GDP) as salvage chemotherapy for patients with relapsed or refractory peripheral T cell lymphoma-not otherwise specified. Ann Hematol 96: 245-251, 2017.
52. Mikesch JH, Kuhlmann M, Demant A, Krug U, Thoennissen GB, Schmidt E, Kessler T, Schliemann C, Pohlen M, Mohr M, *et al*: DexaBEAM versus ICE salvage regimen prior to autologous transplantation for relapsed or refractory aggressive peripheral T cell lymphoma: A retrospective evaluation of parallel patient cohorts of one center. Ann Hematol 92: 1041-1048, 2013.
53. Bachy E, Camus V, Thieblemont C, Sibon D, Casasnovas RO, Ysebaert L, Damaj G, Guidez S, Pica GM, *et al*: Romidepsin Plus CHOP Versus CHOP in Patients With Previously Untreated Peripheral T-Cell Lymphoma: Results of the Ro-CHOP Phase III Study (Conducted by LYSA). J Clin Oncol 40: 242-251, 2022.